ASRM 2022
Scientific Abstracts to be presented at the 78th Scientific Congress
of the American Society for Reproductive Medicine, October 22-26, 2022, Anaheim,
California.

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October 22-26, 2022

These abstracts of research studies, published as submitted by the authors, are
presented in the ASRM 2022 Congress sessions are published in the order of their
presentation. Abstracts of plenary lectures, symposia and interactive sessions are not
included. The abstracts presented have been selected based on peer reviewer scores,
but have not been subject to the rigors of a peer review process characteristic of
scientific publications; thus, the findings should be considered preliminary and are not
appropriate for the direction of clinical care. The conclusions expressed in these
abstracts are those of the authors and do not necessarily reflect recommendations of
the ASRM.
OBJECTIVE: Women with endometriosis can experience significant functional and quality of life (QoL) impairment related to their chronic pain. This analysis evaluated the long-term (up to 2 years) effect of treatment with relugolix combination therapy (Rel-CT) on physical functioning and different QoL domains in women with endometriosis-associated pain using the Endometriosis Health Profile (EHP)-30 questionnaire.

MATERIALS AND METHODS: Premenopausal women with moderate-to-severe pain associated with endometriosis were randomized 1:1:1 in the pivotal SPIRIT 1 or 2 studies to receive Rel-CT (relugolix 40 mg, estradiol 1 mg, and norethindrone acetate 0.5 mg) or placebo for 24 weeks, or delayed Rel-CT (relugolix 40 mg monotherapy for 12 weeks, followed by Rel-CT for 12 weeks). Women completing SPIRIT 1 or 2 were eligible to enroll in the 80-week open-label, single-arm SPIRIT long-term extension (LTE) study where all women received Rel-CT. LS mean changes in the EHP-30 total and domain scores from baseline (pivotal) were analyzed using a mixed-effects model. The proportion of women with a clinically meaningful improvement in the EHP-30 pain domain was assessed, defined as a pre-specified ≥20-point decrease from baseline. Results reported here focus on the Rel-CT group, in which women received the longest duration of Rel-CT treatment (up to 104 weeks); the other groups, in which women transitioned to Rel-CT, provide supportive information.

RESULTS: Of 1261 women randomized in SPIRIT 1 and 2, 1251 were included in the analyses, and 1041 completed these studies. Furthermore, 802 (77%) enrolled in the LTE, of which 681 (85%) and 501 (62%) completed 52 and 104 weeks of treatment, respectively. Baseline dysmenorrhea and non-menstrual pelvic pain Numerical Rating Scale (0 [no pain]–10 [worst imaginable pain]) LS mean scores of 7.7 and 6.0, respectively, declined to 1.6 and 2.1 at Week 104/end of treatment. Correspondingly, EHP-30 LS mean pain domain scores decreased from 59.2 at baseline, with improvements of: 57.8% (LS mean change: −32.8; 95% CI: −35.5, −30.1), 66.4% (LS mean change: −37.7; 95% CI: −40.3, −35.0), and 72.2% (LS mean change: −41.3; 95% CI: −43.9, −38.7) at Weeks 24, 52, and 104, respectively. The proportions of women with clinically meaningful functional improvement on the EHP-30 pain domain were 75.9%, 83.6% and 88.6% at Weeks 24, 52, and 104, respectively. LS mean changes (% improvement) from baseline in EHP-30 total scores were −29.9 (52.6%), −34.4 (60.5%) and −38.2 (66.5%) at the corresponding timepoints. Other EHP-30 domain scores from baseline (pivotal) were analyzed using a mixed-effects model. The proportion of women with a clinically meaningful improvement in each domain was assessed, defined as a pre-specified ≥20-point decrease from baseline. Results reported here focus on the Rel-CT group, in which women received the longest duration of Rel-CT treatment (up to 104 weeks); the other groups, in which women transitioned to Rel-CT, provide supportive information.

IMPACT STATEMENT: Rel-CT represents a potential longer-term treatment for women with endometriosis-associated pain, providing symptom relief and improving daily functioning and various aspects of QoL.
Seventy-nine percent percent reported having delayed or are currently delaying family building due to medical training or career. Among those who specified the duration of delay, 46.2% delayed 0-3 years, 31.4% 3-5 years, and 22.4% ≥ 5 years. The most commonly cited factors influencing timing of childbearing were: moderately, “very much,” or “extremely” they were lack of schedule flexibility (76.0%), lack of time (71.2%), stress (69.7%), and concern about burdening colleagues (49.3%). Thirty-nine percent of respondents had considered egg/embryo freezing for fertility preservation, and 12.6% had frozen eggs/embryos.

Most women (61.1%) stated they were responsible for ≥ 50% of household maintenance roles (e.g., cleaning, groceries, cooking, laundry), and 57.3% stated they were responsible for ≥ 50% of family maintenance (e.g., childcare, eldercare, healthcare appointments, school forms), despite twice as many reporting personally working ≥ 60 hours/week vs. having a partner who worked ≥ 60 hours/week (27.8% vs. 13.6%, p<0.05). In order to accommodate childbearing or parenthood, 34.1% did not take opportunities for career advancement, 33.3% reduced their work hours, 20.5% chose a different specialty, and 18.5% changed their work setting (academic vs. private practice). Twenty-two women (3.0%) had left medicine entirely.

CONCLUSIONS: In this large national survey of female physicians from diverse specialties and practice locations, respondents cited significant career-related pressures coupled with increased household responsibilities that influenced the timing of childbearing and reported marked alterations in career trajectory to accommodate family building and parenthood.

IMPACT STATEMENT: Persistent gender disparities exist in leadership and faculty ranks. There is a need for equal medical education and curricula that include family building and career development.

SUPPORT: Research supported by a grant from the ASRM research institute.

EFFECT OF RACE ON OVARIAN RESPONSE TO GONADOTROPIN STIMULATION IN IN VITRO FERTILIZATION.

OBJECTIVE: There is a well established racial disparity in live birth rates following in vitro fertilization (IVF), but the underlying factors driving this disparity are unclear. This study aimed to determine whether race is associated with differences in ovarian response to gonadotropin stimulation during IVF and if so, how this may relate to live birth rates.

MATERIALS AND METHODS: We conducted a retrospective cohort study among women ages 18 to 45 undergoing ovarian stimulation for any indication from May 2015 to June 2021. Race and ethnicity were self-reported.

The primary outcome was ovarian sensitivity index (OSI) (total oocytes retrieved / total dose of follicle stimulating hormone x 1000), which has been shown to predict live birth following IVF. Linear regression was used to evaluate for an association between race and OSI, adjusting for age, body mass index (BMI), and duration of infertility. Live birth rate (LBR = number of live births/number of stimulation cycles started) was also compared among races, and for each race, logistic regression was performed to determine the association between OSI and live birth after adjusting for confounders.

RESULTS: Of the 4528 fresh cycles included in the study, 3173 (70.08%) were White women, 517 (11.42%) Black, 675 (14.91%) Asian, and 163 (3.60%) Hispanic. Black and Hispanic women were older at time of egg retrieval (p<0.01) and had longer durations of infertility compared to White and Asian women. There was no difference in AMH, total gonadotropin doses, or duration of stimulation among races. Fewer oocytes were retrieved from White (13) and Asian (13) women compared to Black (14.5) and Hispanic (15) women (p<0.02). Unadjusted OSI was similar among races (p=0.14), but after adjusting for age, BMI, and duration of infertility, Black (coefficient 1.43, p<0.001) and Hispanic (coefficient 1.36, p=0.01) women had significantly higher OSI compared to White (coefficient 1) and Asian (coefficient 0.12, p=0.65) women. Results were consistent when including only first ovarian stimulation cycles as well as when excluding fertility preservation and preoperative management cycles. LBR was highest in White women (38.83%), followed by Asian (34.02%), Hispanic (33.11%), and Black (30.29%) women (p=0.01). The association between OSI and live birth was significant only in White (adjusted odds ratio [AOR] 1.09, p<0.001) and Asian women (AOR 1.14, p<0.001).

CONCLUSIONS: Black and Hispanic women had higher OSIs than White and Asian women. Despite this, LBR was still highest in White women, and OSI was not significantly associated with live birth in Black and Hispanic women.

IMPACT STATEMENT: The reasons for the racial disparity in LBR following IVF are poorly understood. Our findings suggest that racial variation in ovarian response to gonadotropin stimulation does not account for the lower LBRs seen in non-White patients and may not predict live birth uniformly across all races. Understanding and addressing the racial disparity in IVF outcomes may require exploration of factors beyond the traditional predictors of live birth.

SUPPORT: None

REFERENCES: None

FAMILY HISTORY RISK ASSESSMENT BY A GENETIC COUNSELOR FOR OVUM DONORS: DATA FOR 582 IN HOUSE OVUM DONORS FROM A SINGLE CLINIC DEMONSTRATES ITS VALUE.

OBJECTIVE: This study was designed to explore the benefits of the genetic counselor’s unique expertise in evaluating egg donor family history as well as to quantify the amount and type of additional information captured during the genetics consultation as well as to determine the reasons for disqualification from the donor program as a result of information derived from the genetics consult.

MATERIALS AND METHODS: The data from this study was collected from an in-house donor program in which all donors are screened by the same genetic counselor. All donors had been pre-screened by the donor coordinator using a family history questionnaire and preliminarily accepted into the donor database, pending genetic testing, psychological evaluation, and family history assessment by a genetic counselor.

RESULTS: Genetic counseling was provided for all ovum donors (n=582) from Jan 2020 until mid-April 2022. Three-generation pedigrees were constructed, and risk assessment was performed. Chart review was performed to categorize the risk factors for which the clinic excluded the donor. Criteria based on the ASRM Minimal Screening for Gamete Donors, 2021 as well as clinic-specific disqualifiers were utilized to determine eligibility.

Of the 582 donors, 74 (13%) were excluded by the clinic due to new health conditions identified during the genetics consult.

Of the excluded donors, the largest categories represented were mental illness (n=35, 74%) and donor or first degree relative with congenital anomalies (n=16, 34%), followed by multifactorial conditions (n=10, 27%), early onset cancer (n=6, 13%) and family history of possible autosomal dominant condition (n=6, 13%), unknown syndrome or developmental delay (n=3, 7%), donor affected with an autosomal recessive condition requiring treatment or carrier of a recessive condition exhibiting symptoms (n=3, 7%), and sibling with autism spectrum disorder (n=2, 4%).

CONCLUSIONS: Family history risk assessment for ovum donors by a genetic counselor provides a thorough, standardized method of screening ovum donors. This data as well as previous studies (2,3,4) clearly and repeatedly demonstrate that a family history taken by a genetic counselor is superior to a questionnaire alone and identifies at least 20% more important family history information. Using a genetic counselor for family history taking allows the clinic or agency to better adhere to the minimum ASRM guidelines that donor candidates should meet and enables the intended parent to have the most comprehensive family history information and assessment of risk to their offspring so they can make informed decisions about potential genetic risks prior to donor selection and pregnancy.

IMPACT STATEMENT: Based on this data, it is reasonable to assert that a genetics consult for every ovum donor as standard practice would benefit the intended parent, the agency, and the IVF clinic.

SUPPORT: None

REFERENCES: None

COUNSELOR FOR OVUM DONORS: DATA FOR 582
UNIQUE SET OF GENETIC VARIANTS REFLECT EARLY-ONSET DIMINISHED OVARIAN RESERVE. Blair R. McCallie, PhD, 1 Mary E. Haywood, PhD, 1 Rachel Makloksi, RN, 2 William B. Schoolcraft, MD, 2 Mandy Katz-Jaffe, PhD 3 CCRM Research, Lone Tree, CO; 4Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Diminished ovarian reserve (DOR) is a condition where the number or quality of oocytes is compromised, significantly impacting a woman’s reproductive potential. While this is expected as women reach their fifth decade, about 10% of younger women (<35 years) will be diagnosed with premature DOR. For these women, the ability to predict the approaching early-onset DOR allows for the opportunity to make critical reproductive decisions. The objective of this study was to perform genome-wide variant discovery associated with premature DOR.

MATERIALS AND METHODS: A diagnosis of premature DOR was defined as maternal age ≤ 34 years (range 27-34), antral follicle count <10, and AMH <1.0 (ng/ml). Whole peripheral blood was collected from maternal, age-matched, female infertility patients with consent and IRB approval: diminished ovarian reserve (DOR; n=36) and normal ovarian reserve (Control; n=30). Maternal exome sequencing was performed (Illumina NovaSeq 6000) with variant calling using Ingenuity Pathway Analysis (Qiagen). Sequencing validation utilized Taqman SNP Genotyping Assays (Applied Biosystems) and oocyte gene expression was performed by RT-PCR (Applied Biosystems). Statistical significance was determined at P <0.05.

RESULTS: Variant analysis revealed 70 unique SNPs in 62 ovarian genes that were completely absent from the control group and predicted to be protein-altering and deleterious (P <0.05). The 10 most significant variants and their associated genes have been implicated in important ovarian biological processes including estrogen response, DNA repair, and cellular respiration, among others. Successful variant validation included gene members of the GR signaling pathway (AGT, KRT6A, KRT19, NCOA2, TAFL1) and key ovarian genes (AHRR, CCDC8, IGFBP5, LRRC17, PCDH11X, PDGFD). Interestingly, 6 protein-altering variants identified in the DOR group were characterized to be genes that are predominantly expressed in the testis (including C5orf52, MEIOB, USP26, and TESX5). Follow up RT-PCR confirmed this unique expression was also seen in human oocytes, including MEIOB, which encodes a factor essential for meiotic recombination. The presence of a MEIOB frame shift mutation has also been correlated with familial POI.

CONCLUSIONS: Women with early-onset DOR exhibited protein-altering, deleterious DNA variants in key ovarian genes associated with GR signaling, estrogen response, and DNA repair. These unique protein altering SNPs could be responsible for contributing to the development of the premature DOR environment. The novel identification of testes-associated deleterious SNPs could be responsible for contributing to the development of key ovarian genes associated with premature DOR.

ORAL ABSTRACT SESSION: ART LAB 1

GROWTH HORMONE IS USELESS IN IVF: THE LARGEST RANDOMIZED CONTROLLED TRIAL. Ali Mourad, M.D., 1 Wael Jamal, M.D., 2 Robert Hemmings, M.D., 3 Artak Tadevosyan, Ph.D. DEPD CSPQ FCACB, 4 Simon Phillips, Ph.D., 5 Isaac-Jacques Kadoch, M.D. 6 1Western University, Montreal, ON, Canada; 2OVO fertility center, Montreal, QC, Canada.

OBJECTIVE: To determine the efficacy and safety of adjuvant growth hormone (GH) therapy in GnRH antagonist cycles on reproductive outcomes in the general In-Vitro fertilization (IVF) population.

MATERIALS AND METHODS: This is a phase III open label randomised controlled trial involving a total of 288 patients who underwent an antagonist IVF cycle at OVO fertility center in Montreal, Canada, between June 2014 and January 2020. The study protocol was registered with Health Canada and approved by VERITAS IRB. The intervention group consisted of patients who received daily 2.5 mg subcutaneous injections of GH starting day 1 of ovarian stimulation until the day of oocyte retrieval, while the control group received standard ovarian stimulation without any adjuvant therapy prior to GnRH antagonist cycles, including embryo transfers (ET), fresh and/or frozen, resulting from this single IVF cycle were included in an intention-to-treat (ITT) and per-protocol (PP) analyses. The primary outcome was clinical pregnancy rate, while the number of retrieved oocytes and good quality embryos, maturation, fertilization, implantation and miscarriage rates and safety endpoints were recorded as secondary outcomes.

RESULTS: A total of 288 patients were recruited and randomly assigned at a 1:1 ratio to the GH or the control group. After removing the cycle cancellations and patients who did not undergo an ET, 105 patients remained in each group. The demographic characteristics in both groups were similar. The overall mean age was 38.0±2.6 years, the mean body mass index was 25.1±4.02 kg/m2 and the mean AMH was 2.51±2.59 ng/ml. The cycle characteristics were also similar between both groups. No differences were noted in terms of total dose of gonadotropin (460.2±467.1 IU) for the GH and control groups respectively, p=0.750, days of stimulation (11.4±11.7 days, p=0.117) and endometrial thickness (10.63±10.94 mm, p=0.372). The ITT and PP analyses detected similar results in terms of both IVF stimulation outcomes and reproductive outcomes. In the ITT analysis, no difference was noted in the number of follicles ≥15 mm (7.8±7.1, p=0.212), oocytes retrieved (11.7±11.2, p=0.613), mature oocytes (8.5±8.6, p=0.881), maturation rate (73.8±78.4%, p=0.06), fertilization rate (64.3±67.2%, p=0.388), good quality embryos (2.5±2.6, p=0.767), implantation rate (42.7±50.8%, p=0.234), miscarriage rate (26.9±29.5%, p=0.761) and clinical pregnancy rate (48.6±58.1%, p=0.167). The number of embryos needed to achieve a clinical pregnancy was 2.9±2.5 in the GH and control groups respectively, with no significant difference (p=0.322).

Finally, no or only mild side effects related to GH injection were noted.

CONCLUSIONS: GH adjuvant therapy in GnRH antagonist cycles is a safe procedure; however, it does not improve the results of IVF stimulation, nor the reproductive outcomes, namely implantation, miscarriage and clinical pregnancy rates.

O-8 11:00 AM Monday, October 24, 2022

IS HOME-BASED MONITORING OF OVULATION TO TIME FROZEN EMBRYO TRANSFER AN EFFECTIVE ALTERNATIVE FOR HOSPITAL-BASED MONITORING OF OVULATION? Tijsske Zaat, M.D., M.S.C., 1 Jan Peter P. De Bruin, M.D., Ph.D., 2 Eva Groenewoud, MD Ph.D., 3 Esther B. Baart, PhD, 4 Wilhelmina Van Baal, M.D., Ph.D., 5 Monique Brandes, Dr., 6 Astrid E. P. Canteine, M.D., Ph.D., 7 Gijs Brouxmans, M.D., Ph.D., Prof., 8 Susanne Gielen, M.D., Ph.D., 9 Mariette Goddijn, Prof., 10 Jeroen Van Dissel dorp, Dr., 11 Arne M. van Heusden, M.D., Ph.D., 12 Eugene M. Kaaikj, M.D., Ph.D., 13 Nicole Klijn, M.Sc. 14 Carolien A. M. Koks, M.D., Ph.D., 15 Cornelia De Koning, Dr., 16 Paul J. Q. Van Der Linden, M.D., 17 Petra Manger, M.D., 18 Lobke Moolenaar, Dr., 19 Robbert Van Oppenraaij, Dr., 20 Quirine Pieterse, Dr., 21 Jesper M. J. Smeenk, M.D. Ph.D., 22 Jantien Visser, MD PhD, 23 Madelon Van Wely, Ph.D., 24 Femke Mol, M.D., Ph.D. 25 Amsterdam UMC, University of Amsterdam, Center for Reproductive Medicine, Amsterdam Reproduction & Development Research Institute, Meibergdreef 9, Amsterdam, Amsterdam, Netherlands; 2 Jeroen Bosch Ziekenhuis, Den Bosch, Netherlands; 3NoordWest Ziekenhuisgroep, Den Helder, Netherlands; 4Erasmus MC University Medical Center, Rotterdam, Netherlands; 5Evelo Hospita l, Department of Obstetrics and Gynaecology, Almere, Netherlands; 6Nij Geest Achmea, Den Bosch, Netherlands; 7Academic Centre Utrecht, Utrecht, Netherlands; 8Franciscus Gasthuis & Vlietland, Rotterdam, Netherlands; 9Antoniou Ziekenhuis, Netherlands; 10 Tergooi Ziekenhuis, Amsterdam, Netherlands; 11Leiden University Medical Centre, Leiden, Netherlands; 12Department of Reproductive Medicine, Maxima Medical Center, Veldhoven/Eindhoven, Netherlands; 13Fergooi Ziekenhuis, Netherland; 14Deventer Ziekenhuis, UMCG, Groningen, Netherlands; 15Amsterdam UMC, University of Amsterdam, Center för Reproductive Medicine, Amsterdam, Netherlands. 16Maastricht Ziekenhuis, Netherlands; 26Haga Ziekenhuis; 27ETZ, Tilburg, Netherlands; 28Amphia Hospital, Breda, Netherlands; 29Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands; 30Amsterdam UMC, University of Amsterdam, Center for Reproductive Medicine, Amsterdam, Netherlands.
OBJECTIVE: Among women who are undergoing in vitro fertilization (IVF), transfer of frozen embryo’s (FET) in the natural cycle (NC) is an effective alternative to FET in the artificial or supplemented cycle in terms of pregnancy outcomes. As NC-FET results in a lower perinatal complication rate that artificial FET, it is a preferred method to transfer frozen embryos in ovulatory women. The standard in NC-FET is modified or hospital-based NC-FET, which involves repeated ultrasounds and triggers the ovulation. From the woman’s point of view, a more natural approach to time FET using LH urine tests to allow a natural ovulation, i.e. true NC or home-based monitoring, may be desired. It is not known whether FET in the true NC results in similar ongoing pregnancy rates compared to modified NC-FET.

MATERIALS AND METHODS: We randomly assigned 1466 infertile ovulatory women who desired a FET. In the true NC group, following timing by a positive urinary LH test, a maximum of two embryos were thawed on the day of transfer. In the modified NC group, a maximum of two embryos were thawed on the day of transfer following timing by a hCG trigger. The primary outcome was ongoing pregnancy after one cycle (per start, per woman randomized). The secondary outcomes were clinical pregnancy and risk of missing the ovulation. We calculated risk difference (RD) and risk ratios (RR) with 90% Confidence Intervals [CI] based on intention-to-treat analysis. Non-inferiority would be shown if the lower limit of the 90% RD confidence interval was less than minus 4%.

RESULTS: At submission of this abstract, data on the primary outcome were available for 1440 women (98%). Ongoing pregnancy occurred in 129 of 720 [17.9%] in the true NC group and in 127 of 720 [17.6%] in the modified NC group (risk ratio in the true NC group 1.02; 90% CI 0.84 to 1.22). This corresponds to a RD of 0.28% (90% CI -3.04% to 3.59%) in the true NC group, indicating non-inferiority. The per protocol analysis confirmed non-inferiority (126/644 versus 126/643: RD 0.03%, 90% CI -3.39% to 3.59%) in the true NC group, indicating non-inferiority. The per protocol analysis confirmed non-inferiority (RR 0.97, 90% CI 0.80 to 1.21). Missing the ovulation occurred in 38/733 [5.2%] in the true NC group and 142/720 [19.7%] in the modified NC group (RR 1.02; 90% CI 0.86 to 1.22). Clinical pregnancy was 145/720 [20.1%] in the true NC group and 220/720 [30.0%] in the modified NC group (risk ratio in the true NC group 1.02; 90% CI 0.84 to 1.22). Ongoing pregnancy occurred in 129 of 720 [17.9%] in the true NC group and in 127 of 720 [17.6%] in the modified NC group (risk ratio in the true NC group 1.02; 90% CI 0.84 to 1.22).

CONCLUSIONS: Among infertile women with ovulatory cycles, the transfer of frozen embryos in the true NC (home-based monitoring) is non-inferior compared to transfer of frozen embryos in the modified NC (hospital-based monitoring) in terms of ongoing pregnancies.

IMPACT STATEMENT: Considering women’s desire for a more natural approach and to feel empowered, true NC (home-based monitoring) should be implemented for FET. True NC also has the benefit of saving direct and indirect medical costs for the woman and for society.

Funded by Dutch Organisation for Health Research and Development (ZonMW843002807). Trial NL6414 (NTR6590).

First enrollment: April 10th 2018; last enrollment April 13th 2022.

SUPPORT: The RCT was funded by Dutch Organisation for Health Research and Development (ZonMW843002807).

REFERENCES: NA

O-9 11:15 AM Monday, October 24, 2022

COMPETENCY AND BENCHMARK VALUES FOR VIENNA CONSENSUS ART LABORATORY KEY PERFORMANCE INDICATORS (KPIs) REDEFINED: REAL-WORLD DATA FROM 80 NORTH AMERICAN IVF LABORATORIES. Jason KM Au, MSc, Sung Ta Tsou, B.SC., May Tian, MSc, Jon C. Havelock, MD, FRCSC, DABOG, Pacific Centre for Reproductive Medicine, Burnaby, BC, Canada.

OBJECTIVE: This study evaluated data from 80 North American IVF clinics as illustrated by the Vienna Consensus Report. The evaluation focused on the 12 Laboratory KPIs to determine the Competency (CV) and Benchmark values (BV) using ~600,000 real-world data points.

MATERIALS AND METHODS: Collaborated with the Electronic Medical Record (EMR) system, anonymized and aggregated Embryology and clinical data surrounding the 12 Vienna KPIs were pulled from all clinics using the EMR over a two-year period (Jan 2018 - Dec 2019). These data contain no identifiers traceable to the clinics or the patients. Before data pulling, each KPI was assessed for its data reliability: 3 KPIs were excluded in this analysis due to the complexity, size, and location of the surveyed data. Datasets with up to 615,310 data points were obtained. Some clinics are excluded from the analysis as KPI data points were determined. The percentages of clinics exceeding the pre-defined CV and percentiles, means (95% confidence interval) and standard deviations were determined. The percentages of clinics exceeding the pre-defined CV (minimum performance level) and BV (aspirational) were also determined.

RESULTS: For 7 of the 9 reported KPIs, ≤10% clinics has achieved this aspirational performance and no clinic has reached the benchmark performance for 3 KPIs.

Table 1. The results of the statistical analyses

<table>
<thead>
<tr>
<th>KPIs</th>
<th>Percentile</th>
<th>No. of clinic</th>
<th>No. of Data point</th>
<th>Mean (95% CI)</th>
<th>% of clinics &gt; CV</th>
<th>% of clinics &gt; BV</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>10% 25% 50% 75% 90%</td>
<td></td>
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<td></td>
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<tr>
<td>ICSI normal fertilization rate (%)</td>
<td>66 71 75 79 82</td>
<td>63</td>
<td>595</td>
<td>487</td>
<td>74.9% (73.5% - 76.4%)</td>
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<tr>
<td>IVF normal fertilization rate (%)</td>
<td>48 57 60 66 70</td>
<td>37</td>
<td>165</td>
<td>655</td>
<td>59.0% (55.9% - 62.1%)</td>
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</tr>
<tr>
<td>ICSI damage rate (%)</td>
<td>13 50 3.7 13.0 9.0</td>
<td>23</td>
<td>220</td>
<td>835</td>
<td>4.4% (2.6% - 6.1%)</td>
<td>87 78</td>
</tr>
<tr>
<td>Cleavage rate (%)</td>
<td>94 96 97 99 100</td>
<td>27</td>
<td>77350</td>
<td>96.9% (95.7% - 98.0%)</td>
<td>81 22</td>
<td></td>
</tr>
<tr>
<td>D2 embryo development rate (%)</td>
<td>46 48 54 68 75</td>
<td>25</td>
<td>75608</td>
<td>96.8% (95.9% - 98.0%)</td>
<td>72 0</td>
<td></td>
</tr>
<tr>
<td>D3 embryo development rate (%)</td>
<td>30 35 43 56 69</td>
<td>63</td>
<td>334</td>
<td>326</td>
<td>45.8% (42.3% - 49.4%)</td>
<td>44 8</td>
</tr>
<tr>
<td>Blastocyst development rate (%)</td>
<td>22 33 45 54 60</td>
<td>80</td>
<td>596</td>
<td>753</td>
<td>43.9% (40.7% - 47.1%)</td>
<td>63 10</td>
</tr>
<tr>
<td>Cleavage Implantation rate (%)</td>
<td>11 14 22 24 28</td>
<td>21</td>
<td>5167</td>
<td>19.8% (16.9% - 22.7%)</td>
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<tr>
<td>Blastocyst Implantation rate (%)</td>
<td>28 34 43 51 55</td>
<td>44</td>
<td>16871</td>
<td>41.5% (37.7% - 45.3%)</td>
<td>73 2</td>
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</table>
CONCLUSIONS: This study suggested that the pre-defined CV and BV may not align with the real-world performance of clinics in North America. Validation study must be done in generating real-world performance benchmarks for clinics/laboratories. This study proposes using the 25% and 75% quartiles as the CV and BV, respectively.

IMPACT STATEMENT: This study aims to use real-world data from clinics to statistically determine the Competency and Benchmark values associated with each Vienna KPI. This study demonstrated the use of Big Data in the validation work on established standards and guidelines.

REFERENCES:

O-10 11:30 AM Monday, October 24, 2022

LOW LACTATE/PYRUVATE MEDIUM IMPROVES GV COMPETENCE. LauraEscrich, PhD, AitorGalbeteUrrutia, BSc,1 Nuria Soler, MSc, Maria FernandaInsua, PH.D,2 MariaJoseEsberaPerez, PhD,3 Noelia Grau, PhD,4 IVIRMA Valencia, Valencia, Spain; 2Instituto de Investigación saysa La Fe, Valencia, Spain; 3Universidad de Valen-

OBJECTIVE: To study the effect of two media on supporting nuclear and cytoplasmic competence of germinal vesicle (GV) oocytes.

MATERIALS AND METHODS: This is an experimental, prospective and randomized study performed on GV. Women < 36 years-old underwent COS and oocyte retrieval (June 2020 - May 2021). After denudation, GV were selected to rescue. Informed signed consent was given to women (IRB approval 0703 E 402 ME).

Briefly, GV were individually cultured in 25µl of either of G-2 PLUSTM (Vi-
trolife) or CSCM–NXC (IrvinScientific) medium in EmbryoS scopes; at 37°C, 5% CO2and 5% O2, in an EmbryoScope. After 24-28h, oocytes reaching MII <24h (rMII) were assessed and the rescue rate calculated (rR: rMII / GV).

Nuclear dynamics was studied in 541 GV. The occurrence time (h) of these events was assessed (denudation was reference time, t0): 1) GV breakdown (GVBBD), marking the start of MI and informing on GV permanence, since denudation; 2) the 1st polar body extrusion (t1PB), marking the end of MI and the beginning of MII. Variables subtraction provided MI duration.

To assess cytoplasmic competence, rMII were activated by A23187 (4µM;5 min) and puromycin (10mg/ml;5h). At 16-20h culture, normal oocyte activation (NOA) was assessed by extrusion of the 2ndPB and presence of one pronucleus. The NOA rate was calculated (NOAR, percentage of rMII displaying NOA response / incubated rMII). Besides, direct morphokinetic variables (pronuclear appearance -PNA- and fading -PNF-) and S-phase duration, were assessed on parthenotes.

Variables were compared by Chi-square test with Yates’ correction. Continuous variables were checked for normality and analyzed by t-tests.

RESULTS: Concerning nuclear competence, comparable rR were observed, regardless media (57.1%); reaching MI in comparable time (19.4±0.2h). However, according to G2 or CSCM–NXC, differences were observed in rGVBBD (4.4±0.2h vs. 3.4±0.2h; p<.05) and MI duration (14.6±0.2h vs. 15.1±0.1h; p<.05).

Regarding cytoplasmic competence, rMII in CSCM–NXC had higher NOAR than rMII in G-2 (9.4% vs. 40.6% respectively; p=.01). However, rMII-derived parthenotes had comparable morphokinetics for PNA (7.7±0.2h), PNF (22.8±1.0h) and S-phase duration (16.9±0.6h), regardless media.

CONCLUSIONS: CSCM–NXC and G2 support nuclear competence; but, rMII in CSCM–NXC, with low lactate/pyruvate ratio, were more competent, at cytoplasm level than those rMII in G2.

CSCM–NXC promotes: 1) reduction on permanence time at GV and longer MI duration, without compromising rR nor t1PB and; 2) improvement on cytoplasmic competence. Alternatively, high glucose/pyruvate ratio of G2 impairs cytoplasmic, but does not nuclear competence.

IMPACT STATEMENT: CSCM–NXC rescues nearly 60% GV and improves cytoplasmic competence. It is currently the medium used in our GV rescue clinic program.

O-11 11:45 AM Monday, October 24, 2022

FIRST PRE-CLINICAL AND CLINICAL VALIDATION OF AN AUTOMATED SPERM INJECTION ROBOT (ICSI-A) IN HUMAN OOCYTES. Nuno Costa Borges, PhD,1 John Zhang, MD, PhD,2 Eduard Albo Plandiura, Eng.,3 Zhuo LU, PH.D,4 Sergio Mas Sabatés, Eng.,5 Carolina Castello, BSc,6 Guilemm Giralt, Eng.,6 Monica Acacio, MSc,7 Enric Mestre, PhD,7 Queralt Matia-Algud, MSc,8 Laura Marquès, PhD,9 Mariona Rius, PhD,9 Carmen Marquez, PH.D,9 Ivette de la Jara Gómez, BSc,10 Aida Pujol Masana, PhD,10 Luis Mallol esto, Eng,5 Gloria Calderon, PhD,9 Santiago Munne, PhD,1 Embryobots, Barcelona, Spain; 2New Hope Fertility Center; 3Overture Life, Barcelona, Spain; 4New Hope Fertility Center, New York, NY; 5Overture Life, Madrid, Spain; 6CRA Barcelona, Barcelona, Spain; 7Ferty; 8Gravidia (CIRHB); 9Cefer; 10Center for Infertility and Human Reproduction CIRH, Eugin Group, Barcelona, Spain.

OBJECTIVE: Intracytoplasmic sperm injection (ICSI) is currently performed manually by skilled embryologists. However, success rates can vary depending on the performance of each operator. Recently, we have developed an automated robot for sperm injection, ICSI-A, which has proven successful in proof-of-concept studies carried out in the mouse, rabbit, and hamster. Here, we evaluated the efficiency of the robot first in human pre-clinical experiments and then in a small clinical trial using human donor oocytes.

MATERIALS AND METHODS: The project received approval from two independent Institutional Review Boards (IRBs). The first one to use human immature oocytes from ICSI cycles discarded for being immature at the moment of the ICSI procedure and the second one to conduct a first clinical validation of the robot in regular oocyte donation cycles. Specific consent was obtained from donors and patients participating in the study. In the pre-clinical experiments, the oocytes were in vitro matured and those showing a first polar body (PB) were used to train artificial intelligence (AI) algorithms in identifying the morphological structures of oocytes (zona pellucida, perivitelline space, oolemma, cytoplasmic inclusions and PB) and then to evaluate the injection efficiency of the robot. The mature oocytes were injected with latex microspheres similar in size to the head of a human sperm and survival rates assessed after overnight culture. In the clinical validations, oocytes from three donation cycles were assigned randomly to be injected with the robot or by conventional ICSI. Once injected, oocytes were cultured uninterrupted in a time-lapse incubator, and fertilization and blastocyst rates assessed on Day 5/6/7 post-ICSI. In both parts of the project, the robot was operated by an engineer with no micromanipulation experience, while conventional-ICSI was performed manually by experienced embryologists. Chi-square test was used to compare results.

RESULTS: In the pre-clinical validations, 84 out of 124 oocytes that were matured in vitro, showed a first PB (66.1% maturation rate) and were used to train the robot. Thirty-one out of 34 vitrified-warmed oocytes that were injected with a microsphere with the ICSI-A robot survived (91.2%) the procedure, showing 8% survival rates were obtained in the control group (n=11). No differences were found when fresh oocytes were used with the ICSI-A robot (n=6, 100% survival) and manual ICSI (n=9, 88.9%). In the clinical validations, 13/14 (92.9%) oocytes injected with ICSI-A fertilized successfully and 61.5% developed into good quality blastocysts. Similarly, 16/18 (88.8%) oocytes injected with conventional ICSI fertilized and 68.8% reached the blastocyst stage. Differences were not statistically different.

CONCLUSIONS: The ICSI-A robot showed high proficiency in injecting human oocytes. However, ICSI-A clinical results are still preliminary, they are promising and are within the KPI competence values described for IVF laboratories.

IMPACT STATEMENT: Automated processes may contribute to reduce the current variability in results associated to certain IVF procedures.

O-12 12:00 PM Monday, October 24, 2022

TURNING THE BLACK BOX INTO A GLASS BOX: USE OF TRANSPARENT ARTIFICIAL INTELLIGENCE TO UNDERSTAND BIOLOGICAL MARKERS USEFUL FOR EMBRYO SELECTION. Cristina Hickman, PhD,1 Nikica Zaninovic, Ph.D,2 Jonas Malmsten, D.P.S,2 Qiansheng Zhan, Ph.D,2 Adriana Brualla Mora, MSc,3 Iris Har-Vardi, PhD,4 Assaf Ben-Meir, MD,5 Fertility, London, United Kingdom; 6Weill Cornell Medicine, New York, NY; 7Fertility, Beer-Sheva, Israel; 8Fertility, Israel.

REFERENCES:
OBJECTIVE: To compare biomarkers automatically annotated by CHLOE EQTM (Fairility) with human annotations, and to better understand their biological relevance.

MATERIALS AND METHODS: 799 day 5 Time-lapse (TL) videos were retrospectively reviewed by 13 morphologically graded and ranked by five experienced embryologists before being assessed by CHLOE for automatic detection of a range of biomarkers.

RESULTS: CHLOE EQTM score was directly related to ranking by all embryologists (p < 0.001). Embryologists rarely agreed with each other (10/3799= 12.9%). Implanted embryos (mean± standard deviation: 0.94±0.2, n=56) had a higher (p < 0.001) CHLOE EQTM score compared to embryos that did not implant (0.85±0.3, n=28). Euploids (0.85±0.2, n=360) had higher (p < 0.001) CHLOE EQTM score than aneuploid/mosaics (0.76±0.3, n=410). Implanted embryos (0.94±0.16, n=28) had higher (p < 0.035) CHLOE EQ score than non-implanted embryos (0.85±0.25). The difference in CHLOE EQ score between embryos leading to LB (0.93±0.2 n=42) and not (0.87±0.2 n=36) approached significance (p=0.08).

Good quality embryos, as determined by CHLOE, were more likely to be euploid (51%/vs 35%, p < 0.001), more likely to implant (71% vs 33%) and more likely to lead to a LB (58% vs 22%) than poor/fair quality embryos.

There was very strong (Correlation Coefficient: r=0.9; t4=0.83; t6=0.80; t7=0.72; t8=0.84; tM=0.81; tSB≈0.95; tB≈0.86), and strong (rPNf≈0.65; t3≈0.76; t5≈0.79; t9≈0.74; tBE≈0.61) levels of agreement between human and CHLOE EQ morphokinetic annotations.

12% of blastocysts were identified as DUCs by CHLOE (97/799), DUC blastocysts had lower euploidy rate (31%, 29/94) compared to non-DUC blastocysts (49%, 332/684, p < 0.001). 2% of A-graded ICM blastocysts were DUC which was a five-fold lower proportion than B-graded (10%) and C-graded (50%) ICM blastocysts (p < 0.001).

22% of embryos were identified as having severe fragmentation by CHLOE (179/799).

Euploid embryos had a larger diameter at 114hpi (166±24 n=359 vs 154±23um n=403, p < 0.001), compared to aneuploid and mosaic embryos. The embryos with an A-graded ICM had a significantly (p < 0.001) larger embryo diameter (179±18um, n=114) than embryos graded B (157±18um, n=165) or C (153±22, n=12) by embryologists. There is a negative relationship between diameter at 114hpi & tSB (r≈−0.7, p < 0.001) and tBE≈(r≈−0.7, p < 0.001).

21% (169/799) of blastocysts collapsed once, 4% (30/799) twice and 0.5% (4/799) 3 times. The severity of the collapse increased with increasing number of collapses (1 collapse: median 23%: 2: 29%; 3.31%; p < 0.001).

CONCLUSIONS: CHLOE can automatically quantify: (a) blastocyst diameter (which increases with expansion); when the blastocyst is expanded; (b) proportion of blastocyst that collapses and the number of times a blastocyst collapses; (c) DUC(d) fragmentation and (e) morphokinetics (comparable to human manual annotations).

IMPACT STATEMENT: Automatic TL quantification allows for a consistent embryo assessment; better fluidity of information between the lab, REI, patient & clinic management; reducing operational costs whilst increasing standards of care through transparency.

SUPPORT: NA

ORAL ABSTRACT SESSION: ENDOMETRIOSIS

O-13 10:45 AM Monday, October 24, 2022

WAVES STUDY – QUANTITATIVE ULTRASOUND MEASUREMENT OF ENDOMETRIAL WAVES IN ADENOMYSIS VERSUS WOMEN WITH NORMAL UTERI. Connie Odette Rees, MD, MSc,1 Yizhou Huang, MSc, PhD,2 Anna De Boer, BSc,1 Blijkke Wessels, BSc,1 Huib Van Vliet, MD, PhD,1 Aleida G. Huppelschoten, MD, PhD,1 Massimo Mischi, PhD,1 Benedictus Christiaan Schoot, MD, PhD1 1Catharina Hospital, Eindhoven, Netherlands; 2Eindhoven University of Technology, Eindhoven, Netherlands; 3Department of Gynaecology and Obstetrics, Catharina Hospital Eindhoven, Eindhoven, Netherlands; 4Department of Electrical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands.

OBJECTIVE: Measurement and analysis of uterine contractions by quantitative 2D transvaginal ultrasound measurements in women with abnormal uteri due to adenomyosis versus women with normal uteri.

MATERIALS AND METHODS: In this multi-centre prospective observational cohort study, 29 women with adenomyosis with a natural menstrual cycle were compared to 70 women with normal uteri and menstrual cycles. Patients were included from September 2014 - January 2022 in 3 centres. Primary endpoints were the contraction frequency (contractions/minute), amplitude, direction, (Cervix-to-fundus, Fundus-to-cervix), and coordination. Women underwent a 4 minute ultrasound of the uterus in mid-sagittal section. Uterine motion analysis was implemented by a dedicated speckle tracking algorithm; with frequency, amplitude, coordination and velocity-related features extracted from the derived signals to characterise uterine contractions. Measurements were carried out at different points of the menstrual cycle (Menstrual phase, Periovulatory phase and Luteal phase).

RESULTS: Results differed most significantly between groups in the periovulatory phase, with women with adenomyosis showing lower frequency (1.44 vs. 1.79 contractions/minute, p = 0.025), higher amplitude (0.09 vs. 0.04, p = 0.0008) and lower velocity of uterine contractions (0.62 vs. 0.83, p = 0.0008). In the menstrual phase, women with adenomyosis showed a trend toward higher contraction frequency (1.37 vs. 1.33 contractions/minute, p = 0.592), amplitude (0.05 vs. 0.04, p = 0.259) and velocity (0.72 vs. 0.67, p = 0.456). Across all phases, women with adenomyosis showed a trend towards reduced contraction coordination (0.23-0.34 vs. 0.15-0.26). This being statistically significant in the late luteal phase (p = 0.018).

CONCLUSIONS: Our results confirm differences in uterine movement in abnormal versus healthy uteri, specifically in the periovulatory and menstrual phases.

IMPACT STATEMENT: Further research in women with (other) benign uterine disorders will hopefully lead to a better understanding of the clinical implications of abnormal uterine contractility in this population. This could add to the aetiological understanding of clinical symptoms of these conditions (i.e. dysmenorrhoea or infertility). The notable difference between groups regarding coordination identifies this features as potential prognostic or therapeutic markers.

SUPPORT: Unrestricted grant GE Healthcare Austria

0-14 11:00 AM Monday, October 24, 2022

TIME TO MINIMAL OR NO PELVIC PAIN WITH RELUGOLIX COMBINATION THERAPY IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED PAIN: RESULTS FROM THE SPIRIT PROGRAM. Sawsan As-Sanie, MD, MPH,1 Neil Johnson, MD,2 Andrea S. Lukes, MD, MPH,3 Juan Camilo Arjona Ferreira, MD,4 Juliet Li, PhD,5 Julie Stein Perry, MD,6 Rachel B. Wagman, MD,7 Linda C. Giudice, MD, PhD1 15100 East Medical Center Drive, Ann Arbor, MI; 2Robinson Research Institute, University of Adelaide, Australia; 3Carolina Women’s Research and Wellness Center, Durham, NC; 4Myovant Sciences Inc., Brisbane, CA; 5Myovant Sciences Inc., Brisbane, CA; 6Myovant Sciences, Brisbane, CA; 7University of California, San Francisco, San Francisco, CA.

OBJECTIVE: In women with endometriosis-associated pain, once-daily relugolix combination therapy (Rel-CT) was associated with maintenance of efficacy on dysmenorrhea (DYS) and non-menstrual pelvic pain (NMPP) through 104 weeks (wks) of treatment (Becker, ESHRE 2022). Here, the time course of when first reported minimal/no pain for either DYS or NMPP was examined.

MATERIALS AND METHODS: Premenopausal women with moderate-to-severe pain associated with endometriosis were enrolled in SPIRIT 1/2 and randomized 1:1:1 to receive Rel-CT or placebo for 24 wks, or delayed Rel-CT (relugolix 40 mg monotherapy for 12 wks followed by Rel-CT for 12 wks). Women who completed the pivotal trials were eligible to enroll in an 80-wk open-label, single-arm, long-term extension (LTE) study, representing outcomes up to 104 wks of treatment with Rel-CT. Primary endpoints of the LTE were proportion of responders for DYS and NMPP, based on daily Numerical Rating Scale (NRS) scores (0=no pain, 10=worst pain imaginable) and analgesic use. Responders were defined as women who achieved a predefined, clinically meaningful reduction from baseline in NRS score and no increase in analgesic use. In this post-hoc analysis, Kaplan-Meier curves were developed for each treatment group to describe time to first reported minimal/no pain (NRS ≤3 for DYS and ≤5 for NMPP, as well as for time to first reported 28-day amenorrhea and becoming analgesic free using pooled SPIRIT 1/2 data and the LTE. Results are reported for the Rel-CT group in which women received continuous Rel-CT treatment for up to 104 wks.

RESULTS: Of 1261 women randomized in SPIRIT 1/2, 1251 were included in the analyses, and 1041 completed these studies. Of these, 802 (77%) women...
entered the LTE and 501 (62%) completed Wk 104, including 172 women in the Rel-CT group. Median time to NRS ≤ 1 for DYS was approximately 8 wks in the Rel-CT group, and was not reached in the placebo group within 24 wks of treatment; 82.5% and 22.4% of women, respectively, reported minimal/no pain at Wk 24. This increased to 94.5% of women in the Rel-CT group at Wk 52 and 93.5% at Wk 104. Reporting patterns for amenorrhea were consistent with those for DYS. For NMPP, median time to NRS ≤ 1 was approximately 32 wks in the Rel-CT group and 40 wks in the placebo group (i.e. placebo transition to Rel-CT); 42.6% and 28.9% of women reported minimal/no pain at Wk 24. This increased to 59.9% of women in the Rel-CT group at Wk 52 and 70.5% at Wk 104. In the Rel-CT group, median time to becoming amenorrheic was approximately 16 wks; 68.8% of women were amenorrheic free at Wk 24, increasing to 86.8% at Wk 52 and 94.9% at Wk 104.

CONCLUSIONS: In women treated with Rel-CT, median time to minimal/no pain associated with DYS occurred within two menstrual cycles and was also observed in nearly all women at the end of the two-year SPIRIT trials. For NMPP, median time to minimal/no pain was achieved in approximately 8 months, and was observed in over half of women at one year and more than two thirds at the conclusion of the SPIRIT trials.

IMPACT STATEMENT: Rel-CT provides meaningful reduction of endometriosis-associated DYS and NMPP, with continued improvement in effect over 2 years.


Differential Uterine Uptake of Estrogen and Progestogen-Based Radiotracers Across the Menstrual Cycle: Moving Towards Improved Radiologic Detection of Endometriosis. Rachel G. Catharine Wilson, PhD,1 Heather M. Sidener, DVM, DACLA,1 Lauren Drew Martin, DVM,1 Jeanne Link, PhD,2 Steven L. Young, M.D., Ph.D.,1 6ove D. Slayden, PhD1 1Oregon Health and Science University, Beaverton, OR; 2Oregon Health & Science University, Beaverton, OR; 1Oregon Health & Science University, Portland, OR; 2University of North Carolina School of Medicine, Chapel Hill, NC.

OBJECTIVE: To examine uterine uptake of radiotracers targeting steroid receptors with the intent to extrapolate our findings to inform the feasibility and development of positron-emitting tomography (PET) imaging to identify endometriosis.

MATERIALS AND METHODS: We performed PET and computed tomography scans on rhesus macaques (Macaca mulatta) with either spontaneous or induced endometriosis. Radiotracers targeted either the estradiol or progesterone (P) receptors, 16-estradiol (estradiol) or progesterone (progesterone). Radiotracer uptake was also noted at an ectopic location that was identified as a site of endometriosis during a prior laparoscopy.

RESULTS: To determine the SUV measurement that would provide the greatest ability to discern endometrium or endometrium-like tissue from surrounding organs, we compared mean and maximum SUVs in the intestines and uterus were similar [8.3 SUVs ± standard error (SE)] in the proliferative phase and 9.2 ± 0.2 SUVs, respectively], intestinal mean uptake was substantially lower than uterine (0.6 ± 0.1 and 4.1 ± 0.1 SUVs, respectively). We then focused on mean SUVs to determine if uterine uptake differed with menstrual cycle phase or radiotracer target. Radiotracer uptake in the uterus significantly differed with scan time (p < 0.01), and the interactions of scan time*cycle phase (p = 0.03) and scan time*radiotracer target (p < 0.01). Peak mean SUV occurred within the first 3.5 minutes with higher peaks for FFNP (6.0 vs 4.8 SUVs, respectively). Radiotracer uptake then dropped until about 7.5 minutes with the lowest levels of FES uptake in the proliferative phase: 2.8 SUVs vs 3.5 SUVs for all other groups. Uptake of FES regardless of cycle phase and FFNP in the proliferative phase reached a semi-equilibrium state approximately 8 minutes post injection. However, FFNP uptake in the secretory phase rose from 3.6 SUVs to 4.2 SUVs during this same time. Radiotracer uptake was also noted at an ectopic location that was identified as a site of endometriosis during a prior laparoscopy.

CONCLUSIONS: Radioactivity uptake profiles in the uterus are dynamic depending on tracer target, scan time, and menstrual cycle phase with greatest uptake of FFNP during the secretory phase and lowest of FES in the proliferative phase. This indicates a kinetic rather than a standardized uptake analysis may be warranted. Further, identification of a likely endometriotic lesion supports the feasibility of the approach.

IMPACT STATEMENT: Targeting progesterone receptors with FENP during the secretory phase appears to provide the highest resolution for identifying endometrium-like tissue suggesting PET represents a non-invasive diagnostic imaging tool for endometriosis.

A Prospective Study of Plasma Protein Markers Associated with Risk of Laparoscopically Confirmed Endometriosis in the Nurses’ Health Study II. Naoko Sasamoto, M.D., Ph.D.,1 Long Ngo, Ph.D.,2 Allison F. Vitonis, M.S.,1 Simon Dillon, Ph.D,2 Stacey A. Missmer, Sc.D.,1 Towa A. Libermann, Ph.D,2 Kathryn L. Terry, Sc.D.1 1Brigham and Women’s Hospital, Boston, MA; 2Beth Israel Deaconess Medical Center, Boston, MA; 3Michigan State University, Grand Rapids, MI.

OBJECTIVE: To identify plasma proteins associated with risk of laparoscopically confirmed endometriosis among premenopausal women using a multiplex aptamer-based proteomics biomarker discovery platform.

MATERIALS AND METHODS: We examined the association between proteins measured in prospectively collected blood samples and risk of endometriosis diagnosis in a case-control study nested within the Nurses’ Health Study II. We measured 1,305 plasma proteins using a validated proteomics biomarker discovery platform, SOMAscan, that included markers for immunity, angiogenesis and inflammation in 200 laparoscopically confirmed endometriosis cases and 200 risk-set sampling matched controls. We used conditional logistic regression to calculate odds ratios (OR) and 95% confidence intervals (CI) per one standard deviation increase in protein levels. Area under the curve (AUC) was calculated to determine the performance of the multi-protein model in discriminating endometriosis cases from controls.

RESULTS: Median age at blood draw was 40.7 years for endometriosis cases and 41.3 years for controls, and most participants were white race (95%). Blood samples from endometriosis cases were collected up to 9 years before endometriosis diagnosis (median 1.4 years before diagnosis). There were 17 proteins associated with risk of endometriosis diagnosis with absolute fold change >1.2 in levels between cases and controls and p-value <0.05. Of these, 15 proteins were associated with increased risk of endometriosis diagnosis and only 2 proteins were associated with decreased risk. Compared to controls, endometriosis cases had higher plasma levels of S100A9 (OR=1.52, 95%CI=1.19-1.94), ANXA1 (OR=1.45, 95%CI=1.15-1.84), HIST1H3A (OR=1.42, 95%CI=1.31-1.78), TOPI (OR=1.95, 95%CI=1.24-3.06), CD5L (OR=1.23, 95%CI=1.00-1.51) and lower levels of IGFBP1 (OR=0.70, 95%CI=0.52-0.94), NPPB (OR=0.70, CI=0.52-0.94). When we developed multi-protein models and assessed its performance to discriminate endometriosis cases from controls, a model including HIS-T1H3A, TOPI, IGFBP1, and CD5L showed an AUC=0.65 (95%CI=0.59-0.70).

CONCLUSIONS: Using an aptamer-based proteomics platform, we identified plasma proteins associated with risk of laparoscopically confirmed endometriosis and developed a multi-protein model discriminating endometriosis cases from controls.

IMPACT STATEMENT: Endometriosis patients suffer on average seven years of delay from symptom onset to diagnosis, and therefore discovery of non-invasive biomarkers that will identify women at greater risk of endometriosis has high potential to allow timely interventions and have significant positive impact on clinical outcomes of endometriosis.

SUPPORT: Financial support: This study was supported by the Department of Defense W81XWH1910318. NHSII cohort was supported by U01CA176726, U01HL145386, and R01CA67262.

FERTILITY & STERILITY® e7
EFFECT OF MICRONAS THAT ARE LINKED TO ENDOMETRIOSIS ON HEPATIC GENE EXPRESSION. Ramanaih Mamillapalli, PhD, Anjali Mangla, BS, Hugh S. Taylor, MD 1Yale University School of Medicine, New Haven, CT; 2Yale University, New Haven, CT.

OBJECTIVE: Endometriosis is a chronic inflammatory gynecological disorder regulated by estrogen and characterized by the growth of endometrial tissue outside the uterus. It causes pelvic pain, infertility and numerous systemic effects. Women with endometriosis have lower body mass index (BMI). Disruption of hepatic gene expression is associated with altered metabolism and weight loss in endometriosis. MicroRNAs that are differentially expressed in endometriosis contributing to the pathogenesis of the disease. Here, we investigate the effects of these miRNAs on liver gene expression to determine if microRNAs may be a mechanism leading to altered metabolism and weight loss.

MATERIALS AND METHODS: HepG2 cells were obtained from ATCC and cultured in EMEM with 10% FBS, and 1% p/s. Cells were transfected with microRNAs (50 nM) miR let-7b, miR 125b-5p, miR 150-5p, and miR 3613-5p or the respective inhibitors or controls using Lipofectamine® RNAiMAX according to the manufacturer’s protocol in a six-well plate (200,000 cells/well). Cells were harvested 48 hours post-transfection and total RNA and protein were extracted using TRIzol method. qRT-PCR and western blot were used to determine the gene expression (miRNA) and protein levels respectively. Predicted miRNA binding sites were found at website targetscan.org. The Mann-Whitney U Test was performed to determine statistical significance using Graphpad prism software.

RESULTS: Microarray study from serum of endometriosis subjects showed differential expression of microRNAs miR let-7b, miR 125b-5p, miR 150-5p, and miR 3613-5p (p <0.05). Bioinformatic analyses revealed that these microRNAs have binding sites in multiple genes that are involved in liver metabolism. qRT-PCR results showed that miR-Let-7b mimic significantly reduced the expression of Mrcl, while it significantly increased the expression of Igfbp1, while miR-3613-5p mimic significantly reduced the expression of Cyp2r1 and Mrc1. miR 125b-5p mimic significantly increased the expression of Fabp4 and significantly reduced the expression of Mrcl and its inhibitor significantly increased the expression of Rock2 and significantly decreased expression of Igfbp1. miR 150-3p mimic significantly increased the expression of Cyp2r1 and Mrc1, while miR 150-3p inhibitor significantly increased the expression of Igfbp1.

CONCLUSIONS: Liver genes, Cyp2r1, Fabp4, Mrc1, Rock2, and Igfbp1, are significantly affected by microRNAs that have been linked to endometriosis. These findings provide new insights into the role of miRNAs in endometriosis and their potential to contribute to the dysregulation of liver gene expression as well as the alteration of metabolism in endometriosis.

IMPACT STATEMENT: Altering these miRNAs in a mouse model of the disease and determining the effect on metabolism, weight and body fat could be an interesting future study to pursue. Continued research in this area has the potential to not only lead to a better understanding of endometriosis as a metabolic and multi-organ disease but also to the identification of novel endometriosis and obesity treatments, with miRNAs serving as potential drug targets.

O-17 11:45 AM Monday, October 24, 2022

SUMOYLATION MEDIATES PROGESTERONE RESISTANCE IN ENDOMETRIOSIS TREATMENT FAILURE AND IMPAIRED IMPLANTATION. Valerie A. Flores, MD, Hugh S. Taylor, MD, Zhihao Wang, BS 1Yale School of Medicine, 2Yale University, New Haven, CT.

OBJECTIVE: Endometriosis is a debilitating gynecologic disease affecting up to 1-in-10 reproductive-aged women. Progesterone resistance is the primary cause of endometriosis treatment failure as well as contributes to endometriosis related infertility, however the mechanisms mediating progesterone resistance are not completely understood. We have previously categorized human endometrial lesions as having high, medium, or low PR expression in women undergoing surgery for endometriosis. While those with low PR failed to respond to PR, those with moderate PR levels also failed to respond, suggesting that posttranslational modifications may mediate progesterone resistance. Small ubiquitin like modifier (SUMO) proteins are able to bind to (i.e. SUMOylate) and repress PR function, without altering PR expression levels. Here, we utilized human endometriosis samples to determine if PR is SUMOylated in endometriosis, contributing to progesterone resistance.

MATERIALS AND METHODS: Matched eutopic and ectopic endometrium were collected from women undergoing laparoscopic surgery for endometriosis (n=11) as well as controls (endometrium from women undergoing laparoscopy for other gynecologic conditions, n= 9). Western Blot was performed on extracted protein to assess PR-A/B and SUMOylated PR-A/B expression. Image J was utilized to quantify protein expression. Response to medical therapy, fertility status and stage of disease were determined from review of the electronic medical record. Student’s t-test was used for statistical analysis.

RESULTS: Women with endometriosis had lower expression of PR Total in eutopic and ectopic endometrium compared to controls (p<0.05). Specifically, there was lower expression of PR-B in eutopic and ectopic endometrium of women with endometriosis compared to controls (p<0.05). While PR-A was higher in controls and eutopic endometrium than endometriosis lesions, PR-A was highly SUMOylated in eutopic and ectopic endometrium of women with endometriosis (p<0.05). All women with endometriosis had previously failed progestin-based therapy.

CONCLUSIONS: We identified PR-A SUMOylation in eutopic and ectopic endometrium of women with endometriosis. SUMOylation of PR-A represses PR function, thereby inhibiting PR’s normal transcriptional activity. Unsumoylated PR-A is critical for PR function in endometrial decidualization. Decidualization is an important molecular mechanism for inducing regression of endometriosis lesions as well as necessary for implantation. SUMOylation of PR-A is a novel mechanism of progesterone resistance (endometriosis-failure) in endometriosis.

ORAL ABSTRACT SESSION: ENVIRONMENT AND REPRODUCTION

O-18 12:00 PM Monday, October 24, 2022

UNHEALTHY AIR QUALITY SECONDARY TO WILDFIRES IS ASSOCIATED WITH LOWER BLASTOCYST YIELD FROM IN VITRO FERTILIZATION. Molly S. Kornfield, MD, Elizabeth S. Rubin, MD, Pamela B. Parker, M.D., M.P.H, Rachel Madding, MD, Bharti Garg, MBBS, MPH, Thomas O’Leary, PhD, Maureen K. Baldwin, MD MPH, Paula Amato, MD, David Lee, MD, Diana Wu, MD, Sacha A. Krieg, M.D., Ph.D. Oregon Health & Science University, Portland, OR; 3Oregon Health and Science University, OR; 4University of Pittsburgh Medical Center, Pittsburgh, PA; 5Oregon Health and Science University, Portland, OR; 6Ohio State University, OR; 7Oregon Health & Science University.

OBJECTIVE: Air pollution exposure is associated with adverse reproductive outcomes; however, the impact of an acute episode of unhealthy air quality on in vitro fertilization (IVF) outcomes has not been studied. The historic September 2020 Oregon wildfires caused an unprecedented air quality crisis with an increase in average air quality index from 26 (Good) in the preceding 2 months to 336 (Hazardous) over a 10-day period. To evaluate the relationship between unhealthy air quality and IVF outcomes, we compared IVF cycle outcomes during a 10-day period of unhealthy air quality to IVF cycles from 2 months prior.

MATERIALS AND METHODS: This retrospective cohort study included IVF cycles at a single academic fertility center. Two studies were performed: one to evaluate a patient exposure (PE) group and another to evaluate an embryo exposure (EE) group. Each were compared to the same control group. The PE analysis included subjects with at least 4 days of stimulation during the air quality crisis. The EE analysis included subjects with at least 1 day of fertilization and/or embryo culture during the crisis. Primary outcomes were fertilization and blastulation rates. Secondary outcomes included numbers of oocytes retrieved, mature oocytes fertilized, and blastocysts obtained. Additional analysis was performed to compare IVF outcomes between PE only, EE only, and both. Fisher’s exact, Wilcoxon rank sum, two sample t tests, Kruskall Wallis, and ANOVA were used for statistical analyses.

RESULTS: Twenty-six IVF cycles were included: 11 PE only; 9 EE only; and both. The PE analysis included subjects with at least 4 days of stimulation during the air quality crisis. The EE analysis included subjects with at least 1 day of fertilization and/or embryo culture during the crisis. Primary outcomes were fertilization and blastulation rates. Secondary outcomes included numbers of oocytes retrieved, mature oocytes fertilized, and blastocysts obtained. Additional analysis was performed to compare IVF outcomes between PE only, EE only, and both. Fisher’s exact, Wilcoxon rank sum, two sample t tests, Kruskall Wallis, and ANOVA were used for statistical analyses.

O-19 10:45 AM Monday, October 24, 2022

UNHEALTHY AIR QUALITY SECONDARY TO WILDFIRES IS ASSOCIATED WITH LOWER BLASTOCYST YIELD FROM IN VITRO FERTILIZATION. Molly S. Kornfield, MD, Elizabeth S. Rubin, MD, Pamela B. Parker, M.D., M.P.H, Rachel Madding, MD, Bharti Garg, MBBS, MPH, Thomas O’Leary, PhD, Maureen K. Baldwin, MD MPH, Paula Amato, MD, David Lee, MD, Diana Wu, MD, Sacha A. Krieg, M.D., Ph.D. Oregon Health & Science University, Portland, OR; 3Oregon Health and Science University, OR; 4University of Pittsburgh Medical Center, Pittsburgh, PA; 5Oregon Health and Science University, Portland, OR; 6Ohio State University, OR; 7Oregon Health & Science University.

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there were no significant differences in IVF outcomes between exposed and controls. In our EE analysis, the exposed group had significantly fewer blastocysts develop compared to controls (median of 2 (IQR 1-5) vs 4 (IQR 2-7), respectively, p<0.049). The EE analysis also demonstrated a significantly higher proportion of cycles with no blastocysts (3/15 cycles (20%) for exposed vs 1/43 (2%) for controls, p<0.049). No differences were found among other secondary outcomes. When comparing IVF cycles among PE only, EE only, and combined exposure groups, there was a significant decrease in absolute blastocyst yield, with the fewest blastocysts from the combined group (p=0.048) and more no-blastocyst cycles in the EE only group (p=0.040).

CONCLUSIONS: Wildfire smoke exposure is associated with lower blastocyst yield when embryo development occurred during unhealthy air quality, despite multiple measures to minimize smoke exposure in the laboratory. This effect was observed when unhealthy air quality was measured during blastocyst development, but not during ovarian stimulation.

IMPACT STATEMENT: Unhealthy air quality during embryo development may impact IVF outcomes. Given the effect of climate change on wildfire frequency and severity, reproductive centers in wildfire-affected areas should work to optimize IVF outcomes against these severe insults to air quality.

0-20 11:00 AM Monday, October 24, 2022

ENVIRONMENTAL EXPOSURE TO INDUSTRIAL POLLUTANTS IS ASSOCIATED WITH DECREASED MALE FERTILITY. Joemy M. Ramsay, PhD, Kiarad Fenderski, MD, Joshua J. Horns, PhD, Kim Vanderslice, PhD,1 Benjamin R. Emery, M.PHIL,2 Kenneth L. Aston, PhD,3 James Hotaling, MD,4 University of Utah, Salt Lake City, UT; 3University of Utah School of Medicine, Salt Lake City, UT; 4University of Utah, Department of Family and Preventive Medicine, Division Of Public Health, UT; 4University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT.

OBJECTIVE: To understand how exposure to industrial air pollution is associated with male fertility by using a cohort of men in the Subfertility, Health and Assisted Reproduction (SHARE) cohort who underwent a semen analysis (SA) between 2005-2017 with ≥1 measured bulk semen parameter (N=16,277). SAs were classified as azoospermic (0 M/mL) or subfertile using World Health Organization cutoffs for concentration (<15 M/mL) and total sperm count (TSC, <39 Ml). We constructed residential histories for each man using residential locations from administrative records linked through the Utah Population Database. Using the Environmental Protection Agency Risk-Screening Environmental Indicators (RSEI) microdata we identified industrial facilities with air emissions of 17 chemical groups that are known endocrine-disruptors and/or are associated with male reproductive toxicity. We geospatially linked RSEI microdata with residential histories and defined exposure to these chemicals as living within 50km of ≥1 industrial facility emitting a chemical of interest in the 5 years prior to each SA. T-tests and chi-square tests were used to examine differences in bulk semen parameters and demographics by whether or not men were exposed to a chemical of interest in the 5 years prior to SA. Single exposure logistic regression models were run for chemical groups with >100 exposed men (n=12), controlling for age at SA and race/ethnicity for each dichotomous fertility outcome. Single exposure associations were considered significant at a Bonferroni-corrected q<0.0042.

RESULTS: 15,905 (97.7%) men lived within 50km of ≥1 industrial facility. Men who lived within 50km of an industrial facility had significantly lower TSC (p=0.04), total motility (p=0.005), and total motile count (TMC, p=0.03). Significantly higher odds of subfertile concentration were observed with exposure to dinitrotoluene (OR=1.7, 95% CI 1.19-2.43, p<0.005). Subfertile TSC was associated with aromatics (OR=1.36, 95% CI 1.05-1.77, p=0.02). Oestradiol was also increased with exposure to dichloroacetonitrile (OR=1.35, 95% CI 1.04-1.76, p=0.03). In our EE analysis, the exposed group had significantly increased odds of subfertile concentration (OR=1.70, 95% CI 1.19-2.43, p=0.004). No significant differences were found comparing single exposure groups, controlling for age at SA and race/ethnicity.

CONCLUSIONS: Wildfire smoke exposure is associated with lower blastocyst yield when embryo development occurred during unhealthy air quality, despite multiple measures to minimize smoke exposure in the laboratory. This effect was observed when unhealthy air quality was measured during blastocyst development, but not during ovarian stimulation.

IMPACT STATEMENT: Unhealthy air quality during embryo development may impact IVF outcomes. Given the effect of climate change on wildfire frequency and severity, reproductive centers in wildfire-affected areas should work to optimize IVF outcomes against these severe insults to air quality.

0-22 11:30 AM Monday, October 24, 2022

IMPACT OF COVID-19 VACCINATION ON ART OUTCOME IN THE CONTEXT OF MALE PATIENTS. Katherine L. Palmerola, MD,1 Maria Bustillo, M.D.,2 Marta Montenebro, BS, PhD2,3 Yaima Valdes, MD,4 Ineabelle Collazo, BS,5 Juergen Eisermann, M.D.,4 Himanshu Arora, B.S.C., M.S.C., PH.D.6 IVFMD, South Florida Institute for Reproductive Medicine, Miami, FL; 6American University of the Caribbean School of Medicine, Miami, FL; 6American University of the Caribbean School of Medicine, Miami, FL; 6American University of the Caribbean School of Medicine, Miami, FL; 6American University of the Caribbean School of Medicine, Miami, FL; 6American University of the Caribbean School of Medicine, Miami, FL.

OBJECTIVE: To determine if COVID-19 vaccination has a significant influence on parameters considered important for Assisted reproductive technology (ART) in men.

IMPACT STATEMENT: Our results highlight the largely unstudied impact of environmental exposure to industrial air pollution on male fertility. SUPPORT: None.
**MATERIALS AND METHODS**: Retrospective analysis of 70 male patients, investigating semen volume (mL), concentration (x10^6), percent sperm motility, Progression, total motile sperm count (TMC) (x10^6) respectively with respect to COVID-19 vaccination status. A total of 70 male patients/donors were included in the analysis. Patients were stratified into two groups based on the COVID-19 vaccination status that 56 patients received at least a single dose of vaccine and 34 did not receive any dose of vaccine. Data was structured within each group with respect to aspects like semen volume (mL), concentration (x10^6), percent sperm motility, Progression, total motile sperm count (TMC) (x10^6) respectively. Statistical analysis included two-tailed Student’s t-test for continuous variables, Chi-squared test for categorical variables, Pearson correlation for correlation matrix analysis, with p < 0.05 defining statistical significance. GraphPad Prism (GraphPad Software) was used for statistical analysis.

**RESULTS**: We compared semen volume (mL), concentration (x10^6), percent sperm motility, Progression, total motile sperm count (TMC) (x10^6) respectively between the vaccinated (n = 56) and non-vaccinated (n = 34) male patients/donors. Results showed that there was no significant difference between the two groups in context of each of the considered parameters (p > 0.05).

**CONCLUSIONS**: Our findings suggest that COVID-19 vaccination does not affect semen volume (mL), concentration (x10^6), percent sperm motility, progression, total motile sperm count (TMC) (x10^6) respectively. Further studies are required to find if additional parameters, such as sperm sorting methods, BMI, age, Testosterone, Leutinizing hormones (LH), Follicular stimulating hormones (FSH) which could be influenced by COVID-19 vaccination. Together these studies will help to overcome vaccine hesitance and establish a clear understanding about vaccines in the context of clinical variables that are considered relevant to ART for successful IVF outcomes.

**IMPACT STATEMENT**: Our findings will help in understanding of the impacts of COVID-19 vaccination on parameters which are considered important for assisted reproductive technology with respect to male partner.

**SUPPORT**: This work was supported in part by the IVFMD, South Florida Institute for Reproductive Medicine.

**OBJECTIVE**: Cell phones emit radiofrequency—electromagnetic radiation (RF-EMR) to transmit data for social media, web browsing, and music / podcast streaming. The advent of Bluetooth earbuds has presumably prolonged the amount of time the cell phone resides in the trouser pockets of men. This places the cell phone and its respective RF-EMR near the testicles for prolonged times. RF-EMR is considered an environmental pollutant and has been postulated to increase oxidative stress and induce free radical formation. Even though previous studies have demonstrated negative effects on sperm parameters, the impact of modern smartphone technology and wireless spectrums (4G, 5G, and WIFI) on sperm motility and viability has not been investigated. We hypothesized that RF-EMR from cell phones has deleterious effects on sperm motility and viability, though these effects can be mitigated with physical barriers or distance.

**MATERIALS AND METHODS**: We studied the impact of RF-EMR on sperm motility and viability from fertile, normozoospermic men, between the ages of 25-35 years old by exposing their ejaculated semen in an in vitro model for a 2-hour duration. Additionally, we placed semen samples within a 37 degrees Celsius incubator to assess for heat effects. We certified exposure to the specimen using a calibrated RF-EMR detection meter. Statistical analysis was performed using SPSS v.28. Continuous variables were presented as medians and interquartile ranges [25th - 75th], and comparison between groups was performed using the U Mann Whitney test.

**RESULTS**: We observed a decrease in sperm motility (50% vs. 38%, p = 0.024) and viability (60% vs 47%, p = 0.003) with WIFI. We did not identify a decrease in sperm motility and viability in semen samples that were exposed to 4G or 5G RF-EMR. As the smartphone with WIFI was noted to be warmer, we analyzed the semen samples within an incubator, and noted a decrease in progressive motility (40% vs 24%, p = 0.04). The addition of a case and increased distance with a smartphone on WIFI lessened the impact on sperm motility and viability (p = 0.01, n = 18).

**CONCLUSIONS**: This pilot, but adequately powered study, we observed that sperm motility and viability are negatively impacted with smartphones placed in close proximity to the WIF spectrum. It appears that heat that is emanated from the device contributes to this effect, as the device was noted to be warmer than when phones were used only with either 4G or 5G. With large variability in smartphones, continued research on exposure effects is needed and the current association should be considered cautiously as hypothesis generating.
IMPACT STATEMENT: Cell phones with data usage through WiFi have deleterious effects on sperm motility and viability, with both RF-EMR and heat contributing to impact.

ORAL ABSTRACT SESSION: INFERTILITY AND CANCER

O-25 10:45 AM Monday, October 24, 2022

TRENDS AND CHARACTERISTICS OF OVARIAN CONSERVATION AT HYSTERECTOMY FOR CERVICAL CARCINOMA IN-SITU

Caroline Violette, MD,1 Rachel S. Mandelbaum, MD,1 Donna Shouple, MD,1 Lynda D. Roman, MD,1 Koji Matsuo, MD, PhD1 University of Southern California, Los Angeles, CA; 2Keck School of Medicine.

OBJECTIVE: The association between early surgical menopause and increased mortality has been well demonstrated in benign gynecologic disease, but data specific to cervical carcinoma in-situ, a pre-malignant gynecologic condition, is unknown. This study examined the contemporary trends and characteristics of ovarian conservation at time of hysterectomy in cervical carcinoma in-situ.

MATERIALS AND METHODS: This is a retrospective observational cohort study examining the National Inpatient Sample. The study population was 6,605 women aged ≤65 with cervical carcinoma in-situ who had hysterectomy from 1/2016-12/2019. Exposure allocation was the adnexal procedure status (ovarian conservation versus oophorectomy). Main outcome measures were temporal trends of ovarian conservation over time and per patient age. Multivariable binary logistic regression model (conditional backward selection) was fitted to identify independent characteristics associated with ovarian conservation. A classification-tree was constructed by recursive partitioning analysis to examine utilization patterns of ovarian conservation.

RESULTS: A total of 2,775 (52.7%) women underwent ovarian conservation at hysterectomy. Ovarian conservation rates unchanged during the study period (P=0.219). Ovarian conservation rates remain stable until age 40 years, ranging from 88.0% to 78.6% (P=0.236), after which time the rate sharply and significantly decreases from 78.6% to 19.1% (P<0.001). In multivariable analysis, younger age, no comorbidity, higher household income, vaginal hysterectomy, and surgery at small bed capacity non-academic hospitals were independent factors associated with ovarian conservation (all, P<0.05). There were 17 utilization patterns of ovarian conservation that the rate changed from 17.2% to 94.4% (absolute rate difference, 77.2%, P<0.05).

CONCLUSIONS: Decrease in the utilization of ovarian conservation at hysterectomy for cervical carcinoma in-situ occurred at age 40 years, which is earlier than expected. There was substantial variability in the utilization of ovarian conservation based on patient, hospital, and surgical factors, suggesting there would be benefit in establishing clinical practice consensus and guidelines.

IMPACT STATEMENT: The decreased utilization of ovarian conservation in patients above the age of 40 is clinically relevant and suggests the need for updated treatment guidelines for patients undergoing surgical management of cervical carcinoma in-situ.

O-26 11:00 AM Monday, October 24, 2022

PLATINUM CHEMOTHERAPY CAUSES REPRODUCTIVE HARM IN FEMALE ADOLESCENT AND YOUNG ADULT CANCER (AYA) SURVIVORS.

Beth Zhou, JD, M.D.,1 Brian Kwan, PhD,2 Milli Desai, MHS, MAS,3 Vinital Nalawade, MS,1 Brian W. Whitcomb, PhD,3 Irene Su, MD, MSCE4 University of California San Diego, La Jolla, CA; 2University of California Los Angeles, Los Angeles, CA; 3University of Massachusetts, Amherst, Amherst, MA; 4San Diego, CA.

OBJECTIVE: The effect of platinum chemotherapy on fertility outcomes is not well characterized. We tested the hypothesis that platinum chemotherapy causes fewer live births and more infertility in AYA cancer survivors, utilizing novel causal inference methods to appropriately account for competing risks such as death which indirectly decrease outcomes by precluding fertility attempts.

MATERIALS AND METHODS: We leveraged de-identified administrative claims data from Optum Labs® to identify females with incident breast, ovarian, and colorectal cancer between ages 15-39 treated with platinum chemotherapy or no chemotherapy and matched females with no cancer. We used the parametric g-formula to estimate 5-year cumulative incidences and direct effects of platinum on live births and infertility adjusting for confounding and accounting for competing events (death, recurrence, and second cancers).

RESULTS: The cohort comprised of 1,292 platinum chemotherapy cancer survivors (44.7% breast, 28.3% colorectal, 27.0% ovarian), 3,196 no chemotherapy cancer survivors (73.6% breast, 8.7% colorectal, 17.7% ovarian), and 34,182 no cancer females contributing 94,271 person-years overall. Median age at diagnosis was 33.8 years old.

Adjusted 5-year incidences of live birth were 8.0% (95% CI 7.5, 8.5) in no cancer, 7.1% (95% CI 5.7, 8.6) in no chemotherapy, and 3.0% (95% CI 2.0, 4.2) in platinum chemotherapy. Accounting for competing events, live birth incidence in platinum chemotherapy rose to 4.4% (95% CI 3.0, 6.2), suggesting that the overall fewer live births is in part due to occurrence of competing events. Adjusted relative risks were lower compared to no chemotherapy (HR 0.48, 95% CI 0.43-0.92) and no chemotherapy (RR 0.54, 95% CI 0.42, 0.89).

Adjusted 5-year incidences of infertility were 24.4% (95% CI 23.8, 25.5) in no cancer, 27.2% (95% CI 24.5, 29.2) in no chemotherapy, and 22.6% (95% CI 20.7, 25.2) in platinum chemotherapy. Accounting for competing events, infertility incidence in platinum chemotherapy rose to 28.9% (95% CI 26.6, 31.6).

Adjusted relative risks were higher compared to no cancer (RR 1.25, 95% CI 1.21, 1.43) and no chemotherapy (RR 1.09, 95% CI 0.97, 1.20).

CONCLUSIONS: Platinum chemotherapy is significantly associated with lower live birth probability and higher infertility both indirectly, through impeding fertility attempts, as well as through direct effects.

IMPACT STATEMENT: We leveraged causal inference methods and administrative claims data to demonstrate direct effects of platinum chemotherapy to provide meaningful estimates for patient counseling.

O-27 11:15 AM Monday, October 24, 2022

TO BIOPSY OR NOT TO BIOPSY? PREVALENCE OF ENDOMETRIAL HYPERPLASIA AND CANCER IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME.

Ravi Agarwal, MD,1 Frank Z. Stanczyk, PhD,2 Jacqueline Ho, M.D.,3 Sharon A. Winer, M.D., M.P.H1 University of Southern California Keck School of Medicine, Los Angeles, CA; 2University of Southern California, Los Angeles, CA; 3Keck School of Medicine, University of Southern California, Los Angeles, CA.

OBJECTIVE: Polycystic ovarian syndrome (PCOS) affects as many as 12% of women of reproductive age, and is characterized by oligo-anovulation, hyperandrogenism, and unopposed estrogen [1]. And though these endocrine disorders put patients with PCOS at a three-fold higher risk to develop endometrial cancer than women without PCOS, no clear guidelines exist for endometrial biopsy in patients with PCOS, burdening physicians to decide based on arbitrary risk factors. The objective of this study was to describe the prevalence of endometrial hyperplasia (EH) and carcinoma in women diagnosed with PCOS, and to assess for clinical characteristics of patients with endometrial disease.

MATERIALS AND METHODS: This was a cross-sectional, retrospective study of patients aged 18-40, being evaluated for oligomenorrhea and/or PCOS between 2016 and 2021, in the Reproductive Endocrinology Clinic at Los Angeles County Hospital. All patients underwent a standardized evaluation including an endometrial biopsy, measurement of serum free and total testosterone levels, random follicle stimulating hormone (FSH) and estradiol levels, hemoglobin A1c (HgbA1c), and calculation of a Ferriman Galwey (FG) score. Endometrial biopsy results and patient characteristics were compared for women diagnosed with PCOS. Statistical analysis was performed with SAS 9.4 software and data analysis was performed via t-test and Chi-square test, as appropriate, and a p-value <0.05 was considered significant.

RESULTS: The Rotterdam criteria [2], a total of 242 patients were diagnosed with PCOS during the study period. Of these patients, only 11 did not undergo an endometrial biopsy, 161 patients (70%) had a normal endometrial biopsy, 18 patients (8%) were biopsied with EH without atypia, 37 (16%) were diagnosed with EH with atypia, and 14 (6%) were diagnosed with endometrial carcinoma. Compared to patients with a normal endometrial biopsy, patients with endometrial disease were older (mean age 31.4 vs 29.8, p=0.02), and had both lower total testosterone levels (34.7 ng/dL vs 62.3 ng/dL, p<0.01) and free testosterone levels (5.4 pg/mL vs 9.3 pg/mL, p<0.001). There were no differences in BMI, parity, FSH, Estradiol, FG score and FG score between patients with a normal endometrial biopsy and those with endometrial disease.

CONCLUSIONS: To our knowledge, this represents the largest cross-sectional study of PCOS patients to undergo a routine endometrial biopsy. Endometrial hyperplasia or carcinoma is prevalent in 30% of PCOS patients, and we demonstrate that younger age and higher androgen levels appear to be protective against endometrial disease.

FERTILITY & STERILITY®
OBJECTIVE: To evaluate markers of ovarian reserve in patients with CHSS to aid in patient counseling for ART and fertility preservation.

MATERIALS AND METHODS: This was a single-center retrospective cohort study of CHSS carriers, without a current cancer diagnosis, who presented for ART or fertility preservation (FP) from 2006-2021. Patients were divided into groups based on whether they completed FP before (PRE) or after (POST) chemotherapy. Patients were compared to the general population who undergoes elective oocyte cryopreservation do not have different markers of ovarian reserve compared to the general population who undergoes elective oocyte cryopreservation do not have different markers of ovarian reserve

RESULTS: Of 293 CHSS patients who presented for at least an initial consultation at our academic center, 79 patients were included and compared to 699 controls. Of the CHSS cohort, 65 were BRCA 1/2 carriers, 5 were Lynch carriers, and 9 others carried either APC, ATM, Cowden, CHEK2 and NF1 or NF2. Due to low sample size, patients who carried mutations other than BRCA or Lynch were grouped into their own subgroup for analysis, labeled as “Other”. Mean age (33.4 ± 4.8 vs 34.4 ± 3.3 years, p<0.001) and BMI (24.7 ± 6.5 vs 23.4 ± 4.2 kg/m², p<0.001) varied significantly between CHSS and control groups. Mean AMH was not different between CHSS patients and age and BMI-matched controls (3.5 ± 2.7 vs 3.4 ± 2.8 ng/mL, p=0.07) or by CHSS type (Table 1). Mean AFC was also not different between CHSS carriers and age and BMI-matched controls (16.60 ± 8.74 vs 17.83 ± 8.39, p=0.07).

CONCLUSIONS: Patients who are CHSS carriers without cancer at time of cryopreservation do not have different markers of ovarian reserve compared to the general population who undergoes elective oocyte cryopreservation.

IMPACT STATEMENT: CHSS carriers can be counseled that their markers of ovarian reserve are similar to the general elective fertility preservation (FP) population and can expect similar outcomes with ART/FP.

<table>
<thead>
<tr>
<th>BRCA</th>
<th>65</th>
<th>33.4 (4.5)</th>
<th>3.5 (2.8)</th>
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<td>0.30</td>
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Table 1: Comparison of AMH and AFC means in CHSS Carriers Compared with Controls
RESULTS: 450 cancer patients presented for initial consultation, of which 205 completed at least 1 FP cycle during the study period. 5 oocyte cryopreservation (OC) (all PRE) and 30 EB/IVF cycles (22 PRE vs 8 POST) were included in the analysis. Cancer diagnoses included breast (n=32), ovarian (n=1) and bladder cancer (n=2). During the study period, 15 patients in the PRE group completed a cumulative 27 thaw cycles (7.3% rate) and 5 patients in the POST group completed a cumulative 8 thaw cycles (2.4% rate). All 5 OC patients underwent oocyte thaw with a mean survival rate of 0.8 (SD 0.14). Blastocyst formation rate was 0.51 (SD 0.002) and PGT utilization rate was 0.8.

Time between freeze and thaw varied significantly between PRE and POST groups (mean 3.7 PRE vs 0.75 years POST; p < 0.01). Use of PGT was 18.5% in the PRE group and 100% in the POST group. No significant difference was found in median embryo grade between groups (1 PRE vs 1 POST; p=0.683). Median number of embryos transferred did not vary between groups (1 PRE vs 1 POST; p=0.60).

There was no significant difference in SAB, biochemical pregnancy or live birth rate between groups (X^2 = 5.54, p=0.136). Gestational age (36.58 ± 1.22 PRE vs 37.48 ± 0.84 weeks POST, p = 0.15) and birth weight (3083 ± 563 PRE vs 3548 ± 145 g POST, p = 0.07) did not vary significantly between groups.

CONCLUSIONS: FET utilization and pregnancy outcomes from embryos created PRE vs POST chemotherapy were not different. Thus, cancer patients who present for ART/FP following chemotherapy do not have compromised fertility when compared to the general population before chemotherapy were not different. Thus, cancer patients who present for ART/FP following chemotherapy do not have compromised fertility when compared to the general population.

OBJECTIVE: To investigate the differential impact of GnRH-agonist (GnRHa), hCG, or dual trigger, on the embryological outcomes in the general infertility population.

MATERIALS AND METHODS: Retrospective cohort study of all patients undergoing IVF with autologous oocytes in a GnRHa antagonist cycle, from July 2015 to December 2020, at a single private fertility center. GnRHa and dual trigger groups were matched to comparable hCG controls, using propensity score matching. Multivariable logistic regression analysis was used to compare the dual trigger group to GnRHa group. The confounding variables controlled for included: age, previous pregnancy history, infertility diagnosis, AMH, BMI, ethnicity, length of stimulation, and total gonadotropin dose. Mode of fertilization (conventional insemination versus ICSI) was accounted for in the fertilization rate assessment. Primary outcomes included number of oocytes retrieved, number of mature oocytes, oocyte recovery rates per follicle aspirated, mature oocytes/total oocytes ratio, fertilization, number of embryos, number of usable blastocysts, and blastocyst development rate. P-values and 95% confidence intervals were computed for the adjusted mean differences.

RESULTS: A total of 828 patients were included, 77 (9%) in the GnRHa group, 166 (20%) in the dual group, and 585 (71%) in the hCG group. Dual trigger, compared to hCG trigger, resulted in higher number of retrieved oocytes (20.92 vs. 17.17, 95% CI for estimated difference: 1.89-6.11), higher number of mature oocytes (13.78 vs. 11.33, 95% CI for estimated difference: 1.26-3.93), higher number of 2PNs (9.75 vs. 7.63, 95% CI for estimated difference: 1.15-3.27), and higher number of usable blastocysts (4.63 vs. 3.69, 95% CI for estimated difference: 0.3-1.76). GnRHa agonist trigger, versus hCG trigger, resulted in higher number of retrieved oocytes (32.65 vs.
pregnancy or clinical pregnancy loss rate in IUI cycles with natural cycles or cycles.

is a useful tool to assess ovarian reserve, this study suggests that it should among patients with varying levels of AMH in IUI cycles. While AMH no difference in ongoing pregnancy rates or clinical pregnancy loss rates when comparing AMH

was no difference in clinical pregnancy loss rate in adjusted analysis when excluding DOR patients due to completely confounding the dual trigger group.

CONCLUSIONS: Compared to the standard hCG trigger, dual trigger improves embryological outcomes among low responders, normal responders, and high responders.

IMPACT STATEMENT: Dual trigger, in the absence of any contraindication for its use, and with the dose of hCG component adjusted on a sliding scale for the risk of OHSS, should be considered the standard of care in IVF.

O-33 11:15 AM Monday, October 24, 2022

THE PREDICTIVE VALUE OF ANTI MULLERIAN HORMONE IN INTRAUTERINE INSEMINATION CYCLES. Chelsea M. Canon, MD,1 Sarah Roger, MD,1 Joseph A. Lee, BA,2 Carlos Hernandez-Nieto, MD,2 Kimberley Thornton, MD,2 Beth McAvey, M.D., M.S.,3 Alan B. Copperman, MD,2 Lucky Sekhon, MD4 Icahn School of Medicine at Mount Sinai, New York, NY; 2Reproductive Medicine Associates of New York, New York, NY; 3Reproductive Medicine Associates Long Island IVF (RMALIVF), Garden City, NY.

OBJECTIVE: Many patients with ovulatory dysfunction or unexplained infertility proceed with intrauterine insemination (IUI) as first line fertility treatment. Ovarian reserve, especially as predicted by anti mullerian hormone (AMH), is often assessed at initial consultation, and the result used to help determine the treatment plan. While AMH has been well demonstrated to be a predictor of ovarian responsiveness to gonadotropins, it has not been validated as an independent marker of natural fertility or for outcomes in IUI cycles in the infertile population. Thus, our study investigated whether AMH levels are associated with ongoing pregnancy or clinical pregnancy loss in patients undergoing IUI cycles.

MATERIALS AND METHODS: This study included patients undergoing natural cycle or ovulation induction and superovulation with oral medication (clomiphene citrate or letrozole) with IUI using partner sperm from 2016 to 2022. Patients were included only if serum AMH was measured in a single endocrine lab, total motile sperm count was >10 million, and a hysterosalpingogram was performed and showed ≥1 patent fallopian tube. Patients were grouped based on AMH (Group 1: AMH <1; Group 2: AMH between 1-5; Group 3: AMH >5). Demographic and cycle characteristics were collected. The primary outcome was ongoing pregnancy rate. The secondary outcome was clinical pregnancy loss rate. Comparative statistics were performed with ANOVA, Kruskal-Wallis, and chi-square. Data was also analyzed using a multivariate regression analysis fitted with a general estimation equation (GEE) model. A sample size of 356 patients per group was calculated in order to have 80% power to detect a 10% difference in ongoing pregnancy rate (alpha=0.05).

RESULTS: A total of 8,643 cycles were identified. There was a significant difference in ongoing pregnancy rate (0.0004) between the groups in an unadjusted analysis. There was no difference in clinical pregnancy loss rate (p=0.77) between the groups in an unadjusted analysis. After adjusting for patient age, partner age, BMI, endometrial thickness, medication type and number of follicles ≥16 mm, there was no difference in ongoing pregnancy rates when comparing AMH <1 to AMH between 1-5 (aOR 0.89, 95% CI 0.65, 1.21) or AMH >5 (aOR 1.24, 95% CI 0.87, 1.77). Similarly, there was no difference in clinical pregnancy loss rate in adjusted analysis when comparing AMH <1 to AMH between 1-5 (aOR 0.35, 95% CI 0.10, 1.21) or AMH >5 (aOR 0.55, 95% CI 0.13, 2.29).

CONCLUSIONS: There is a common clinical misconception that AMH level can be used as a marker of fertility. Yet, we demonstrated that there is no difference in ongoing pregnancy rates or clinical pregnancy loss rates among patients with varying levels of AMH in IUI cycles. While AMH is a useful endocrine tool, this study suggests that it should not be over-interpreted as a predictive tool for reproductive potential in IUI cycles.

IMPACT STATEMENT: AMH is not associated with the odds of ongoing pregnancy or clinical pregnancy loss rate in IUI cycles with natural cycles or those augmented with oral agents.

SUPPORT: None

O-34 11:30 AM Monday, October 24, 2022

ENDOMETRIN PLUS INTRAMUSCULAR (IM) PROGESTERONE EVERY THIRD DAY HAS SIGNIFICANTLY LOWER PREGNANCY RATES COMPARED TO DAILY IM PROGESTERONE ALONE IN PATIENTS UNDERGOING PROGRAMMED FROZEN EMBRYO TRANSFER. Luke Y. Ying, MD,1 Bradley S. Hurst, MD,2 Michelle Matthews, MD,2 Rebecca Usadi, MD,3 Charles C. Coddington, MD,2 Ying Ying, Ph.D.,4 Ashley M. Eskew, MD, MSC1 1HCA Healthcare/USF Morsani College of Medicine GME; Brandon Regional Hospital, Brandon, FL; 2Atrium Health Carolinas Medical Center, Charlotte, NC; 3Atrium Health, Charlotte, NC; 4Atrium Health Reproductive Medicine, Charlotte, NC.

OBJECTIVE: To determine whether use of Endometrin plus IM progesterone on every third day (VIM) is associated with lower ongoing pregnancy rates compared to daily IM progesterone in programmed frozen embryo transfer (FET) cycles.

MATERIALS AND METHODS: FET cycle data from a single academic program between November 2018 and December 2021 were used for this retrospective case-control study. Inclusion criteria were women undergoing programmed FETs with either 50 mg daily IM progesterone only (control) or 200 mg Endometrin twice daily plus 50 mg IM progesterone on every third day, with transfer of a single day 5 or 6 frozen embryo. Exclusion criteria were transfer of ≥2 embryos, or use of a gestational carrier. Clinical outcomes included positive hCG, clinical pregnancy, miscarriage, and live birth/ongoing pregnancy rate. Appropriate parametric and nonparametric tests were used for statistical analysis.

RESULTS: A total of 903 FETs were analyzed for this study, including 504 FETs in the IM group, and 399 FETs in the VIM group. There were no significant differences in patient age, BMI, endometrial thickness, blastocyst quality, or infertility diagnosis between the groups. The VIM group had significantly lower positive hCG and clinical pregnancy rates compared to the IM group (72% vs 60.2% and 56.7% vs 40.6%, respectively, see Table 1). Ongoing pregnancy rate was 36.1% in the VIM group, compared to 50.6% in the IM group (p < 0.0001); these findings also remained significant when excluding FETs with donor egg (35.9% vs 50.7%, p < 0.0001).

Table 1. Pregnancy outcomes compared between IM and VIM protocols

<table>
<thead>
<tr>
<th>Parameters</th>
<th>IM (n = 504)</th>
<th>VIM (n = 399)</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive hCG (%)</td>
<td>72.0</td>
<td>60.2</td>
<td>0.0002</td>
</tr>
<tr>
<td>Clinical pregnancy (%)</td>
<td>56.7</td>
<td>40.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>Biochemical loss per positive hCG (%)</td>
<td>21.2</td>
<td>32.5</td>
<td>0.002</td>
</tr>
<tr>
<td>Clinical loss per clinical pregnancy (%)</td>
<td>11.9</td>
<td>11.1</td>
<td>0.81</td>
</tr>
<tr>
<td>Total pregnancy loss per positive hCG (%)</td>
<td>30.6</td>
<td>40.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Live birth/ongoing pregnancy rate (%)</td>
<td>50.0</td>
<td>36.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Live birth/ongoing pregnancy rate excluding FETs with donor eggs (%)</td>
<td>50.7</td>
<td>35.9</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CONCLUSIONS: This study demonstrates that the combination of Endometrin and IM progesterone every third day for luteal support in a programmed FET cycle yields significantly lower clinical and ongoing pregnancy rates compared to daily IM progesterone alone.

IMPACT STATEMENT: IM progesterone alone may be preferable to combined Endometrin and IM progesterone in patients undergoing programmed frozen embryo transfer.

O-35 11:45 AM Monday, October 24, 2022

SHORTER TELOMERE LENGTH IS ASSOCIATED WITH LOWER ANTRAL FOLLICLE COUNT AND POORER IN VITRO FERTILIZATION OUTCOMES IN WOMEN OF ADVANCED REPRODUCTIVE AGE. Xiaojie P. Zhou, MD,1 Dana Smith, PhD,2 Jue Lin, PhD,2 Marcelle I. Cedars, MD1 University of California, San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; 1University of California San Francisco, San Francisco, CA.

E4 ASRM Abstracts
OBJECTIVE: To determine if telomere length in peripheral blood mononuclear cells (PBMCs) is associated with ovarian reserve measures and in vitro fertilization (IVF) outcomes in women of advanced reproductive age.

MATERIALS AND METHODS: In this prospective cohort study performed at a single academic center, women between the ages of 35 and 42 with unexplained infertility or diminished ovarian reserve were enrolled between November 2020 and June 2021. Average telomere lengths in PBMCs were measured during ovarian stimulation using quantitative polymerase chain reaction. Linear regression models were used to assess the relationship between telomere length and antral follicle count (AFC), anti-müllerian hormone (AMH) level, peak estradiol (E2) level, oocyte yield, number of fertilized oocytes (2PNs), number of good quality day 3 embryos and number of useable blastocysts. The models were adjusted for age.

RESULTS: A total of 40 women were enrolled with a mean age of 38.7 years (SD 2.0). Shorter telomere length was associated with a significantly lower baseline AFC (p = 0.04), as well as lower peak E2 (p = 0.04), lower oocyte yield (p = 0.02) and fewer 2PNs (p = 0.02), after adjustment for age. Telomere length was not associated with baseline AMH level (p = 0.46), number of good quality day 3 embryos (p = 0.11) or number of useable blastocysts (p = 0.10).

CONCLUSIONS: There is a well-studied association between shortened telomeres and biological aging. This study suggests that this association may extend to ovarian aging given the correlations observed between telomere length, ovarian reserve measures and quantitative IVF outcomes, independent of age, in infertile women who are of advanced reproductive age.

IMPACT STATEMENT: Although these results should be interpreted with caution given the limited sample size, this study invites the possibility that telomere length in PBMCs may be used prospectively to identify a premature reduction in ovarian quantitative aging.

O-36 12:00 PM Monday, October 24, 2022

LOW POST-WASH TOTAL PROGRESSIVELY MOTILE SPERM COUNTS YIELD COMPARABLE INTRAUTERINE INSEMINATION PREGNANCY RATES. Peter N. Dietrich, MD1, Claire Stevens-Haas, MS1, Jayme S. Bosler, MD1, Robert Rydze, MD1, Shunping Wang, PhD1, Stephanie Gunderson, M.D.,1 Jay L. Sandlow, MD1, Kate D. Schoyer, MD1, Medical College of Wisconsin, Milwaukee, WI;2Medical College of Wisconsin, Menomonee Falls, WI;3Froedtert Hospital, Menomonee Falls, WI.

OBJECTIVE: Existing literature cites post-wash total motile sperm counts (pwTMC) as a useful parameter for evaluating IUI pregnancy rates. Specific pwTMC threshold recommendations range from 5-10 million, with most sources reporting significantly lower pregnancy rates (per cycle) below this range. However, there have been no reported outcomes for utilizing post-wash total progressively motile (TPMC) pregnancy rates. The objective of our study was to determine if pregnancy outcomes in women between the ages of 20 and 40 were similar with a specific TPMC utilizing post-wash total progressively motile sperm counts.

MATERIALS AND METHODS: We conducted a retrospective review of couples who underwent IUI at our clinic with a pwTPMC < 5 million sperm between 2015-2022. Our main outcome was positive pregnancy test following IUI. Additional parameters evaluated include age, pwTMC and pwTPMCs, as well as the percentage of male partners who had > 5 million pwTMC. Patients were included regardless of infertility diagnosis.

RESULTS: A total of 348 patient charts were reviewed, with 120 patients who elected not to proceed with insemination due to less than 5 million pwTPMC, resulting in 228 patients included in the analysis. The mean female partner age was 33 years. Overall, there was an 11.4% pregnancy rate per cycle. The pregnancy rate was similar for a pwTPMC from 2-5 million, but decreased significantly when pwTPMC was below 1 million, with higher pregnancy rates at these cutoffs with female age < 35 (table 1). A female age of > 39 was a poor predictor of success, with no pregnancies if pwTPMC was 4 million or less. Interestingly, up to 55% of patients with a pwTPMC < 5 million still achieved pregnancy due to adequate pwTPMC.

CONCLUSIONS: Patients who underwent IUI with a pwTPMC of 1-5 million were found to have pregnancy rates comparable to those who underwent IUI with > 5 million pwTPMC, with higher rates in female patients. Post-wash TMC, which is often used for IUI eligibility, was below 5 million in a majority of patients, suggesting post-wash TPMC offers better pregnancy predictability.

IMPACT STATEMENT: Our findings suggest that pwTPMC is a better predictor of IUI success than pwTMC. This data allows for more accurate counseling of couples, and may alter treatment recommendations especially in younger patients with male factor.

SUPPORT: No financial support.
LAWSUITS OVER DISPUTED FROZEN EMBRYO OWNERSHIP AFTER DIVORCE OR SEPARATION: CLAIMS BASIS AND RESOLUTIONS. Gerard Letterie, MD,1 Dov Fox, JD, DPhil, LLM2 Seattle Reproductive Medicine, Seattle, WA; 3Professor of Law and Director of the Center for Health Law Policy and Bioethics at the University of San Diego, San Diego, CA.

OBJECTIVE: Contested disposition and ownership of embryos are a frequent basis of claims during domestic separation and divorce proceedings with possible clinical liabilities. The objective of this study is to review claims basis, decisions, and clinic liability in lawsuits over disputed embryos after divorce or separation and to gain insight into causes and areas for improvement.

MATERIALS AND METHODS: The study is a retrospective analysis of case law involving disputed embryo status since 1980 to identify allegations, claims and contributing factors to final settlement. Case status was identified in Westlaw directory using the terms assisted reproductive technology; IVF; frozen embryos; ownership; clinic and patient contracts; rights to implant or discard embryos; unused or abandoned embryos; divorce; separation. Cross referencing terms within this set of cases included embryo OR pre-embryo OR pre-embryo AND implantation OR disposition OR IVF OR "in vitro fertilization" OR fertility OR fertility OR divorce OR separation. Closed cases were evaluated for the following: disposition after filing (destroy or permit transfer); details of clinic contract regarding embryo disposition and clinic liability. Additional data extracted included state and location in federal or state courts.

RESULTS: The search returned 449 and 572 results from federal and state courts respectively from 2 from Puerto Rico. These cases were then manually searched and reviewed. Allegations and claims were based on the plaintiff’s complaint. There were 62 final cases that met entry and compose the final study group. 43% of cases had either no contract or no stipulation regarding ownership in event of divorce. In these cases, the court directed destruction of the embryos in 40% and maintain in storage in 52% of cases. No decision was possible in 8% of cases as the female partner was pregnant with disputed embryo at the time of filing. When an agreement was present and disputed, the courts reversed the expressed intent of the contract in half the cases. These decisions were made apart from any contractual arrangements prior to securing embryos in storage. Claims to ownership were equally divided between male and female members of the couple. In no case was a clinic held liable.

CONCLUSIONS: This review suggests that disputes regarding ownership and disposition of frozen embryos were brought regardless of informed consent agreements prior to the IVF process. One third of clinics had no agreement for any aspect of the cycle in place prior to cycle start. These data suggest that claims will continue regardless of informed consent documentation and that due diligence of the IVF centers is completely absent in 30% of cases identifying areas where improvement in counseling is clearly needed.

IMPACT STATEMENT: These data suggest that significant shortcomings exist in contractual arrangements for the disposition of frozen embryos in the setting of divorce or separation at times marked by a complete absence of any signed documents. Improvements in documentation and the contractual options offered by clinics are essential next steps to avoid or minimize these events.

SUPPORT: None
REFERENCES: None

EXPLORE THE REPRODUCTIVE BLACK MARKET: FERTILITY MEDICATIONS ON THE DARK WEB. Zhengyi Li, MSc, Kyle Nguyen Le, MD, Xiaojing Liao, PhD,1 Brent C. Monseur, MD, ScM2 Indiana University Bloomington, Bloomington, IN; 2Cooper University Hospital, Camden, NJ; 3Stanford Hospitals and Clinics, Sunnyvale, CA.

OBJECTIVE: This study aims to characterize the illegal trading of fertility medications on the dark web (a segment of the Internet not accessible by routine web browsers). Using specialized software, we reviewed anonymous marketplaces that sell illegal services/goods, e.g., forgery documents, drugs, prescription medications, etc. for the presence of fertility medications.

MATERIALS AND METHODS: Fertility medications were identified via a search using Micromedex with the terms “female reproductive agents” (n=77) and “male reproductive agents.” (n=20). Veterinary reproductive medications were also included. Synonyms of terms (e.g., common, chemi- cal, and trade names) were identified and included using PubChem. The “IVFCandy” hashtag was searched on multiple social media platforms to identify jargon. With a total of 1,264 terms, we conducted a word-matching search implementing a crawler through Python (a technique to index large volumes of dark web content) of illicit drug data from anonymous online market- places (n=10) and forums (n=6). From 2011-2015, we extracted data on vendor name, product, price, advertised origins, and acceptable shipping destinations.

RESULTS: Fertility medications were present in five anonymous marketplaces (i.e., Alphabay, Pandora, Agora, Evolution, and Hydra). There were 954 product listings (22.8% included multiple medications, n=227) from 154 unique fertility suppliers and 471 fertility-related forum threads. The most common fertility medications encountered were for erectile dysfunction: sildenafil (n=772, $9.60/g), tadalafil (n=246, $15.70/g) and vardenafil (n=73, $195.0g). The next most common class of medications was ovulation induction agents (e.g., clomiphene, $15.60/g [n=68]; letrozole, $269.90/g [n=37]), followed by IVF medications (i.e., human chorionic gonadotropin [n=29, $30.80/ial], somatropin [n=4], cabergoline [n=18], estradiol [n=6]) and miscarriage/abortion medications (i.e., misoprostol [n=7], mifepristone [n=2]). One listing was for gender affirming hormone therapy (i.e., estradiol and spironolactone). Most listings shipped to worldwide destinations originating from the United States (29.6%), Germany (18.3%), India (16.9%) and the United Kingdom (9.9%).

CONCLUSIONS: This is the first study to explore the presence of fertility medications in illicit marketplaces on the dark web. Due to stigma, drug shortages and high cost of treatments, patients will continue to resort to illegal means of obtaining fertility medications despite significant risks of using drugs without a prescription (e.g., counterfeit, contamination, and presence of untested substances).

IMPACT STATEMENT: Physicians should be aware of the increasing use of illicit online marketplaces to purchase prescription medications as a significant public health issue (e.g., drug misuse/abuse) as well the risks of serious health consequences including death due to substances and falsified medical products. Advocating for better coverage of fertility services may help curtail the use of illicit means to obtain fertility medications on the reproductive black market.

SUPPORT: None

A MIXED-METHODS EVALUATION OF EGG DONORS' PHYSICAL, PSYCHOSOCIAL, AND DISCLOSURE EXPERIENCES DURING POST-DONATION. Kirby Adlam, PhD, APRN-FPA, CNM,1 Mary Dawn Koenig, PhD, 2 Crystal L. Patil, PhD,3 Sana M. Salihi, MD,4 Alana Steffen, PhD,4 Wendy Kramer, B.A.,5 Patricia Hersberger, PhD, APRN, FNP-BC, FAAN3 1University of Illinois at Chicago; 2University of Illinois Chicago; 3845 S. Damen Ave, MC 802, Chicago, IL; 4University of Illinois at Chicago, Chicago, IL; 5Donor Sibling Registry, Nederland, CO.

OBJECTIVE: To explore physical, psychosocial and disclosure experiences among people who donated eggs.

MATERIALS AND METHODS: Using a cross sectional, mixed-methods design, an anonymous online survey using REDCap was developed and pre-tested among anonymous egg donors. The refined survey was emailed to participants of the Donor Sibling Registry and Facebook groups that targeted egg donors. Descriptive statistics, Chi Square, and Fischer’s Exact tests were used to analyze quantitative data; conventional content analysis was used for qualitative data analysis.

RESULTS: Among the 363 participants (Age: 22-71 years, M = 38.8 years), the majority identified as white race (92.8%), donated more than 1 time (75%; M = 3.3), and were anonymous donors (82.4%). The average time from egg donation to study participation was 13.75 years. Most donors (89.5%) reported a positive overall experience. Changes to menstrual cycle, ovulation, or fertility occurred in 21% of participants post-donation. Many (41.4%) reported procedural related pain (6.7/10 average), and 10.5% reported ovarian hyperstimulation syndrome. Anxiety (25.8%) and depression (23.2%) were the most common self-reported medical diagnoses. Validated measures (PROMIS Bank V1.0 Depression, PROMIS Bank V1.0 Anxiety)
were also used to assess mild or greater anxiety and depression with similar results (25.1% & 17.6%, respectively) (t-score > 55). Participants reported clinically significant rates of alcohol/drug use (11.5%) (≥ 2 CAGE-AID), and half of those also reported experiencing depressive symptoms (p < 0.01). Donor gamete recipients were more likely to report the most common qualitative response for reported emotional distress (17%) and regret (20%). Most participants (94.3%) were not contacted by clinics for medical updates post-donation, despite 25% feeling there were important medical changes to report. Most donors felt positive about and disclosed their donation to friends (95%), partners (91%), and parents (82%), but fewer (52%) shared with their own offspring. Participants’ qualitative data indicated the three most important concerns to adherents were: 1) improved communication with clinics (n = 39), 2) desire for less anonymity (n = 36), and 3) more information on long-term health outcomes related to egg donation (n = 31).

CONCLUSIONS: Most participants felt their egg donation experience was positive despite reported pain, menstrual cycle changes, and emotional distress. Depression and anxiety were the most common medical diagnoses, with depression rating higher than national prevalence. Elevated CAGE-AID was associated with depression, indicating the importance of screening egg donors for mental health and drug/alcohol use. Egg donors may benefit from pre- and post-donation counseling on disclosure with future offspring.

IMPAK STATEMENT: Post-treatment screening for anxiety, depression and drug/alcohol use could improve health outcomes among former egg donors. Decreasing barriers in communication, improving follow-up, and more data on long-term health outcomes would be beneficial to egg donors.

SUPPORT: Seth and Denise Rosen Graduate Research Award University of Illinois at Chicago.

O-41 11:45 AM Monday, October 24, 2022

FACTORS, MOTIVATIONS AND EXPERIENCES OF INFERTILITY PATIENTS WHO INITIALLY CONSIDERED EMBRYO DONATION (ED) WITH SUPERNUMERARY EMBRYS. Seth Jacob Barishansky, M.D., MSc.1 Jeanne E. O’Brien, MD, MSc.1 Kathleen Devine, MD, MSc.1 Angela K. Lawson, Ph.D.1.1 The George Washington University, Washington, DC; 5Shady Grove Fertility Center, Rockville, MD; 3Shady Grove Fertility, Washington D.C., DC; 3Northwestern University, Chicago, IL.

OBJECTIVE: To assess characteristics and reasons why patients initially consider ED with supernumerary embryos.

MATERIALS AND METHODS: A 123-item survey was emailed to 240 randomly selected patients at a single infertility practice who expressed interest in embryo donation from 2015-January 2020. Demographics, treatment history, and motivations for considering ED were queried. Statistical analysis was performed using chi-square analysis. A $25 gift card was offered for participation. This study was approved by WIRB Copernicus Group’s IRB.

RESULTS: Out of 54 (54%, 130/240) of eligible patients completed the survey. On average, initial donation inquiry occurred 5.5 years from the patient’s initial clinic visit. Mean age at donation inquiry was 38.7 years. Most patients learned about ED from their clinic (68.2%). The majority of patients were Caucasian (77.3%), married (83.3%), women (90.2%) with at least a Bachelor’s degree (85%). Almost a quarter (24.2%) utilized PGT-A and 62.5% of those did, indicated that the genetic results provided motivation to consider ED. Most (50.8%) utilized expanded carrier screening (ECS) and only 28.8% indicated that the results provided motivation to consider ED. 77.3% of those who considered ED were aware that children from ED may utilize direct-to-consumer DNA testing to identify genetic relatives in the future. The three most important reasons when considering ED were to help another couple (n = 39), 2) desire for less anonymity (n = 36), and 3) more information on long-term health outcomes related to egg donation (n = 31).

CONCLUSIONS: Most participants felt their egg donation experience was positive despite reported pain, menstrual cycle changes, and emotional distress. Depression and anxiety were the most common medical diagnoses, with depression rating higher than national prevalence. Elevated CAGE-AID was associated with depression, indicating the importance of screening egg donors for mental health and drug/alcohol use. Egg donors may benefit from pre- and post-donation counseling on disclosure with future offspring.

SUPPORT: Seth and Denise Rosen Graduate Research Award University of Illinois at Chicago.

DIFFERENCES IN GENETIC CARRIER SCREENING (CS) PANELS NECESSITATE INTENDED PARENT (IP), EDUCATION FOR GAMETE DONOR SELECTION. Andria G. Besser, MD, CCRC.1 Orah Yvonne Salamah, BSN, RN,2 Mary Elizabeth Fino, M.D.3 1NYU Langone Health Fertility Center, New York, NY; 2New York University Langone Fertility Center, New York, NY; 3NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: Given the lack of standardization of genetic CS panels between different laboratories and the continued evolution of these products, IPs and their selected gamete donors may not have been tested for the same autosomal recessive (AR) conditions. The purpose of this study was to determine how often IPs select gamete donors with CS results that are compatible with their own and, to determine the efficacy of an educational material created to assist with donor selection.

MATERIALS AND METHODS: We reviewed all cases in which an IP submitted a gamete donor profile for review of CS results between January 2020 and March 2022. Donor submissions were classified as “cleared” if the donor had negative results for all autosomal recessive (AR) genes that the IP was known to carry and the IP had negative results for all AR genes that the donor was known to carry, versus “not cleared” if either the donor or IP was not tested for a condition that the other carried or if both the donor and IP were known to carry the same AR condition. In April 2021, we created and began distributing an educational guide, which provided detailed instructions about verifying CS results between the donor and IP. Frequencies of “cleared” and “not cleared” donors were tallied, and chi-square tests were used to determine if implementation of the educational guide altered these frequencies.

RESULTS: 1046 donors were submitted by IPs for CS review during the study period, of which data were available for 794 donors. 665/794 (83.8%) involved only sperm donors, 82/794 (10.3%) involved only egg donors, and 47/794 (5.9%) involved both egg and sperm donors. In total, 656 donors (82.6%) were deemed “cleared” for CS results. Of the remaining 138 donors, 135 (17.0%) were “not cleared” due to a lack of testing for either the donor or IP; while 3 (0.4%) were because the donor and IP carried variants in the same gene and had an increased reproductive risk. The ratio of “cleared” to “not cleared” donors was not significantly different (X2=1.5; p=0.2) between sperm donors (117/665, 17.6%) and egg donors (108/82; 12.2%). Among “not cleared” cases involving a single gamete donor, the donor required additional testing in 83.1% of cases (103/124), while the IP required additional testing in 16.1% of cases (20/124), and both donor and IP required additional testing only once. Before distribution of the educational guide, 77.8% of donors (273/351) were “cleared”, while after distribution this proportion increased significantly to 86.5% (383/443; X2=10.3; p=0.001).

CONCLUSIONS: Prior to distribution of an educational material about donor selection, nearly a quarter of donors selected by IPs had CS results that were not compatible with their own. While this was reduced after distribution, this proportion was not reduced to a level of donor selection prior to treatment whenever possible.

IMPAK STATEMENT: This study demonstrated that additional IP education about CS results in improved genetic risk mitigation through informed donor selection.

FERTILITY & STERILITY®

e17
ORAL ABSTRACT SESSION: GENETIC COUNSELING

O-43 10:45 AM Monday, October 24, 2022

DISCOVERY OF GERMLINE Mosaicism, Non-Penetrant Disease, and More Following Diagnosis of Autosomal Dominant Disorders in Donor-Conceived Offspring. Jessica Park, MS, CGC, Jennifer Luque, MGC, CGC, Crystal Chan, MD, MSc, FRCSC, Cris Amo, MD, MSc, FRCSC, Celia D. Garcia, MD, MSc, FRCSC, Heather Shapiro, MD, FRCSC, Toronto, ON, Canada; University of Toronto, Toronto, ON, Canada; Markham Fertility Centre, Markham, ON, Canada; Dr. Roy’s Fertility Centre, New York, NY; Columbia University Fertility Center, New York, NY.

OBJECTIVE: Current counseling recommendations following a diagnosis of an apparently de novo autosomal dominant (AD) disorder in a child cite a recurrence risk of approximately 1% due to the possibility of germline mosaicism [REF; Clarke 8th Edition (Harper) p.32]. When an AD disorder is identified in a donor-conceived offspring, investigation for germline mosaicism in the donor can help clarify reproductive risks for other recipient families. Here we summarize experience from investigations of AD diagnoses in donor-conceived offspring to illustrate why such investigations are warranted.

MATERIALS AND METHODS: A retrospective review of reports of AD conditions in donor-conceived offspring from 2016 to 2022 was performed. Results of donor testing and management are summarized.

RESULTS: AD disorders were reported in 35 offspring. Genetic testing for the causative mutation was performed for the donor in 28 (80%) cases. Testing was not able to be performed for the remaining 7 cases because the diagnosis was not clinically confirmed in 2 cases, a causative mutation was not identified in 4 cases, and in 1 case, the donor was unavailable to participate in testing. Of the cases where testing was performed:

- 1 donor (11%) was identified to have the tested mutation and be at risk for disease symptoms themselves: Lynch syndrome, CHEK2-associated inherited cancer risk, and hypertrophic cardiomyopathy. In each case, the donor’s history was negative for any features of the disease.
- Inconclusive results were reported for 1 (3.7%) case, with suspicion for a complex rearrangement.
- Negative results were reported for 21 (75%) cases. 19 were tested on semen. 1 was tested via blood as the testing was not possible on semen. 1 case was tested via blood, buccal, and semen, and remains suspicious for parental mosaicism because two full siblings have the same mutation.

Donors with negative results may still be mosaic, but the mutation was not present in the sample tested, or not detectable due to limitations of detecting low-level mosaicism.

CONCLUSIONS: It is appropriate to investigate the risk for mosaicism or unrecognized AD disease in an apparently unaffected donor following diagnosis of an AD condition in an offspring. These investigations allow for informed decision-making and appropriate medical management for recipients and donor-conceived offspring, as well as for donors and their own families. It is recommended that donor programs establish protocols for managing and investigating these cases. The availability of validated molecular testing on DNA from semen samples is a significant limitation in the assessment of germline mosaicism.

IMPACT STATEMENT: Germline mosaicism and undiagnosed disease are potential causes of AD disorders in an individual’s offspring. Managing the possibility of germline mosaicism or undiagnosed AD disease risks requiring applicable donor program policies, appropriate recipient counseling, and availability of appropriate genetic testing.

SUPPORT: None

REFERENCES: Clarke 8th Edition (Harper) p.32

O-44 11:00 AM Monday, October 24, 2022

OBSERVATION: Current counseling recommendations following a diagnosis of an apparently de novo autosomal dominant (AD) disorder in a child cite a recurrence risk of approximately 1% due to the possibility of germline mosaicism [REF; Clarke 8th Edition (Harper) p.32]. When an AD disorder is identified in a donor-conceived offspring, investigation for germline mosaicism in the donor can help clarify reproductive risks for other recipient families. Here we summarize experience from investigations of AD diagnoses in donor-conceived offspring to illustrate why such investigations are warranted.

MATERIALS AND METHODS: A retrospective review of reports of AD conditions in donor-conceived offspring from 2016 to 2022 was performed. Results of donor testing and management are summarized.

RESULTS: AD disorders were reported in 35 offspring. Genetic testing for the causative mutation was performed for the donor in 28 (80%) cases. Testing was not able to be performed for the remaining 7 cases because the diagnosis was not clinically confirmed in 2 cases, a causative mutation was not identified in 4 cases, and in 1 case, the donor was unavailable to participate in testing. Of the cases where testing was performed:

- 1 donor (11%) was identified to have the tested mutation and be at risk for disease symptoms themselves: Lynch syndrome, CHEK2-associated inherited cancer risk, and hypertrophic cardiomyopathy. In each case, the donor’s history was negative for any features of the disease.
- Inconclusive results were reported for 1 (3.7%) case, with suspicion for a complex rearrangement.
- Negative results were reported for 21 (75%) cases. 19 were tested on semen. 1 was tested via blood as the testing was not possible on semen. 1 case was tested via blood, buccal, and semen, and remains suspicious for parental mosaicism because two full siblings have the same mutation.

Donors with negative results may still be mosaic, but the mutation was not present in the sample tested, or not detectable due to limitations of detecting low-level mosaicism.

CONCLUSIONS: It is appropriate to investigate the risk for mosaicism or unrecognized AD disease in an apparently unaffected donor following diagnosis of an AD condition in an offspring. These investigations allow for informed decision-making and appropriate medical management for recipients and donor-conceived offspring, as well as for donors and their own families. It is recommended that donor programs establish protocols for managing and investigating these cases. The availability of validated molecular testing on DNA from semen samples is a significant limitation in the assessment of germline mosaicism.

IMPACT STATEMENT: Germline mosaicism and undiagnosed disease are potential causes of AD disorders in an individual’s offspring. Managing the possibility of germline mosaicism or undiagnosed AD disease risks requiring applicable donor program policies, appropriate recipient counseling, and availability of appropriate genetic testing.

SUPPORT: None

REFERENCES: Clarke 8th Edition (Harper) p.32

O-45 11:15 AM Monday, October 24, 2022

CLINICAL IMPLICATIONS OF EXPANDED CARRIER SCREENING (ECS) FOR FERTILITY CARE AND INDIVIDUAL HEALTH. Laura C. Gemmell, MD, MSc, Jessica L. Giordano, MS, Jeri J. Forman, MD, Paula Brady, MD, New York, NY; Columbia University Medical Center, New York, NY; Columbia University Fertility Center, New York, NY.

OBJECTIVE: To evaluate incidence of expanded carrier screening (ECS) results with possible clinical implications on patient health and/or fertility treatment planning.

MATERIALS AND METHODS: Retrospective chart review of ECS (283 conditions) completed through a single academic fertility practice in New York City from 2018 to 2020 was performed. Results with possible ramifications for an individual patient’s health were recorded. This included individuals identified through ECS to have a genetic condition due to homozygous or compound heterozygous findings and those with heterozygous findings associated with an elevated risk for premature ovarian insufficiency, metabolic crisis, cardiovascular disease, or malignancy. Rates of positive ECS results and carrier-carrier couples were also reported, excluding carrier-carrier couples without a reproductive risk for a serious clinical outcome (specifically, alpha thalassemia single gene deletions).
RESULTS: ECS was performed in 3147 patients; 2332 (74%) carried at least one condition. Forty-three patients (1.4%) were homozygous or compound heterozygous for a recessive genetic condition. One percent were high-risk heterozygote carriers in recessive disease gene: ataxia-telangiectasia (n=7), familial hypercholesterolemia (n=13), fumarase deficiency (n=3), Nijmegen breakage syndrome (n=10). Fourteen female carriers of X-linked conditions were identified (0.6%), including 6 fragile X pre-mutation carriers. When restricting analysis to couples in which both completed ECS (n=891), 25 couples (2.8%) carried the same genetic condition.

CONCLUSIONS: The majority of patients undergoing ECS screening for a panel of 283 conditions will have a positive result. However, 44% of results may impact decisions regarding fertility care (elevated reproductive risk for recessive or an X-linked condition). A small group of patients (2.4%) received results with possible implications for their own health.

IMPACT STATEMENT: ECS is utilized for fertility treatment planning, but patients should also be counseled those results could have relevance to their own health. Homozygosity, compound heterozygosity, or high-risk heterozygous results require extensive counseling, referrals to geneticists and other specialists, and may impact eligibility for life and disability insurance. Using ECS during the preconception period can allow patients ample opportunity for earlier monitoring and timely intervention.

SUPPORT: None

REFERENCES: None

O-46 11:30 AM Monday, October 24, 2022
PGT-SR OBSERVED SEGREGATION PATTERNS ALLOW FOR TAILORED RISK ASSESSMENT. Lauren Walters-Sen, PhD, FACMG, Dana Neitzel, MS, CGC, Julia Wilkinson, MS, CGC, Sarah Poll, PhD, Nicole Faulkner, PhD, FACMG, Swaroop Aradhya, PhD, FACMG Invitae, San Francisco, CA.

OBJECTIVE: To report rates of gamete segregation patterns in carriers of balanced rearrangements as determined by PGT-SR.

MATERIALS AND METHODS: A retrospective analysis of trophectoderm biopsies from patients with a confirmed parental reciprocal or Robertsonian translocation (Rec-T or Rob-T, respectively) was performed to determine segregation patterns: Alternate, Adjacent (Rob-T), Adjacent-1 (Rec-T), Adjacent-2 (Rec-T), 3:0 (Rob-T), and 3:1 (Rec-T). All testing was performed using a modified FAST-SeqS NGS-based PGT method. Differences in segregation rates were analyzed using Welch’s unpaired t test.

RESULTS: PGT-SR was performed on 1755 embryos (52 patients/87 cycles with Rob-Ts, 172 patients/285 cycles with Rec-Ts). Overall, maternally-derived translocations led to higher derivative-abnormal rates, with a more pronounced parent-of-origin effect for Rob-Ts (37.8% maternal vs. 17.7% paternal) than Rec-Ts (60.5% maternal vs. 49.5% paternal). When gamete segregation patterns were analyzed, significant differences were observed in rates of Alternate and Adjacent segregation between maternally and paternally-derived Rob-Ts. Similarly, parent-of-origin differences were significantly different for Alternate, Adjacent-2, and 3:1 segregation patterns for Rec-Ts. Of note, when Rec-Ts involving acrocentric chromosomes were analyzed, the rates of unbalanced segregation were higher than Rec-Ts without acrocentrics, particularly of 3:1 segregation (18.6% vs. 10.1% maternal, 7.9% vs. 5.5% paternal).

CONCLUSIONS: We observed a clear parent-of-origin effect when comparing rates of balanced vs. unbalanced embryos from translocation carriers. Maternal rearrangements led to a higher rate of unbalanced embryos as compared to those paternally-derived. However, abnormal rates in trophectoderm biopsies are not as grim as those depicted by common references for gametes (approximately 70% derivative-abnormal for maternal Rec-Ts, 45% derivative-abnormal for maternal Rob-Ts), likely due to decreased viability of abnormal embryos even before the blastocyst stage. Finally, greater knowledge of the segregation patterns of translocations can improve counseling on the complicated reproductive potential of patients with these rearrangements.

IMPACT STATEMENT: These rates, derived from the largest published cohort to date, can be a valuable tool in counseling patients with balanced translocations regarding the potential success of their reproductive journey with IVF/PGT-SR.

SUPPORT: This study was funded by Invitae.

FERTILITY & STERILITY®
OBJECTIVE: Genetic recombination at the target gene can affect linkage-based diagnosis calls in preimplantation genetic testing for monogenic disorders (PGT-M). This study assesses potential increased risk for recombination in specific genes and/or chromosomes to provide guidance in genetic counseling for families with anticipated PGT-M technical challenges and results of testing.

MATERIALS AND METHODS: PGT-M cases with at least one biopsy sample impacted by genetic recombination were identified from cases tested between January 2020 and December 2021. CooperSurgical laboratories tested 4,138 cases for PGT-M during that time period. PGT-M analysis was based on the Illumina karyotyping platform, with direct mutation analysis via Sanger sequencing included when possible. Compiled data was analyzed for distribution across chromosomes, gene frequency, and inheritance pattern. Microdeletion and microduplication disorders were considered a single gene finding.

RESULTS: Of 4138 cases, 247 (6.0%) were identified to have at least one sample; there were 273 recombinant samples total. Three cases reported out for two conditions, each of which had recombination identified for at least one sample.

Recombination was identified in genes on all chromosomes except for 14 and Y. The top five recombinant chromosomes are X (13 genes), 2 (11 genes), 17 (10 genes), 1 and 16 (9 genes each). Recombination occurred in 110 genes and 5 microdeletions/microduplications, with 13 (11.3%) being X-linked, 52 (45.2%) autosomal recessive, and 50 (43.5%) autosomal dominant. The top 10 genes or groups of genes by case are: DMD (28), CFTR (22), BRCA1 (13), HBB (12), PKD1 (10), GJB2 (10), BRCA2 (8), SMN1 (6), and FMR1, DMPK and Htt (5 each).

Recombination was of maternal origin for 64 of the 113 (56.6%) recombinant autosomal recessive gene samples, and for 57 of the 101 (56.4%) recombinant autosomal dominant gene samples.

CONCLUSIONS: Recombination occurs throughout the genome, affecting dominant and recessive conditions almost equally; however, based on distinct gene count, the X chromosome is most impacted, with DMD being most frequently recombinant. Autosomal recessive CFTR is second, and third is autosomal dominant BRCA1. Recombination events may also reduce the number of transferrable embryos in some PGT-M cases, highlighting the importance of tracking these events.

IMPACT STATEMENT: With a recombination rate of 6% for PGT-M cases, anticipatory guidance regarding risk of recombination could be considered when performing PGT-M genetic counseling. This is especially important for X-linked genes, particularly DMD, which may benefit from additional counselling regarding potential technical challenges caused by recombination events and available solutions.

ORAL ABSTRACT SESSION: LGBTQ

O-49 10:45 AM Monday, October 24, 2022

CONCURRENT TESTOSTERONE (T) DURING OVARIAN STIMULATION NEGATIVELY AFFECTS EMBRYO DEVELOPMENT AFTER IN VITRO FERTILIZATION (IVF) IN A TRANSMASCULE MOUSE MODEL. Amanda R. Schwartz, MD,1 Min Xu, PhD,1 Nicholas Henderson, PhD, MA,1 Cynthia Dela Cruz, PhD,2 Daniel Plau, PhD,3 Vasantha Padmanabhan, MS, PhD,3 Ariella Shikanov, PhD,3 Molly B. Moravec, MD, MPH4 University of Michigan, Ann Arbor;1 University of Michigan, Ann Arbor, MI.

OBJECTIVE: Current data on the impact of T on ovarian function show variable results with potential for a detrimental effect on reproductive capacity and uncertain reversibility. The objective of this study was to determine the impact of active T treatment and T cessation on IVF outcomes in a mouse model of masculinizing hormone treatment. We hypothesized that current or prior T treatment would not have an impact on IVF outcomes.

MATERIALS AND METHODS: CS75BL/6N (n = 40) female mice were assigned to 4 treatment groups: 1) current T implant 2) current sham implant 3) T cessation 4) control. All mice were received silastic tubing implants with ethanol alone or 10 mg T enanthate in ethanol at 10 weeks. Daily cytology was performed prior to implantation and continued until all T treated mice ceased cycling and biweekly serum samples were collected throughout the study duration. At 12 weeks post implantation, group 1 and 2 mice were stimulated with 0.2 mL intraperitoneal CARD HyperOva followed by 7.5 IU human chorionic gonadotropin (hCG) 48 hours later. Oocytes were collected at 14 hours post hCG, fertilized in vitro with sperm from B6D2F1/J male mice and cultured to blastocyst stage. Group 3 and 4 mice were explanted after 12 weeks and stimulated two weeks post fertilization using the same protocol. The study was designed to have 90% power to detect a 28% difference in the number of blastocysts between the current T and sham groups. Data were analyzed using Chi square and unpaired t-tests with Prism 9.0. Results: Compared to current sham, current T mice had significantly higher terminal T (2.87 vs 0.26 mg/mL; p < 0.0001), lower terminal progesterone (32.19 vs 43.02 mg/mL; p = 0.009) and lower single ovari weight (8.26 vs 10.78 mg; p = 0.002) with no difference in terminal anti-mullerian hormone or estradiol. Mice with current T treatment had fewer total oocytes (15.00 vs 32.60; p < 0.0001), mature oocytes (14.40 vs 32.56; p < 0.0001), 2 cell embryos (12.50 vs 30.44; p < 0.0001), 4-8 cell embryos (12.40 vs 20.88; p < 0.0001), morulas (11.90 vs 30.13; p < 0.0001), blastocysts (10.00 vs 25.00; p < 0.0001), and hatching blastocysts (5.00 vs 11.00; p = 0.0003) compared to controls. Fertilization rate was reduced in mice with current T implant (86.81% vs 93.52%; p = 0.019) vs controls. When comparing the T cessation group to sham cessation, there was no difference in oocyte yield (25.60 vs 33.20; p = 0.084), 2 cell embryos (24.60 vs 29.29; p = 0.261), 4-8 cell embryos (24.40 vs 28.30; p = 0.356), morulas (23.70 vs 27.10; p = 0.401), blastocysts (22.10 vs 23.10; p = 0.799) or hatching blastocysts (12.50 vs 10.50; p = 0.560).

CONCLUSIONS: In a mouse model of gender-affirming T treatment, current T treatment negatively impacted oocyte yield, fertilization and embryo development; however, these negative effects were not seen following T cessation.

IMPACT STATEMENT: The effect of concomitant T treatment during ovarian stimulation in transmasculine people is currently unknown. If translatable to humans, further research is needed to determine the optimal T cessation period and to balance the benefit of T cessation on IVF outcomes with the potential for increased gender dysphoria.

O-50 11:00 AM Monday, October 24, 2022

OPINIONS OF TRANSGENDER, GENDER NON-CONFORMING, AND NON-BINARY PEOPLE ON VALUE OF FERTILITY PRESERVATION: A CROSS SECTIONAL SURVEY. Jawaria Amir, MD,1 Sara Twiehaus, DO,1 Monica Dhokia, BS,1 Maria Amir, BS,1 Sloane L. York, MD MPH,3 Jennifer Hirshfeld-Cytron, MD3 Rush University, Chicago, IL;1 Fertility Centers of IL, Deerfield, IL.

OBJECTIVE: To query gender-diverse (GD) individuals on their opinions regarding fertility preservation (FP), family planning, and perceived barriers to access care.

MATERIALS AND METHODS: An anonymous, questionnaire-based study was distributed between November, 2021 and February, 2022 to online listservs and Facebook groups for GD community. Data was collected through Research Electronic Data Capture. Eligibility criteria included self-identification along the GD spectrum (e.g. transgender, non-binary, gender non-conforming). Questions investigated demographic characteristics, fertility desires, use of gender-affirming treatments, FP counseling, and experiences with healthcare providers. To assess degree of knowledge regarding fertility topics, participants were asked to choose between three answer choices: “a little,” “some,” or “a lot.” Data analyses were performed using SPSS version 21.0. A p value <0.05 was considered to be statistically significant.

RESULTS: Of the 103 participants, median age was 24.4 years and most identified as white (86.4%). Sixty-seven percent (69), regardless of sex- assigned at birth or gender identity did not desire biological parenthood but up to one-third would consider adoption to parent. No significant difference was found by any demographic factor, inducing age (p=0.12) among those that did vs. did not desire biological parenthood. Self-reported knowledge about fertility preservation (i.e cryopreservation) and family building options (i.e gestational carriers/surrogacy and adoption) was low (10-16%), though more reported “a lot” of knowledge around the impact of gender-affirming (GA) treatments on fertility (37-45%). Sixty-three percent (n=65) reported feeling supported by their healthcare provider when discussing family planning goals. More transgender individuals (82.8% transgender males and 75.0% of transgender females) endorsed feeling supported by their healthcare provider when discussing family planning goals (p=0.009). GD individuals may not prioritize genetic reproduction in either their youth or adulthood. While counseling
regarding FP should be thorough to avoid decisional regret among GD people, assessing desire for FP and biological parenthood among the GD population is equally as important as studying barriers to access. While it reassuring that a majority of respondents endorsed knowing that GA treatments could impact future fertility, some subjects such as gestational carriers, cryopreservation and adoption are not as well-understood. Improved health-care professional’s engagement with GD communities is needed to improve patient education and support for a future.

IMPACT STATEMENT: There is an ongoing need to improve fertility counseling, discussion of strategies to achieve parenthood if desired, and availability of information for the GD population.


O-51 11:15 AM Monday, October 24, 2022
CURRENT ACCESS TO FERTILITY CARE FOR TRANS AND GENDER DIVERSE PATIENTS ACROSS UNITED STATES HOSPITALS, Samantha Lauren Estevez, M.D.,1 Isabelle Band, MD, 1 Alysa Hernandez, MD, Atoosa Ghofranian, MD,1 Keri Bergin, B.S., M.D.,2 Carlos Hernandez-Nieto, MD, 3 Joseph A. Lee, BA, 1 Danielle Soltész, MPH, MBA, 3 Alan B. Copperman, MD, 1 Icahn School of Medicine at Mount Sinai, New York, NY; 1Albany Medical Center, Albany, NY; 2Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: There are nearly two million trans and gender diverse (TGD) people in the United States (U.S.). Most research about TGD patients has been focused on the initiation and completion of gender-affirming care. Because some aspects of gender-affirming care might affect future fertility, it is important to assess whether fertility preservation is an established part of hospital services and comprehensive care models. While websites may not accurately represent all care offered by a facility, they serve as an initial gateway for TGD patients to access care. We surveyed publicly available websites of U.S. hospitals and evaluated access to fertility care for TGD patients.

MATERIALS AND METHODS: The study included U.S. adult and children’s hospitals sourced from the American Hospital Directory, the Children’s Hospital Association, and U.S. medical school websites. A minimum of five hospitals were included from each state and the District of Columbia. Specialty hospitals (e.g., orthopedics, psychiatric, or oncology) and military/veteran care centers were excluded. Two researchers independently surveyed each hospital website and collected the following data: location; medical school affiliation; adult or pediatric care; religious affiliation; presence or absence of a reproductive endocrinology and infertility (REI) division or affiliate providing fertility care; availability of TGD care and, if provided, through a designated program or solo clinicians; the field(s) of medicine in which TGD care was provided, including surgery, endocrinology, primary care, gynecology, urology, psychiatry, otolaryngology, infectious disease, dermatology, sleep therapy, physical therapy, social work, and legal aid; and presence or absence of TGD fertility care.

RESULTS: Of the 654 hospital websites surveyed, 335 (51.2%) offered some form of TGD care. The most common specialties included primary care (37.00%), endocrinology (36.85%), psychiatry (33.03%), and surgery (22.05%). Of the 335 U.S. hospitals that did provide TGD care, 22.99% (n=77) offered TGD-specific fertility care (including counseling, cryopreservation, and in vitro fertilization). Referrals to fertility care were offered at five (0.76%) hospitals. Medical school affiliations were found at 501 hospitals (76.61%), and 165 hospitals (25.23%) had religious affiliations.

CONCLUSIONS: Our findings highlight a significant gap in access to information for TGD-specific fertility care in the U.S. hospital websites that serve as the means by which TGD patients can assess if TGD care is readily available. Of the 654 U.S. hospitals surveyed, 48.78% (n=319) did not provide any form of TGD care for the patients within their communities. TGD fertility care was offered at only 11.77% (n=77) of hospitals surveyed. Having readily available information about, and access to, multidisciplinary care is of tantamount importance to TGD patients.

SUPPORT: None
REFERENCES: N/A

O-52 11:30 AM Monday, October 24, 2022
TRANSGENDER FEMALE PATIENTS WHO UNDERWENT ORCHIECTOMY ARE AT INCREASED RISK OF MAJOR ADVERSE CARDIAC EVENTS (MACE), Chase Carto, BS, Thomas A. Masterson, III MD University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: To assess the risk of MACE after gender-affirming orchiectomy in patients undergoing male to female transition.

MATERIALS AND METHODS: TriNetX, a large, multicenter electronic health record database, was utilized to establish the experimental cohort. Patients were included in the cohort if they had a personal history of sex reassignment (ICD-10-CM Z87.890), and at least one of the following diagnoses/procedures: acquired absence of other genital organ(s) (Z90.79), intersex surgery; male to female (CPT 55970), laparoscopy, surgical; orchietomy (54600), orchietomy, with or without testicular prostheses, scrotal, and or inguinal approach (54520). The primary outcome of the analysis was the development of MACE within 5 years of gender-affirming orchietomy, as defined by subsequent documentation of MACE, including myocardial infarction, venous embolism, cerebral infarction, pulmonary embolism, transient ischemic attack and related syndromes (ICD-10-CM I21, I22, I23, I26, I63, I82, Z66.718, G45). Two control cohorts were created, one comprised of cisgender male and the other cisgender female patients without documented history of sex reassignment or surgical orchietomy. Cohorts were balanced using propensity score matching prior to analysis for age and preexisting hypertensive disorders. Statistical analysis was run comparing development of MACE in the experimental cohorts versus each control. Patients who had MACE outcomes prior to receiving gender-affirming surgery were removed from analysis, in addition to any patient that received surgery more than 20 years ago due to incomplete data within the TriNetX network. Statistical significance was assessed at p < 0.05.

RESULTS: A total of 566 patients were identified in the transgender cohort. The mean age was 43 (26 – 60), and the cohort consisted of predominantly white patients (80%). The risk of developing MACE within 5 years of gender-affirming surgery in the transgender cohort was 6.35%. Analysis revealed a significant increase in risk of MACE in the transgender cohort when compared to both male (OR = 2.47, 95% CI: 1.31 – 4.31, p = 0.0032) and female (OR = 3.149, 95% CI: 1.58 – 5.75, p = 0.0004) controls.

CONCLUSIONS: In this cross-sectional study of a large, multicenter database, transgender female patients who underwent gender-affirming orchietomy appear to be at increased risk of developing MACE.

IMPACT STATEMENT: Receiving gender-affirming orchietomy in patients undergoing male-to-female gender transition may place these patients at heightened risk of future MACE. These patients may warrant close evaluation of preexisting risk factors and clinical follow-up in the years after surgery to prevent adverse cardiovascular outcomes.

O-53 11:45 AM Monday, October 24, 2022
ASSISTED REPRODUCTIVE TECHNOLOGY TREATMENT OUTCOMES IN TRANSGENDER MALES WITH HISTORY OF GENDER AFFIRMING HORMONE THERAPY. Atoosa Ghofranian, MD, Samaatars Lauren Estevez, M.D.,1 Caroline Gelfman, MD,1 Dmitry Gounko, B.S., M.A.,1 Joseph A. Lee, BA,2 Jovana Lekovic, MD,1 Kimberley Thornton, MD,1 Alan B. Copperman, MD, Icahn School of Medicine at Mount Sinai, New York, NY;2 Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: There has been increased access to assisted reproductive technology (ART) treatment for transgender and gender diverse (TGD) patients. Yet, limited research has assessed fertility in patients who undergo gender affirming hormone therapy (GAHT). We evaluated the effect of testosterone (T) therapy in transgender men and ART treatment outcome.

MATERIALS AND METHODS: The study included all transgender male patients who sought treatment at a single academic reproductive center between 2013-2021. For patients with a history of GAHT, T dose range, level at intake, time on/off treatment were collected. Primary outcome included ovarian reserve characteristics.

RESULTS: 77 transgender males were included. 82.1% of patients presented to care after 2016. 46 patients underwent fertility preservation counseling. Six patients proceeded to ART treatment (IVF, co-IVF, IUI, egg freezing, embryo freezing), 1 patient underwent IVF, 3 patients underwent co-IVF, 4 patients underwent IUI, 6 patients underwent egg freezing, and 2
patients underwent embryo freezing. The 1 patient that completed an IVF cycle achieved live birth. Of the 30 patients who completed co-IVF cycles, 1 achieved pregnancy. Of the 4 patients who completed IUI cycles, 1 achieved live birth and 1 achieved pregnancy.

CONCLUSIONS: Transgender males with a history of prior GAHT can successfully achieve fertility preservation, pregnancy and live births. The number of transgender males who utilized fertility services increased since our TGD care initiative in October 2016. With 12 major academic centers in New York City, a formal referral system would aid in a better understanding of the barriers that preclude access to fertility care for TGD patients.

IMPACT STATEMENT: Multi-center studies that include a larger number of TGD patients could assess the impact of concurrent or prior T therapy on stimulation outcome and reduce the gender dysphoria associated with discontinuation of GAHT.

SUPPORT: None

REFERENCES: N/A

OBJECTIVE: Although many transgender men seek fertility care, critical knowledge gaps on their use of assisted reproductive technology (ART) continue to limit effective counseling. We used fertility benefits claim data to identify a multicenter cohort of transgender men with inclusive fertility benefits who presented for fertility care and assessed their treatment progression and ART outcomes.

MATERIALS AND METHODS: We performed an IRB-approved, multi-center, retrospective case series of transgender men within a single provider of employee sponsored fertility benefits. Study subjects were identified by claims from December 2017 to April 2022. Clinical information and cycle outcomes were provided by individual clinics.

RESULTS: A total of 17 transgender patients utilized fertility benefits at one of 14 clinics. The majority, 15 (88.2%) pursued treatment. A total of 7 (41.2%) underwent oocyte cryopreservation (OC), 6 (35.3%) underwent in vitro fertilization (IVF), and 2 (11.8%) underwent intrauterine insemination. Of the remaining, 1 only had a consultation and 1 utilized oocyte storage. Of those that underwent IVF, 4 pursued freeze-all cycles, and 2 pursued transfer–1 frozen and 1 fresh. Clinical information and cycle outcomes were available for 5 OC/IVF patients, 4 of whom had prior testosterone (T) therapy (Table 1). One patient (Table 1, Case 5) underwent IVF with PGT-A and had a fertilization rate of 75% (n = 6/8), and 4 blastocysts, 2 of which were euploid.

CONCLUSIONS: In this case series of transmasculine patients with fertility benefits, a majority pursued treatment after initial consultation. This case series increases our knowledge on health access disparities for transgender individuals and suggests reassuring ART outcomes in transmasculine patients with fertility benefits.

IMPACT STATEMENT: Pervasive economic and health disparities exist for gender minority patients; however, inclusive fertility benefits may reduce barriers to access to care. Given the sparse data on ART for transgender men, case series remain important for counseling patients regarding expectation for outcomes. Fertility benefit claims may represent a path for identifying larger cohorts of sexual and gender minority subjects for multi-center studies.

SUPPORT: None

Table 1: Demographics, T use and Ovarian Stimulation Cycle Data

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<th>Patients (n)</th>
<th>All (16)</th>
<th>Prior T Use (11)</th>
<th>No T Use (5)</th>
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<td>Demographics</td>
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<td>Mean Age (Years)</td>
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<td>Mean BMI (kg/m2)</td>
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<td>24.3 ± 3.7</td>
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<td>History of Gender Affirming Top Surgery (%)</td>
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<td>Ovarian Stimulation Cycle Data</td>
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<td>T Level Range at Cycle Start (nmol/L)</td>
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<td>Mean AMH (ng/mL)</td>
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<td>Mean Basal AFC</td>
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<td>Mean Follicles at Cycle Start</td>
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<td>Mean Cycle Length (Days)</td>
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<td>Mean Total Gonadotropin (IU)</td>
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<td>Mean Peak E2 (pg/mL)</td>
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<td>Mean Oocytes Retrieved</td>
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O-54 12:00 PM Monday, October 24, 2022

MULTICENTER CASE SERIES OF TRANSGENDER MEN WITH FERTILITY BENEFITS: ACCESS TO CARE AND NAVIGATING OBSTACLES. Elizabeth S. Rubin, MD,1 Yishin Yang, BA,2 Melody Qiu, MSc,2 Joseph A. Lee, BA,3 Alan B. Copperman, MD,4 Angelia Liang, BS,5 Mark P. Leondires, M.D.,6 Brent C. Monseur, Ford Hospitals and Clinics, Sunnyvale, CA.

REFERENCE: N/A

SUPPORT: None

Table 1: Demographics, T use and Ovarian Stimulation Cycle Data

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<tr>
<th>Case</th>
<th>Age</th>
<th>Cycle Type</th>
<th>Time on T (mo)</th>
<th>Time off T (mo)</th>
<th>AMH (ng/mL)</th>
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<th>Starting GN dose (IU)</th>
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AMH anti-mullerian hormone; AFC antral follicle count; GN gonadotropin; E2 estradiol

*Not reported
IMPROVING ONCOLOGY FERTILITY PRESERVATION - AREAS OF IMPACT. Jason B. Huang, MD, Susana Elena Berrios, B.A.,1 Yael Simons, MD,2 David Dulce, BA, MS,1 Shabab Patel, BA,1 Bingtian Xiang, BA,1 Samuel Ohlander, M.D.1 1University of Illinois College of Medicine, Chicago, IL; 2University of Illinois Chicago, Chicago, IL.

OBJECTIVE: Fertility preservation (FP) services are often underutilized in oncologic care despite the availability of services and society recommendations. Eleven states, including Illinois, have enacted laws requiring insurance coverage of FP costs for iatrogenic infertility, including for cancer patients. We conducted a collaborative quality improvement (QI) initiative to establish a male FP program and to identify and address the provider-level barriers to implementation.

MATERIALS AND METHODS: We surveyed oncology providers before and after reproductive health awareness initiatives to understand perceived barriers to FP services. Survey results guided the design of QI initiatives. We identified males diagnosed and treated for cancer at our institution, an urban academic tertiary referral center, between January 2019 to December 2019 and then after a series of QI interventions from September 2020 through December 2021. State mandated FP coverage went into effect January 1, 2020. We retrospectively reviewed patient charts to determine rates of discussion and utilization of FP services.

RESULTS: Fourteen of 14 providers responded to surveys. The 2 most common barriers to discussion of FP were knowledge deficits among providers (25% of respondents) and difficulty with documentation (25%); other reasons were assumptions about the patient (22%), perceptions regarding FP (14%), and comfort discussing FP (14%). Our interventions thus included 2 lectures to oncologists and oncology fellows, with an emphasis on guidelines and awareness of our institution’s FP services, and provision of quick reference guides. During our intervention period, our institution transitioned to a new electronic medical record system (EMR) that included a FP referral suggestion for all new chemotherapy orders. Prior to QI interventions, a total of 205 patients with newly diagnosed and treated cancer were reviewed. 29 (14.1%) of these patients had documented FP counseling and 11 proceeded with cryopreservation. During our post-intervention period, we identified 233 patients meeting inclusion criteria over a 15-month period. Following a 4-month interventional period, 17.0% of patients had documented FP discussions in the first 3 months. This decreased to 4.0% in the next 3 months, 2.3% in the following 3 months, and 7.7% in the remaining 2 months.

CONCLUSIONS: Despite recognition of the importance of FP and increasing support and availability of FP services, significant barriers to access remain. Educating and collaborating with providers outside of fertility specialists leads to meaningful impacts in patient care, but these advances may be transient. Continued investment in these relationships is critical to durable increases in counseling rates and utilization of FP services.

IMPACT STATEMENT: Our findings highlight provider-level barriers to FP access, the effectiveness of cross-specialty collaborations to improve fertility care, and the importance of establishing and formalizing such FP initiatives for durable improvements in FP access for cancer patients.

SUPPORT: None

O-56 10:55 AM Monday, October 24, 2022

SPERM DNA METHYLATION PREDICTS HUMAN AGING IN FERTILE AND INFERTILE MEN. John Tucker Sigalos, M.D.,1 Junxi Feng, High School Diploma,2 Liudmilla Rubbi, PhD.,3 Jesse Mills, M.D.,4 Matteo Pellegrini, PhD.,5 Srim R. Eleswarapu, M.D., Ph.D.1 1David Geffen School of Medicine at UCLA, Los Angeles, CA; 2UCSF, Los Angeles, CA.

OBJECTIVE: Epigenetics refers to heritable changes in gene expression that do not involve changes in the underlying DNA sequence. One of the most studied mechanisms of epigenetic change is DNA methylation. It is postulated that adverse outcomes related to advanced paternal age and assisted reproductive technologies (ART) are due to epigenetic changes. Prior studies have described accurate age estimation based on human somatic cell DNA methylation. We sought to evaluate the DNA methylation patterns of somatic cells and sperm from fertile men and men with idiopathic infertility.

MATERIALS AND METHODS: Men at least 18 years old were recruited in an academic andrology clinic during presentation for vasectomy consultation (fertile men) or presentation for infertility evaluation (men with idiopathic infertility) from August 2021 through March 2022. Men underwent history and physical examination, semen analysis, and serum sex hormone testing. Swabs of buccal mucosa and freshly ejaculated semen were collected. DNA was extracted from these samples for targeted bisulfite sequencing DNA methylation analysis.

RESULTS: 48 patients (25 men with idiopathic infertility and 23 fertile men) were enrolled. Using a ridge linear regression model to predict age based on DNA methylation pattern versus actual chronicologic age, buccal swabs showed a correlation coefficient of 0.54 between epigenetic age and actual age with mean error of 3.45 years difference. Prediction of age based on sperm DNA methylation pattern revealed a correlation coefficient of 0.52 between epigenetic age and actual age with mean error of 3.35 years difference.

CONCLUSIONS: Sperm DNA methylation can be used to predict chronologic age in a similar fashion to that predicted by somatic cell epigenetic changes. Further research may focus on subsets of infertile men, such as men with varicocele or hypogonadism.

IMPACT STATEMENT: These data show that sperm are subject to many of the epigenetic changes seen in somatic cells. Further work will need to evaluate how these epigenetic changes reflective of aging affect ART and offspring outcomes.

SUPPORT: This work is supported in part by the H. & H. Lee Surgical Research Scholars Program via the L.B. Research and Education Foundation

O-57 6:57 AM Monday, October 24, 2022

BREAKING IT DOWN: ADHERENCE TO GUIDELINES FOR DNA FRAGMENTATION TESTING IN MALE INFERTILITY PATIENTS. Arienne N. Shami, BS,1 Marie Menke, MD, MPH, James M. Dupree, M.D., M.P.H,2 Samantha B. Schon, M.D., M.S.3 1University of Michigan, Ann Arbor, MI; 2Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI; 3Michigan Medicine, Ann Arbor, MI.

OBJECTIVE: To create a reference guide for six of the major U.S. religions for use by reproductive health specialists to provide patient-centered care for a culturally diverse patient population.

MATERIALS AND METHODS: We utilized primary source reviews of various religious texts and verified electronic databases to examine perspectives on use of, in vitro fertilization (IVF), intrauterine insemination (IUI), sterilization procedures such as vasectomy and tubal ligation, and surrogacy for six major U.S. religions: Catholicism, The Church of Jesus Christ of Latter-Day Saints (LDS), Hinduism, Judaism, Buddhism, and Islam. Each statement of religious belief was either taken directly from primary source documents or cross-referenced across several secondary sources to ensure accuracy. Perspectives were compiled into a reference document and table for clinical use.

RESULTS: Most religions have focused statements concerning assisted reproduction and vasectomy. While there are caveats for most religions, IVF and IUI are largely opposed only by the Catholic church, surrogacy is not permissible in the LDS Church, Catholic Church, and Islam, and vasectomy is not permissible for the Catholic Church, LDS Church, Judaism, and Islam. Similarly, tubal ligation is also not permitted for these religions with the exception of Judaism of which while vasectomy is considered a violation of the Torah, sterilization of a woman is not explicitly discussed in the old testament. Instead, a rabbinic decree states permanent female sterilization as against the views of the faith. The religions with the most lenient rules concerning reproduction and permanent contraception explored include Buddhism and Hinduism each of which have no reservations pertaining to IVF, IUI, surrogacy, or permanent sterilization.

CONCLUSIONS: Religion often plays a significant role in patients’ attitudes towards use of ART, permanent sterilization, and surrogacy. Familiarity with the religious beliefs and perspectives is important for the reproductive health specialist in order to provide appropriate counseling for their patients.

IMPACT STATEMENT: A summative reference guide can help provide patient-centered care for reproductive health and family planning.

O-05 10:45 AM Monday, October 24, 2022

THE UROLOGIST’S GUIDE TO RELIGION AND MALE FERTILITY TREATMENTS. Samuel Ross Donnenfeld, M.D.,1 Akanksha Mehta, M.D., M.S.2 Emory University, Atlanta, GA; 2Emory University School of Medicine, Atlanta, GA.

OBJECTIVE: To create a reference guide for six of the major U.S. religions for use by reproductive health specialists to provide patient-centered care for a culturally diverse patient population.

MATERIALS AND METHODS: We utilized primary source reviews of various religious texts and verified electronic databases to examine perspectives on use of, in vitro fertilization (IVF), intrauterine insemination (IUI), sterilization procedures such as vasectomy and tubal ligation, and surrogacy for six major U.S. religions: Catholicism, The Church of Jesus Christ of Latter-Day Saints (LDS), Hinduism, Judaism, Buddhism, and Islam. Each statement of religious belief was either taken directly from primary source documents or cross-referenced across several secondary sources to ensure accuracy. Perspectives were compiled into a reference document and table for clinical use.

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CONCLUSIONS: Religion often plays a significant role in patients’ attitudes towards use of ART, permanent sterilization, and surrogacy. Familiarity with the religious beliefs and perspectives is important for the reproductive health specialist in order to provide appropriate counseling for their patients.

IMPACT STATEMENT: A summative reference guide can help provide patient-centered care for reproductive health and family planning.
OBJECTIVE: The use of DNA fragmentation assays for infertility patients remains controversial. Guidelines published by ASRM/AUA in October 2020 recommend offering testing in the setting of recurrent pregnancy loss. They also note that some causes of DNA fragmentation are easily rectifiable, and testicular biopsy may be best in select cases. The objective of this study is to better understand current national practice patterns for use of DNA fragmentation testing, treatment options, and patient costs.

MATERIALS AND METHODS: Electronic surveys were distributed to members of the Society for Reproductive Endocrinology and Infertility (SREI) between March and April 2022. Survey data collected general provider characteristics, DNA fragmentation utilization patterns including reasons for against testing, test type, cost, treatment plans, patient use, and changes to practice due to ASRM/AUA guidelines.

RESULTS: A total of 82 SREI members responded (9.9% response rate). All participants were Reproductive Endocrinologists, with a mean of 19.51 years in practice. Over half of participants offered sperm DNA fragmentation testing (59.8%). The most common reason to not offer testing was an expectation that the results would not change treatment (69.7%). Of those using DNA fragmentation testing, just over half utilize ASRM/AUA societal guidelines on when to offer testing. Many respondents did not make changes to their practice based on these guidelines (44.4%), though 33% did begin offering testing to more patients. In practices where testing was utilized, an average of 15.2% of patients were offered testing, most frequently in the context of recurrent pregnancy loss or previous IVF cycle with poor fertilization or embryo development. The primary testing modality used was sperm chromatin structure assay (SCSA, 89.6%), typically performed as a send-out test. Once offered the test, respondents estimated that an average of 73.3% of patients completed testing. Though many providers (30.6%) did not know the cost of the test, others estimated it to range between $100-300 (24.5%) or $300-500 (34.7%). Further, respondents report that the most common reason for patients declining testing was due to cost (59.2%). This was followed by the patient perceiving that the test would not change their treatment plans (49%). When changes in treatment were offered, these most often included oral antioxidants (59.2%) and IVF with (51%) or without (36.7%) testicular sperm. Other common interventions were IVF with microfluidic sperm sorting (28.6%) or frequent ejaculation (28.6%).

CONCLUSIONS: Despite the release of ASRM/AUA guidelines in 2020, the field remains divided on their utility in clinical practice. High costs and unclear interventions remain factors limiting their use from both a provider and patient standpoint.

IMPACT STATEMENT: These data provide insight into barriers to implementation and standardization of practice patterns with regards to DNA fragmentation, highlighting the need for further translational research into these assays and whether pregnancy outcomes could improve with targeted testing and specific interventions.

O-58 7:03 AM Monday, October 24, 2022

THE EFFECT OF LEPTIN ON TESTICULAR MICRO-IMMUNE-ENVIRONMENT IS INFLUENCED BY BMI. Deepa Seetharam, PhD,1 Alexandra Dullea, MS,2 Kajal Khodamoradi, PhD,2 Ranjith Ramasamy, M.D.,2 Fangliang Zhang, PhD,2 Ranjith Ramasamy, M.D.,2 University of Miami Miller School of Medicine, Miami, FL; 2University of Miami Leonard M. Miller School of Medicine, Miami, FL.

OBJECTIVE: Testosterone (T) deficiency is estimated to affect up to 20% of males. T is primarily produced by Leydig Cells (LC) and LC dysfunction can lead to T deficiency (TD). The development and function LC is influenced by paracrine factors released by the testicular micro-environment (TME), including Leptin. Our previous work has demonstrated the role of Leptin in the development of LC into Adult Leydig Cells, capable of producing androgen. In this study, we evaluated the effect of Leptin on the testicular immune micro-environment (TMIE) in mice with a normal body habitus. There is also significant research linking obesity and TD. However, the effect of leptin on TMIE in different BMI conditions is not understood. Therefore, we evaluated the effects of leptin on the TMIE in different BMI conditions (lean and obese).

MATERIALS AND METHODS: We evaluated the effect of leptin on the TMIE using a murine model C57/BL mice. The mice were fed with high-fat and low-fat diet for 8 weeks (n=10) to make them obese and lean for the study. The weights of the animal were measured weekly to ensure the proper obese or lean body habitus. Following 8 weeks of the diet, we injected leptin (100ug and 100ug) intraperitoneally into the obese and lean group for 7 days. After 7 days of leptin injections, the mice were euthanized, blood and spleen were collected. Blood was subjected to differential complete blood count (CBC) profiling and spleen was subjected to comprehensive immunophenotypic panels.

RESULTS: The CBC profiling data was significant for differences the experimental mice when compared to control in 6 CBC values. In obese mice, high-dose leptin treatment resulted in significant changes in neutrophils, lymphocytes, and monocytes (p<0.05). In the obese, high-dose leptin group, neutrophils were increased, and platelets were decreased (p<0.05). Finally, in the lean high-dose leptin group, red blood cells were increased (p<0.05). Immunophenotypic panels also highlighted a differential impact of Leptin on several immune cells (Myeloid derived suppressor cells, T-cells (CD8, CD4), PMN-MDSCs) with respect to BMI.

CONCLUSIONS: The results demonstrate that low dose of leptin has a differential impact on the TMIE, as demonstrated by the differences in CBC profiling, and immune phenotypic panels which is significantly influenced by BMI. Future studies will explore the influence of leptin on hormonal regulation in different BMI conditions.

IMPACT STATEMENT: This is the first study of its kind to evaluate impact of Leptin in regulating testicular immune microenvironment with respect to BMI. Further research will open new doors to the use of Leptin as a personalized medicine for men with testosterone deficiency.

SUPPORT: Supported by the Clinician Scientist Development award from American Cancer Society to RR and Research Scholar Award from American Urological Association to HA.

O-59 7:03 AM Monday, October 24, 2022

MECHANISTIC INSIGHTS INTO A RARE MUTATION IN NACAD AS A POSSIBLE CAUSE OF COVID ORCHITIS. Christian K. Ramsoomair, BS,1 Deepa Seetharam, PhD,1 Balaji T. Moorthy, PhD,2 Fangliang Zhang, PhD,1 Ranjith Ramasamy, M.D.1 1University of Miami Miller School of Medicine, Miami, FL; 2University of Miami Leonard M. Miller School of Medicine, Miami, FL.

OBJECTIVE: Aiming to uncover causal mechanisms of COVID-19 sequelae outside of pulmonary symptomology, a recent study from our group identified a variant of the NACAD protein (120bp coding sequence deletion) associated with COVID-19 orchitis, a risk factor for male infertility. Interestingly, these patients had decreased ACE2 serum levels. NACAD is proposed to prevent inappropriate targeting of non-secreted peptides to the endoplasmic reticulum. We hypothesized that a defect in NACAD function/processing will decrease ACE2 serum levels by disrupting extracellular transport and endoplasmic reticulum interaction. We explored whether intracellular levels of ACE2 levels were altered and if cell membrane protein deposition was increased, which may result in more severe effects to SARS-CoV-2 infection.

MATERIALS AND METHODS: We obtained testis biopsies from men undergoing sperm retrieval for infertility. After siRNA NACAD knockdown, we analyzed total ACE2 expression using Western blot and qPCR as well as immunofluorescence/H&E staining for co-localization (with NACAD). Membrane-anchored ACE2 (mACE2) levels were quantified using immunostaining and flow cytometry while secreted ACE2 (sACE2) was analyzed by ELISA and Western blot.

RESULTS: NACAD and ACE2 co-localize in both the Leydig and germ cells. When NACAD is knocked down, primary testes cells show 80% decreased mRNA and 50% total protein levels of ACE2. The secreted ACE2 was also reduced by nearly 50%. However, when we specifically measured the level of mACE2 on the cell surface, we found that the knock-down of NACAD did not lead to reduction.

CONCLUSIONS: NACAD likely specifically affects the level of sACE2, which is speculated to act as a protection factor by retaining the virus in situ, preventing cells from triggering an immune response. NACAD knockdown reduces sACE2 and mACE2 levels, and we speculate that this reduction may contribute to decreased semen parameters. We hope that establishing a relationship between NACAD and ACE2 expression will prove useful not only to elucidate why some men with COVID develop orchitis but, ultimately, why some men develop multiorgan failure with COVID infection whereas most do not.

IMPACT STATEMENT: We expect that men with a history of orchitis and an increased level of ACE2 receptors will present with a higher and prolonged risk of impaired semen parameters. By identifying the impact of COVID-19 infection on male fertility, we can determine whether recommendations are warranted for sperm cryopreservation for men at high risk of contracting the infection, such as healthcare workers.
ORAL ABSTRACT SESSION: OVARIAN STIMULATION

O-61 10:45 AM Monday, October 24, 2022

THE RELATIONSHIP BETWEEN THE NUMBER OF MATURE OR STIMULATED FOLLICLES AND MULTIPLE PREGNANCY RATES IN LETROZOLE INTRATRIGERINE INSEMINATION (IUI) CYCLES IN WOMEN 18-40 YEARS OF AGE. Alyson M. Digby, MD, Bsc, Michael H. Dahan, M.D. Division of Reproductive Endocrinology and Infertility, McGill University Health Care Center, Montreal, QC, Canada.

OBJECTIVE: Recent ASRM guidelines have recommended limitations in the number of dominant follicles (DF) produced during ovarian stimulation (OS) due to the risk of multiple gestation. Our study aims to assess the incidence of multiple pregnancy according to the number of follicles identified on ultrasound after treatment with letrozole, which is lacking from the literature.

MATERIALS AND METHODS: A retrospective cohort study of 418 cycles from 01/2013 to 12/2018 at a single academic fertility center including women aged 18-40 years who underwent OS with letrozole 5 mg orally for 5 days in the early follicular phase and IUI. Correlation coefficients and multivariate logistic regression were used to measure the association between the data. Data is mean±SD.

RESULTS: Age of the females was 33.6±4.04 years. Ejaculate volume was 2.2±1.5 mL. Prewash sperm concentration was 50.5±31.6 mil/mL, motility 42±16%, post wash sperm concentration 59.7±38.7 mil/mL and motility was 85±17%. The max endometrial thickness was 7.9±1.9 mm. The overall clinical pregnancy rate (CPR) was 10.5% and multiple pregnancy rate (MPR) was 0.9% per cycle and 9% of clinical pregnancies (CP). We assessed the relationship between pregnancy outcomes and number of total follicles ≥10mm, or DF ≥14 mm or DF ≥16 mm. There was no relationship between the number of follicles ≥10mm in mean diameter and the likelihood of a CP (r= -0.04, p=0.40), the # of follicles (FS) (r= -0.32, p=0.51) or the # of follicles identified (FHB) (r= -0.17, p=0.73). The relationship between the number of DF ≥14 mm and CP (r= -0.009, p=0.86), the number of FS (r= -0.003, p=0.94) and FHB (r= 0.007, p=0.88) were non-significant. The relationship between DF ≥16 mm and CP (r= 0.036, p=0.47), FS (r= 0.037, p=0.45) or FHB (r= 0.054, p=0.27) were not significant. Multivariate logistic regression analysis including female age, pre sperm vol, post sperm concentration and motility, max endometrial thickness and either # follicles ≥10mm (OR 0.88, 95% CI 0.57-1.38) or # follicles ≥14mm (OR 0.97, 95% CI 0.58-1.67) or # follicles ≥16mm (OR 1.18, 95% CI 0.67-2.05) failed to find predictors of CP in letrozole OS and IUI. Few subjects had ≥ 4 DF at the time of hCG trigger, making conclusion at these levels tenuous.

CONCLUSIONS: There is no relationship between the number of follicles or DF (1 to 3) and the number of FS or FHB. It may not be necessary to cancel women with 3 DF undergoing letrozole IUI as recently recommended by the ASRM for other agents.

IMPACT STATEMENT: Letrozole cycles with 3 or less DF should not be cancelled.

SUPPORT: No financial support was received for this study.

O-62 11:00 AM Monday, October 24, 2022

OVARIAN STIMULATION OUTCOMES IMPROVE ON SUCCESSIVE RETRIEVAL CYCLES REGARDLESS OF CHANGE IN GONADOTROPIN DOSE OR PROTOCOL. Michael Fanton, Ph.D.1, Valerie L. Baker, MD.2 Kevin E. Loewke, Ph.D.1 1Alife Health, Inc., San Francisco, CA; 210751 Falls Road, Lutherville, MD; 3Alife Health, Inc.

OBJECTIVE: To investigate whether particular changes in gonadotropin dose or stimulation protocols can improve ovarian stimulation outcomes for patients undergoing successive retrieval cycles.

MATERIALS AND METHODS: We analyzed 64,585 patients with multiple completed retrieval cycles from 2014-2019 in the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System (SART CORS). The primary outcomes were the number of eggs retrieved, 2PNs, and blastocysts (transferred plus frozen). Comparison of outcomes between successive cycles may be biased by the decision to stop or continue treatment. To help mitigate this bias, we compared outcomes between the first and second cycles among (a) patients with two or more successive cycles, and (b) patients with three or more successive cycles. Lastly, we stratified outcomes by patients given more or less FSH per day on their second cycle, and by patients with or without protocol changes between cycles. Results were calculated for four quantiles of patient AMH (ng/mL) at the start of the first cycle.

RESULTS: On average, patients retrieved more eggs and created more 2PNs and blastocysts on their second cycle compared to their first cycle, regardless of change in FSH dose. Patients who changed protocols between first and second cycles had a greater improvement in outcomes.

CONCLUSIONS: We observed improvements in outcomes between first and second retrieval cycles regardless of change in dosing or protocol. Future work should further investigate whether these findings are due to patient behaviors (such as better adherence to medication or reduced stress), an inherent biological factor such as ovarian priming, or lessons learned by clinicians from first cycle outcomes.

IMPACT STATEMENT: Patients who decide to undergo multiple retrieval cycles appear on average to have slightly more eggs, 2PNs, and blastocysts on their second retrieval.

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FERTILITY & STERILITY®

e25
OBJECTIVE: During controlled ovarian stimulation cycles, ovulation inhibitors play the pivotal role of suppressing a premature LH surge, however their influence on oocyte maturation has remained unclear. We incrementally evaluated the dose-dependent influence of cetrorelix, GnRH antagonist (GnRH-ant) which has been traditionally used, or chloramidine acetate (CMA), an oral progestin which is used as an alternative to GnRH analog in the progesterin-primed ovarian stimulation (PPOS), on oocyte maturation rate in patients with normal ovarian reserve.

MATERIALS AND METHODS: This retrospective cohort study was performed in a reproduction center between March 2018 and October 2020 which included 977 patients with normal ovarian reserve undergoing PPOS with CMA (n=299), or GnRH-ant with cetrorelix (n=608) in their first IVF cycle. The inclusion criteria were patients aged <40 years and AMH >1.1ng/ml, with conventional autologous oocyte retrieval with freeze-all strategy. In PPOS protocol, CMA 2mg/day was co-administered with gonadotropin from spontaneous menstrual cycle day 3-5 to the day before trigger. The dosage of CMA was increased to the maximum dose of 5mg/day, according to the value of serum LH. In GnRH-ant protocol, cetrorelix at 0.25 mg/day every other day was administered with gonadotropin from spontaneous menstrual cycle day 3-5. Outcome was oocyte maturation rate and the secondary outcome was fertilization rate. After adjusting for 16 covariates such as age, AMH, total gonadotropin dose, and type of trigger, we calculated adjusted relative risk (aRR) and 95% CI of 1mg CMA or cetrorelix in a dose-dependent manner.

RESULTS: In the PPOS group, the median total dosage of CMA was 22 mg (IQR 18.0-32.0), 78.9% (236/299) patients had a fixed daily dose of CMA. In the cetrorelix, the median total dosage of cetrorelix was 0.5 mg (IQR 0.5-0.5). The unadjusted relative risk of maturation rate was 1.00 (1.00-2.00) with PPOS (p=0.01) and 1.12 (0.99-1.26) with GnRH-ant (p=0.16). The unadjusted RR of fertilization rate was 1.00 (1.00-1.01) with PPOS (p=0.08) and 1.18 (1.00-1.35) with GnRH-ant (p=0.02). The aRR of maturation rate was 1.00 (0.99-1.00) with PPOS (p=0.70) and 1.00 (0.99-1.01) with GnRH-ant (p=0.16). The aRR of fertilization rate was 1.01 (1.00-1.02) with PPOS (p=0.22) and 1.00 (1.00-1.01) with GnRH-ant (p=0.50).

CONCLUSIONS: In this population, no dose-dependent influence of CMA or cetrorelix on either oocyte maturation or fertilization rate in normal ovarian reserve patients was observed.

IMPACTION STATEMENT: In PPOS or GnRH-ant protocol, dosage of ovulation inhibitors was not associated with maturation and fertilization of oocytes.

METHODS- From a single center, 108 women with poor ovarian response (stratified according to POEISDON criteria) were randomised to either receive growth hormone (group A-intervention arm; n=52) along gonadotropins or only gonadotropins (group B-comparator; n=56) in antagonist protocol. The inclusion criteria were women aged 21-39 years with low reserves (AMH < 1.2 ng/ml or AFC < 5) or recovery of < 4 oocytes in prior cycles, with normal uterus. Women with severe endometriosis, suffering severe systemic illness and undergone radiochemotherapy were excluded, besides those on other adjuvants including DHEA, testosterone or antioxidants. Couples with severe male infertility demanding ICSI were also excluded. Subjects in group A received growth hormone (GH) (Norditropin, Novo Nordisk) daily at 8IU, along with gonadotropines, while the controls (Gr B) received only gonadotropins [r-FSH + r-LH (Gonal F + Luveris, Merck Serono)]. The primary outcome was clinical pregnancy (CPR), live birth rate (LBR) and miscarriage rate, while secondary outcome was dose and duration of gonadotropines, cycles cancelled, number of mature oocytes, fertilization, cleavage rate, number of good grade and surplus embryos for freezing and implantation rate.

Data analysis was carried out using statistical software STATA version 14.0. For all statistical tests, a two-sided probability of p < 0.05 was considered as statistically significant.

RESULTS: Both groups were comparable for demographic profile. There was no significant difference in LBR (13.4% vs 14.3%; p=0.99), CPR (15% vs 16%; p=0.762) and miscarriage rate (12.5% vs 11.1%; p=0.99) between two groups. There were significantly lower dosages (3415 ± 909.4 IU vs 3973.1 ± 582.3 IU; p=0.00) and higher AMH (0.7 days; p=0.001) in women in Group A, compared to controls. However, there was no significant differences between groups as regards to other secondary outcomes.

CONCLUSIONS: Growth hormone as adjuvants during ovarian stimulation does not improve ART outcome in women with poor ovarian response classified by POEISDON criteria.

IMPACT STATEMENT: Routine use of GH in poor ovarian response patients is not recommended. Need for larger studies addressing cost effectiveness is urged.

SUPPORT: none.
OUTCOME OF RANDOM-START OVARIAN STIMULATION IN CASE OF EMERGENCY FERTILITY PRESERVATION DEPENDING ON THE DAY OF PROTOCOL ONSET.

Sarah Amari, Associate Professor,1 Marouen Braham, Associate Professor,1 Siwar Jouou, Medical degree,1 Sana Chtourou, Assistant Professor,1 Linda Debabi, Medical Doctor,1 Khadija Kacemi Berjeb, Associate Professor,1 Anis anis Padhlouai, professor,1 Noura Chakroun, Professor,2 Fethi Zhioua, Dr 1 Gynecology, Obstetric and Reproductive Medicine Department. Aziza Othmana University Hospital, Tunis, Tunisia; 2Aziza Othmana University hospital, Tunis, Tunisia; 3Tunis, Tunis, Tunisia; 4Aziza Othmana University Hospital, Reproductive Medicine and Gynecology Laboratory, Tunis, Tunisia; 5Aziza Othmana University Hospital, Reproductive Medicine and Cytogenetic Laboratory, Tunis, Tunisia; 6Aziza Othmana University hospital, Gynecology, Obstetric and Reproductive Medicine Department, Tunis, Tunisia; 7FERTILLIA center, Tunis, Tunisia.

OBJECTIVE: To analyze and compare the outcome of a Random Start Controlled Ovarian Stimulation (COS) either at the early, late follicular or luteal phase of the cycle in emergency fertility preservation (FP) patients in the Department of Obstetrics, Gynecology and Reproductive Medicine of the Aziza Othmana Hospital in Tunis.

MATERIALS AND METHODS: We conducted a prospective, monocentric study including 301 FP referral patients from January 2015 to September 2020 in the Reproductive Medicine Department of the Aziza Othmana Hospital.

301 out of the initial 531 referral FP patients underwent emergency random-start COS. Depending on the day of the menstrual cycle on which COS was initiated, patients were subdivided into 4 random-start subgroups: Group A early follicular phase (from day 1 to day 9 of the cycle), Group B+D defined as late follicular phase from day 10 to 14 (Group B was administered hCG for triggering prior to COS, whereas Group C wasn’t) and finally Group D luteal phase COS (past day 14 of the cycle).

RESULTS: Referral patients had breast cancer in 217 cases. 150 patients had Hodgkin’s lymphoma, 40 had another malignant blood disease, while the other 124 had various other illnesses. Only 301 patients (56.7%) underwent a FP procedure in our department, and it was successful in 265 cases (89.3%).

Out the 265 patients, 77 had started ovarian stimulation in the early follicular phase (Group A); 46 in late follicular phase (Group B+C) and 142 in luteal phase of the cycle in emergency fertility preservation (FP) patients.

The mean duration of stimulation was shortest in Group B (4.66 days) and longest in Group D (9.93 days). The difference was statistically significant (p = 0.007).

Furthermore, Group A was administered the lowest total dose of gonadotropins (2478.35 ± 539.03 Units) whereas Group B+C significantly required the highest dosage (562.52 Units) (p = 0.002).

On the other hand, the mean number of follicles larger than 15 mm in ultrasound on the day of triggering was similar in all subgroups (8.95 ± 5.53; 8.96 ± 5.9; 8.69 ± 5.6; P = 0.92). No statistically significant difference was found between the different groups in terms of total number of vitrified oocytes (8; 8; 8; p = 0.13) and metaphase II oocytes (6.93; 6.98; 7.92; p = 0.88).

CONCLUSIONS: Random start is nowadays considered the Gold standard for emergency ovarian stimulation in Fertility preservation, as it allows FP patients to undergo protocol without delay. Depending on the day of onset, duration of stimulation and therefore total dose of gonadotropins administered may vary, without impacting overall outcome and especially the total number of oocytes retrieved and mature oocytes vitrified. Random Start protocol has proven its overall convenience and efficiency. IMPACT STATEMENT: Our daily challenge is to expand our purpose, raise awareness, better inform our peers, fellow colleagues in various specialties throughout the country and patients, potentially exposed to gonadotoxic treatment, before it is implemented. Furthermore, our call is also a healthcare and social cause, to ensure that FP is made accessible to all, to lift financial limitations and social taboos.

ORAL ABSTRACT SESSION: PREIMPLANTATION GENETIC TESTING I

POLYGENIC EMBRYO RISK SCORES: A SURVEY OF PUBLIC KNOWLEDGE AND PERCEPTION.

Alexandra Peyser, M.D.,1 Cailey Brogan, BS,1 Lilli D. Zimmerman, MD,1 Randi H. Goldman, M.D.,1 Northwell Health Fertility, Zucker School of Medicine at Hofstra Northwell, Manhasset, NY; 2Northwell Health Fertility, Northwell Health, Manhasset, NY.

OBJECTIVE: To evaluate the opinions and attitudes of the general US public regarding preimplantation genetic testing for polygenic conditions (PGT-P).

MATERIALS AND METHODS: A web-based questionnaire consisting of 26 questions was administered to a nationally representative sample of adult US residents according to age and sex. The survey contained a description of PGT-P followed by questions with Likert scale-responses ranging from strongly agree to strongly disagree. Survey topics included the safety, costs, utilization, and ethics surrounding PGT-P. Respondents who disagreed with the use of IVF for any indication were excluded from final analyses. Demographic data of respondents were collected and ordinal logistic regression was used to assess the association between the socio-demographic characteristics of the respondents and perceptions regarding PGT-P.

RESULTS: Of the 715 respondents recruited, 673 (94%) completed the survey. Thirty-eight respondents disagreed with the use of IVF for any indication and were excluded from the final analysis. Two responses were excluded due to incomplete responses. Of the remaining 633 (88%) responses, 465 (73%) supported and 39 (6%) opposed use of PGT for detection of aneuploidy (PGT-A) or monogenic disorders (PGT-M). Most respondents agreed that use of PGT-P is ethical (53%) and another 37% were neutral; however, approximately 1 in 10 respondents disagreed and were opposed to the use of PGT-P. Those that opposed PGT-P cited that it was “unethical” (46%), “not natural” (39%), beloved children can be negatively affected (31%) or that it went against their religion (15%). Sixty-two percent of respondents believed PGT-P should be covered by insurance, whereas 10% did not. The majority of respondents did not know whether PGT-P was safe for embryos (68%) or children (67%) and responded that anyone (53%) can utilize it. Most respondents (71%) felt research on PGT-P should continue. When asked about cost, 42% of respondents would be willing to pay $200-500/embryo for PGT-P, while 35% reported they would not pay for it at all. Age (<45yo vs. 45+, OR:0.68, p=0.04), religion (Christian vs. Muslim, OR:3.97, p=0.003) and educational status (OR:2.41, p<0.001) were more likely to support PGT-P use.
CONCLUSIONS: Half of respondents support the use of PGT-P. Respondents who disagree with use of PGT-P report concerns regarding safety, technological uncertainty, and ethical use. However, most believe research regarding this technology should continue. A future study that includes public perception of this emerging technology is essential.

IMPACT STATEMENT: The US public supports use of PGT-P, however concerns regarding its safety and ethical implications persist.

O-68 11:00 AM Monday, October 24, 2022

IS PGT-A BENEFICIAL FOR PATIENTS WITH ONLY ONE BLASTOCYST? A 2014-2018 NATIONAL STUDY OF OVER 21,000 FREEZE-ALL CYCLES. Alexis K. Gadson, MD,1 Meghan C. H. Ozcan, M.D.,2 May-Tal Sauerbrun-Cutler, M.D.,3 Christina Raker, SeD,4 Jennifer L. Eaton, MD, MScT1 Warren Alpert Medical School of Brown University; Women & Infants Hospital, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Providence, RI;4 Warren Alpert Medical School of Brown University; Women & Infants Hospital of Rhode Island, Providence, RI;4 Warren Alpert Medical School of Brown University; Women & Infants Hospital, Providence, RI;4 Warren Alpert Medical School of Brown University, Women & Infants Hospital, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Providence.

OBJECTIVE: Women with only one blastocyst have been largely excluded from studies on preimplantation genetic testing for aneuploidy (PGT-A) due to cost and theoretical risk of embryo damage. Existing data on the benefit of PGT-A in this specific context are therefore sparse. Our objective was to use a large, national database to test the association between PGT-A and live birth rate among women with only one embryo achieving blastocyst stage.

MATERIALS AND METHODS: We utilized de-identified data from the 2014-2018 Society for Assisted Reproductive Technology Clinical Outcomes Reporting System (SART CORS) to identify all autologous freeze-all cycles in which only one blastocyst was cryopreserved. Cycles were included in the analysis if the retrieval was linked to a subsequent thaw or was not linked because there were no embryos suitable for transfer. Exclusion criteria were female age greater than 44 years, embryo banking for fertility preservation, and the use of preimplantation genetic testing other than PGT-A. Patient data including demographics, baseline fertility evaluation, in vitro fertilization cycle outcomes, and pregnancy outcomes were obtained. The primary outcome was live birth per cycle start. Generalized estimating equation (GEE) models for binary data with a logit link were used to test the effect of PGT-A on live birth while adjusting for covariates and the correlation induced by repeated cycles within a patient.

RESULTS: Of the 21,658 cycles in which a single blastocyst was frozen, PGT-A was performed in 16,591 cycles (76.6%) and not performed in 5,067 (23.4%) cycles. The live birth rate was 14.8% in PGT-A cycles compared with 28.9% in non-PGT-A cycles (p < 0.001). Live birth rates in the non-PGT-A group were 37.4% in patients less than 35 years, 30.5% if 35-37 years old, 17.9% if 38-40 years old, and 8.1% if over 40 years old. After adjusting for covariates, 12,497 cycles with complete covariates were included in the regression model. The aOR for live birth per cycle start was 0.72 (p < 0.001) for patients who underwent PGT-A in comparison to those who did not. Live birth rates were significantly decreased for patients who had a blastocyst transfer and underwent PGT-A if less than 35 years old (24.6%, aOR 0.62, p < 0.001) or between 35-37 years old (20.7%, aOR 0.65, p < 0.001). There was no difference in LBR for patients undergoing PGT-A if 38-40 years old (15.7%, aOR 0.93, p = 0.54) or over 40 years old (8.1% < aOR 1.08, p = 0.73).

CONCLUSIONS: The likelihood of live birth per cycle start was significantly decreased in patients who underwent PGT-A with only one high quality blastocyst for biopsy who were younger than 37 years old while those over 38 years of age experienced no significant change in LBR after PGT-A. This data can be used to counsel patients regarding the use of PGT-A despite low embryo yield. Future prospective studies should be performed to further confirm the efficacy of PGT-A in this specific patient population.

IMPACT STATEMENT: For patients that have only one frozen blastocyst available, use of PGT-A significantly decreased LBR in patients less than 38 years of age while offering no significant benefit to older patients.

O-69 11:15 AM Monday, October 24, 2022

THE NATURE OF SEX CHROMOSOME ANEUPLOIDIES IN HUMAN BLASTOCYSTS. Ann Korkidakis, M.D., M.P.H.;1 Abigail Groff, PhD;1 Jaimin S. Shah, M.D.,1 Riwa Sabbagh, MD,1 Alan B. Copperman, MD,1 Samantha Lauren Estevez, M.D.,4 Russell A. Foulk, MD, HCLD,3 Joseph A. Lee, BA,3 Dana Neitzel, MS, CGC,3 Sarah Poll, PhD,3 Lauren Walters-Sen, PhD, FACMG,3 Alan S. Penzias, M.D.,1 Denny Sakkas, PhD8 1Boston IVF-The Eugin Group/Beeth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA;2Whitehead Institute for Biomedical Research, Cambridge, MA;3Icahn School of Medicine at Mount Sinai/Reproductive Medicine Associates of New York, New York, NY;4Icahn School of Medicine at Mount Sinai, New York, New York;5Utah Fertility Center, Pleasant Grove, UT;6Reproductive Medicine Associates of New York, New York, NY;7Invitae, San Francisco, CA;8Boston IVF - The Eugin Group, Waltham, MA.

OBJECTIVE: Post-implantation studies suggest that certain sex chromosome aneuploidies (SCA) do not result from maternal meiotic non-disjunction and hence may have different characteristics than autosomal trisomies. Our aim was to characterize SCA in the human blastocyst in terms of frequency, relationship with female age, and association with day of development.

MATERIALS AND METHODS: Retrospective analysis of consecutive trophectoderm biopsies performed between August 2015 and March 2022 evaluated with Next Generation Sequencing by a single genetics laboratory. Biopsy results were examined by age of female and day of biopsy using Chi-square goodness-of-fit. The SCA group included all embryos with X, XXX, and XYY results. Embryos by indeterminate results or segmental abnormalities involving sex chromosomes were excluded.

RESULTS: A total of 36,841 SCA results were obtained from an analysis of 249,274 embryos (incidence 147.8/1,000 blastocysts). The most frequent SCA was X followed by XXX, and XYY (145.2, 1.3, 0.7, and 0.6/1,000 blastocysts, respectively). The proportion of X significantly increased with advancing female age (p < 0.001); however, there was no age association for other SCAs (Table 1). When excluding embryos with autosomal aneuploidy from the X category, the association differed with a lower proportion in the ≥40 age group (p < 0.001). Analogous to autosomal aneuploidies, there was a significantly greater proportion of X blastocysts biopsied on day 6/7 compared to day 5 (p < 0.001).

CONCLUSIONS: A notable proportion of human embryos carry SCAs at the blastocyst stage, predominantly X. There is an association between X embryos and advancing female age that is not seen with other SCAs. When excluding embryos with autosomal aneuploidies, the relationship between X embryos and age changes, indicating that X embryos without other abnormalities may be less frequent in older women. The higher proportion of X embryos biopsied on day 6/7 suggest delayed embryo development.

<table>
<thead>
<tr>
<th>Age group (yrs)</th>
<th>X*</th>
<th>XXX</th>
<th>XXY</th>
<th>YY</th>
<th>XX/XY* (Euploid)</th>
<th>XX/XY* (Aneuploid)</th>
<th>Ploidy Error</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤30</td>
<td>3,695 (10.9)</td>
<td>31 (0.1)</td>
<td>45 (0.1)</td>
<td>22 (0.1)</td>
<td>21,219 (62.5)</td>
<td>8,509 (25.0)</td>
<td>454 (1.3)</td>
<td>33,975</td>
</tr>
<tr>
<td>31-33</td>
<td>6,007 (11.9)</td>
<td>39 (0.1)</td>
<td>68 (0.1)</td>
<td>45 (0.1)</td>
<td>29,623 (58.8)</td>
<td>13,943 (27.7)</td>
<td>644 (1.3)</td>
<td>50,369</td>
</tr>
<tr>
<td>34-36</td>
<td>8,875 (14.0)</td>
<td>40 (0.1)</td>
<td>81 (0.1)</td>
<td>33 (0.1)</td>
<td>32,466 (51.4)</td>
<td>20,870 (33.0)</td>
<td>827 (1.3)</td>
<td>63,192</td>
</tr>
<tr>
<td>37-39</td>
<td>9,843 (17.0)</td>
<td>41 (0.1)</td>
<td>74 (0.1)</td>
<td>25 (0.0)</td>
<td>22,458 (38.7)</td>
<td>24,776 (42.7)</td>
<td>825 (1.4)</td>
<td>58,042</td>
</tr>
<tr>
<td>≥40</td>
<td>7,769 (17.8)</td>
<td>27 (0.1)</td>
<td>64 (0.1)</td>
<td>17 (0.0)</td>
<td>9,611 (22.0)</td>
<td>25,376 (58.1)</td>
<td>832 (1.9)</td>
<td>43,696</td>
</tr>
</tbody>
</table>

*p < 0.05 using Chi-square
1. Haploid, triploid, tetraploid embryos
2. Counts (% total for age group)
IMPACT STATEMENT: At the human blastocyst stage, there is an association between X embryos and advancing female age that is not evident with other SCAs.

O-70 11:30 AM Monday, October 24, 2022

TRENDS AND OUTCOMES FOR PRE-IMPLANTATION GENETIC TESTING FOR MONOGENIC DISORDERS IN THE UNITED STATES, 2014-2018. Anisha R. Chada, M.D.,1 Sara Crawford, Ph.D.,2 Heather S. Hipp, MD,3 Jennifer F. Kawwass, MD3 Atlanta, GA;4 University of Mount Union, Alliance, OH;5 Emory University School of Medicine, Division of Reproductive Endocrinology and Infertility, Atlanta, GA.

OBJECTIVE: To describe national trends in and characteristics and outcomes of pre-implantation genetic testing for monogenic disorders (PGT-M) in in-vitro fertilization (IVF) cycles in the United States.

MATERIALS AND METHODS: This was a retrospective cohort study of data reported to the Society for Assisted Reproductive Technology Clinic Outcome Reporting system from January 1st, 2014, to December 31, 2018. We reported trends, patient and cycle characteristics, and perinatal outcomes of fresh autologous and donor oocyte cycles that used PGT-M. We evaluated trends in the number and proportion of cycles using PGT-M and detailed cycle and pregnancy outcomes among cycles using PGT-M.

RESULTS: From 2014 to 2018, the absolute number of oocyte retrieval cycles utilizing PGT-M increased from 1,249 to 2,072 (p = 0.0183), and the percentage of all retrieval cycles using PGT-M increased from 1.19% to 1.58% (p = 0.0413). PGT-M was more commonly performed in cycles of younger nulliparous patients who had never undergone in vitro fertilization (IVF). The majority of PGT-M use (70.6%) were in cycles with patients who did not have an infertility diagnosis. Although serious childhood onset conditions, such as Cystic Fibrosis and Spinal Muscle Atrophy, were among the top reported indications for PGT-M use, use was also reported for serious adult-onset conditions, including BRCA mutations and Huntington Disease. Cumulative live birth rates (LBR) per cycle decreased in patients of increasing age. In retrievals with at least one transfer, the LBRs were ≥55.0% in all age categories. Among all age strata, >80% of live births were full term infants and infants with a birth weight >2500g.

CONCLUSIONS: Cycles utilizing PGT-M have increased in number. They were utilized primarily in cycles among nulliparous patients with no known infertility and no prior IVF history. The indications for which PGT-M are used include both the classic childhood onset conditions as well as serious adult onset, non-lethal conditions, and cancer predisposition genes. Pregnancy and perinatal outcomes are reassuringly positive across all age categories among cycles that result in an embryo transfer.

IMPACT STATEMENT: This is the first available study on the prevalence of use of PGT-M among oocyte cycles in the United States. Cycles utilizing PGT-M are increasing, however they still make up a small minority of cycles, given the potential therapeutic benefit of the technology. PGT-M use may increase with increased availability of preconception genetic screening, education about the technology, and decreased financial burden to patients.

SUPPORT: None.

O-71 11:45 AM Monday, October 24, 2022


OBJECTIVE: The objective of the current study was to determine the sustained implantation rates (SIR) of mosaicism masked, whole chromosome aneuploid (WCA) negative embryo transfers that after unmasking of the raw data were putative mosaic, in comparison to transfers of WCA-negative embryos without any signs of mosaicism.

MATERIALS AND METHODS: This was a blinded, non-selection, retrospective cohort study completed with embryo transfers between February 2020 to February 2022. Patients underwent IVF with ICSSI followed by trophectoderm biopsy and PGT-A using PGTsSeq, a validated, next generation sequencing based platform. Mosaicism was selected in cases of whole chromosome mosaicism and segmental mosaicisms of unknown significance after appropriate counseling. For patients who opted to only report WCA, the diagnostic results identified embryos as negative and positive for WCA while masking the mosaic status of the WCA-negative embryos. After IRB approval, the raw data, including the mosaic status of the WCA-negative embryos, was unblinded and pregnancy outcomes were evaluated. Mosaic embryos analyzed in this study belonged to two groups: those with whole chromosome mosaicism only and those with segmental mosaicism only.

The primary outcome was SIR. SIR was compared between groups using likelihood ratio tests based on nested logistic regression models with mixed effects. Fixed effects include oocyte age, day of blastocyst cryopreservation (day 5, 6, 7), and embryo grade (expansion score, inner cell mass grade and trophectoderm grade). Patient was considered as a random effect.

RESULTS: 4,895 mosaicism masked, frozen single embryo transfers were included for analysis. These consisted of 4,187 (85.5%) WCA-negative embryos without signs of mosaicism as the control group, 441 (9.0%) embryos with segmental mosaicism only, and 267 (5.5%) with whole chromosome mosaicism only. SIR among the control, segmental mosaic, and whole chromosome mosaic embryos were 63.7%, 60.8%, and 55.1%, respectively. Association tests between embryo type and outcome yielded non-significant differences between the segmental mosaic group and the control group (p = 0.41). The results are similar for comparing embryos with whole chromosome mosaicism and the controls (p = 0.06).

CONCLUSIONS: Transfer of putative mosaic embryos in a blinded, non-selected population, in which these embryos are not intentionally deprioritized, does not impact clinical outcomes. Sustained implantation rates were similar to WCA-negative, mosaicism-negative embryo transfers.

IMPACT STATEMENT: Preimplantation embryos diagnosed as putative mosaic by a validated PGT-A platform appear to have similar SIR as WCA-negative embryos without evidence for mosaicism.

SUPPORT: None.

O-72 12:00 PM Monday, October 24, 2022

INTERNAL INVESTIGATIONS OVER A 4-YEAR PERIOD HIGHLIGHT THE CONSISTENCY OF PREIMPLANTATION GENETIC TESTING (PGT), THOUGH IDENTIFY PREVENTABLE REPEATED CAUSES OF DISCREPANT PGT RESULTS. Nicholas C. Paolino, MS, CGC,1 Elizabeth Cameron, M.S.,2 Pore Colls, Ph.D,2 Kristine McWilliams, MD, PhD3 CooperSurgical, Livingston, NJ;4 CooperSurgical, Trumbull, CT.

OBJECTIVE: No test is 100% accurate. PGT laboratories should investigate reported concerns regarding specific PGT results. Outcomes of these investigations should be shared to communicate potentially preventable causes of discrepant PGT-A results.

MATERIALS AND METHODS: From May 2018 to March 17, 2022, we received 143 inquiries regarding CooperSurgical PGT results. PGT testing related to these requests was performed from 2015 to 2021. During this period, CooperSurgical performed over 120,000 PGT cases. Following clinical evaluation, 129 inquiries were further investigated, which involved review of prior test results and reanalysis via the laboratory’s current PGT platform. When PGT results remained consistent, secondary investigation by DNA fingerprinting was offered.

RESULTS: CooperSurgical received PGT investigation requests in 0.12% of cases (143/120,000). PGT results were consistent in 92% of investigated cases (119 of 129 cases), with 6% (8 of 129 cases) identified as laboratory errors (6 manual transcription errors; 2 processing errors), and two cases (2%) inconclusive due to degradation of retained sample. 119 families were offered secondary investigation. 29% of couples (34/119) pursued this testing. 85% (29/34) of secondary investigations identified a root cause for the claimed discrepancy between PGT-A and prenatal results (Table 1). 15% of secondary investigations (5/34) were inconclusive due to degradation of the original PGT-A sample. The most frequent identified root cause was sex chromosome discrepancy caused by maternal cell contamination (MCC) within the biopsy provided for PGT-A (10/21; 48%).

CONCLUSIONS: Requests to investigate PGT-A results are infrequent and the findings from the investigations typically confirm the original PGT-A results. A source of PGT laboratory error is manual interpretation and transcription of results. This highlights the benefit of PGT
technologies that include automated analysis and report generation, as our laboratory now utilizes. The most frequent cause of PGT-A error by the IVF laboratory is maternal cell contamination within the provided biopsy specimen.

IMPACT STATEMENT: Discrepancies in PGT results can and will occur. A thorough investigation into discrepancies affords opportunities to improve IVF laboratory practices and develop PGT technologies to proactively identify potential sources of error, such as contamination present within biopsy specimens.

ORAL ABSTRACT SESSION: PUBLIC HEALTH AND REPRODUCTIVE HEALTH

O-73 10:45 AM Monday, October 24, 2022

IMPACT OF THE COVID-19 PANDEMIC ON SOCIAL OOCYTE CRYOPRESERVATION TRENDS. Alex Raghunandan, BS,1 Nina Vyas, MD,2 Ashley Aluko,3 Steven D. Spandorfer, MD,4 Zev Rosenwaks, M.D.4 1Monroe Township, NJ; 2Weill Cornell Medicine, New York, NY; 3NewYork-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY; 4The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: We aimed (1) to quantify the impact of COVID-19 on the number of oocyte cryopreservation cycles performed, and (2) to characterize the demographics of fertility preservation patients both before and during the pandemic.

MATERIALS AND METHODS: We performed a retrospective analysis of patients who underwent social oocyte cryopreservation at a large university-affiliated REI practice. Cycles were divided into two 22-month study periods: pre-pandemic (May 2018–February 2020) and post-pandemic (March 2020–December 2021). Oocyte cryopreservation cycles for medical indications (e.g., cancer diagnosis) were excluded. A Student’s t-test was used to compare parametric variables between the two groups, while a Wilcoxon Rank-Sum was used for non-parametric variables. A Chi-squared test was used to compare non-parametric variables between the two patient groups.

RESULTS: During the pandemic, there was a decrease in total ovarian stimulation cycles (n = 6,343) compared to the pre-pandemic period (n = 6,653). In contrast, there was an 18.9% increase in the number of oocyte cryopreservation cycles seen in the post-pandemic group versus the pre-pandemic group (n = 1,165 and n = 980, respectively). Overall, there was a difference in the proportion of oocyte cryopreservation cycles performed at our institution pre-pandemic and post-pandemic (14.7 vs. 18.3%, p < 0.001). In addition, the age of post-pandemic oocyte cryopreservation patients decreased (36.2 vs. 35.7yr, p = 0.004). There was no significant difference found in the BMI, AMH, and number of cryopreserved oocytes per cycle between the two patient groups.

CONCLUSIONS: Although total ovarian stimulation cases declined following the pandemic, the number of social oocyte cryopreservation cycles increased proportionally. This suggests a shift in patients who present to REI clinics for proactive reproductive planning versus infertility care. More studies are needed to elucidate if this is due to a trend toward delayed childbearing, increase in ART, and/or the pandemic.

O-74 11:00 AM Monday, October 24, 2022

VACCINE AND BOOSTER ACCEPTANCE IN WOMEN CONSIDERING OR UNDERGOING FERTILITY TREATMENTS DURING THE OMICRON SURGE OF THE COVID-19 PANDEMIC. Luce A. Kassi, MD, Amelia Swanson, PhD, Angela K. Lawson, Ph.D., Shriya Shah, BA, Mary Ellen Pavone, MD Northwestern University, Chicago, IL.

TITLE: Vaccine and booster acceptance in women considering or undergoing fertility treatments during the omicron surge of the COVID-19 pandemic.

OBJECTIVE: To evaluate perceptions of COVID-19 vaccination and vaccine booster during the omicron surge in women considering or undergoing fertility treatment.

MATERIALS AND METHODS: IRB approval was obtained. Cross-sectional anonymous surveys of patients were collected from a single academic fertility center. Participants were randomized 1:1 to receive a one-page graphic of supplemental education, which provided basic facts regarding the association between infertility and COVID-19 vaccination and boosters based on the ASRM COVID-19 taskforce recommendations. Beliefs related to COVID-19 vaccination and boosters were assessed with dichotomous, Likert scale and multiple-choice questions. Assessment of trust in the medical system was conducted via the Medical Mistrust Index (MMI). Descriptive data and chi-square analysis were used to compare the intervention v. no intervention groups.

RESULTS: To date, a total of 422/2558 surveys have been received, response rate = 16.5%. The participants were 36.40 years old (SD = 4.28), married (89.3%), nulliparous (63.3%), White (82.5%), Asian (5.9%), Hispanic (4.0%), and Black (3.3%) and 47.7% had a history of at least one pregnancy loss.

Among the participants who reported their vaccination status (n = 408), 96.8% of the study population were fully vaccinated, 86.3% had received their booster dose, 4.5% were fully vaccinated but did not plan on receiving a booster, while only 2.4% did not plan on getting vaccinated. Of those able to be vaccinated during pregnancy, 23.5% were vaccinated during pregnancy. Patients with vaccine hesitancy had higher medical mistrust scores (r = .21, p < .001).

Participants with higher MMI scores had higher PHQ-8 scores (p < .001) and GAD-7 scores (p < .001), were more likely to have a loved one diagnosed with COVID-19 (p = .002), were less likely to

<table>
<thead>
<tr>
<th>Chromosome Involved in Claimed Discrepancy</th>
<th>MCC</th>
<th>Other Contamination</th>
<th>Different Embryo Transferred</th>
<th>Probable Mosaicism</th>
<th>Prenatal Test Error</th>
<th>Spontaneous Pregnancy</th>
<th>Inconclusive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (22)</td>
<td>10</td>
<td>2</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Autosome (12)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 1. Identified causes of discrepant PGT-A results from DNA fingerprinting analysis

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Proportion of ovarian cryopreservation/total stimulation cycles n/N (%)</td>
<td>980/6,653 (14.7%)</td>
<td>1165/6,343 (18.3%)</td>
</tr>
<tr>
<td>Age (years) mean ± SD</td>
<td>36.2 ± 3.6</td>
<td>35.7 ± 3.6</td>
</tr>
<tr>
<td>BMI (kg/m²) mean ± SD</td>
<td>23.8 ± 4.8</td>
<td>24.0 ± 5.0</td>
</tr>
<tr>
<td>AMH (ng/dL) median [IQR]</td>
<td>1.7 [1.0–3.2]</td>
<td>1.8 [1.0–3.2]</td>
</tr>
<tr>
<td>Cryopreserved oocytes (n) median [IQR]</td>
<td>9 [4–14]</td>
<td>9 [5–14]</td>
</tr>
</tbody>
</table>
have lost their job due to the COVID-19 pandemic (p = .017) and reported concerns about vaccine side effects on miscarriage (p = .006).

Participants who received the educational material were more likely to know that pregnant women with COVID-19 had an increased risk of delivering preterm birth and perinatal death (p = .017).

CONCLUSIONS: Two years after the onset of the COVID-19 pandemic, the majority of women in this study were vaccinated and had already received their booster dose. Participants with the greatest medical mistrust expressed concerns about COVID-19 vaccination and risk of miscarriages. The intervention increased patients’ knowledge regarding maternal and fetal risks associated with COVID-19 infection.

IMPACT STATEMENT: Though the vaccination rate was significantly higher among the survey participants compared to the national vaccination rate, vaccine hesitancy was higher in patients with increased level of medical mistrust. Educational handout appears to be a reliable strategy to correctly inform patients on the risks associated with COVID-19 and pregnancy though they did not change vaccine hesitancy.

O-75 11:15 AM Monday, October 24, 2022

PROCEDURAL SPECIALISTS FAMILY BUILDING PATTERNS AND USE OF ASSISTED REPRODUCTIVE TECHNOLOGY. Padmaja Sundaram, B.A., Amelia G. Kelly, MD,2 Morgan S. Levy, BS,3 Arghavan Salles, M.D., Ph.D,4 Vineet Arora, M.D.1 Albany Medical College, Irvine, CA; NYU Langone Health, NEW YORK, NY; Boynton Beach, FL; Stanford University; University of Chicago.

OBJECTIVE: Physicians in procedural specialties are likely to require longer training, work hours, and intensive physical demands relative to non-procedural ones. However, little is known about family building patterns of proceduralists. This cross-sectional study examines variations in the experience of infertility, family building, and usage of assisted reproductive technology (ART) between procedural and nonprocedural physicians.

MATERIALS AND METHODS: Between April-May 2021, a sample of physicians and physicians-in-training were recruited through social media and organizational listservs to complete a questionnaire. Participants reported demographics and family building path, including experience with ART. Only current physicians that chose a specialty were included. Proceduralists were compared to non-procedural physicians. Analysis was conducted using SPSS 28, with statistical significance at p < .05.

RESULTS: Of the 2,510 qualifying respondents, 52.5% (n = 1319) were nonprocedural and 47.5% (n = 1191) were procedural. Top procedural specialties were Obstetrics and Gynecology, General Surgery, and Emergency Medicine; top nonprocedural specialties were Family Medicine, Pediatrics, and Internal Medicine. Procedural and nonprocedural specialists did not differ significantly by age, relationship status, sexual orientation, or rates of infertility. However, there were clear differences in the opportunities for family building between those in procedural vs non-procedural specialties. Proceduralists were more likely to be childless (40.1% vs. 36.1%, p < 0.001). They also reported fewer children (1.12 vs. 1.25, p = 0.015). Proceduralists were more likely to have children during residency (40.7% vs. 34.7%, p < 0.001). Proceduralists were also more likely to use ART (26.9% vs. 22.7%, p = 0.024). Non-procedural respondents spent more years trying to conceive prior to starting ART than proceduralists (3.34 vs. 3.10, p = 0.024). Amongst respondents who pursued ART, those in nonprocedural fields pursued more cycles than those in procedural fields (5.41 vs. 4.38, p = 0.034). Nonprocedural fields were more likely to use daycare as childcare (61.6% vs. 43.9%) (p < 0.001), whereas those in procedural fields were more likely to rely on nannies (50.4% vs. 40.6%) (p < 0.001).

CONCLUSIONS: This study demonstrates concerning differences in family building patterns between physicians in procedural vs non-procedural specialties. Procedural fields face a larger burden during family building and have less time to dedicate to trying to conceive with or without ART. Such discrepancies likely come at a financial and emotional cost. This warrants investigation into barriers procedural physicians face regarding family building as well as interventions to create more suitable environments for proceduralists who want to build families.

IMPACT STATEMENT: Those in procedural specialties face larger barriers in family building and the use of ART compared to those in non-procedural ones. This highlights a forced tradeoff between career and family, especially for those in procedural specialties.
OBJECTIVE: To examine the efficacy of a telehealth based approach to effective weight management interventions in women with obesity seeking treatment for infertility.

MATERIALS AND METHODS: In this observational study (2020-2021) women with obesity and infertility attended IVF centers in MA and NY. Weight loss was recommended prior to conception and patients were referred to Form Health, a multi-disciplinary obesity management program delivered through a telehealth platform. Each referred patient is matched with a board-certified obesity medicine physician and a registered dietician. A smart phone application enables regular communication as well as monthly video visits. The outcomes of the first 97 patients referred from the infertility treatment team to the obesity management program were examined.

RESULTS: 97 women with infertility (mean age 34.5 years, mean weight 261.5 lbs, mean BMI 43.2 kg/m²) enrolled in the obesity treatment program. Mean duration in program to date is 3.8 months. 47 (48.5%) patients were prescribed metformin. Mean HBA1C was 5.6% for this cohort. Weight loss outcomes correlated with time in program, with mean weight loss 4.3% (of starting weight) after 3 months, 7.6% after 6, 9.9% at 9 months, and 9.7% at 12 months. 37% achieved a BMI <40 kg/m². 38% (35 of this cohort had starting BMI >45 kg/m²), and of those 32.4% achieved BMI below 45 kg/m². 84 patients underwent ovulation induction +/- intrauterine insemination and, thus far, 13 patients in this cohort underwent IVF with embryo transfer (3 fresh 10 frozen transfers). 15.4% patients are currently pregnant. CONCLUSIONS: Access to medical obesity treatment is limited, and tele-health delivery has the potential to increase geographic access to safe, effective and evidence-based weight loss treatment for women with obesity seeking infertility care. This study shows that a multidisciplinary telehealth approach to weight loss can be effective. This program was introduced during the Covid-19 pandemic and our study indicates that this strategy may improve patient compliance beyond the pandemic.

IMPACT STATEMENT: Telehealth access to an obesity medicine program for women seeking infertility treatment has shown to help these patients sustain weight loss. Weight loss management program can increase conception rates for obese patients and ultimately improve perinatal outcomes.

ORAL ABSTRACT SESSION: REPRODUCTIVE SURGERY AND PROCEDURES

O-79 10:45 AM Monday, October 24, 2022

ENDOMETRIAL SCRATCHING IN PATIENTS WITH UNEXPLAINED INFERTILITY UNDERGOING INTRAUTERINE INSEMINATION: PRELIMINARY REPORT OF A RANDOMIZED CONTROLLED TRIAL. Karen Keely, MD,1 Roland Antaki, MD,1 William A. Pardoe, BSc, MM, MSc,2 Simon Benoit Dube, M.D,3 Isaac-Jacques Kadoch, M.D.,4 Simon Phillips, Ph.D.,3 Louise Lapensee, M.D.3 1Ovo Clinic, University of Montreal, Montréal, Québec, Canada; 2University of Montréal; McGill University Health Center Glen Site, Montreal, QC, Canada; 3Clinique Ovo, Montréal, QC, Canada; 4OVO FERTILITY, Montreal, QC, Canada; 5OVO Clinic, Montréal, QC, Canada.

OBJECTIVE: To evaluate the impact of endometrial scratching in patients with unexplained infertility undergoing ovarian stimulation and intrauterine insemination.

MATERIALS AND METHODS: A prospective randomized controlled trial was conducted at a university-affiliated private IVF clinic in Montreal, Canada, between May 2018 and March 2022.

Two hundred seventy-five women with a diagnosis of unexplained infertility and an indication for intrauterine inseminations were recruited. One hundred thirty-one patients were randomized to intervention group (endometrial scratching) and one hundred forty-four patients to no intervention group (control). All patients received ovulation induction with either letrozole or letrozole plus gonadotrophins. Patients were monitored by ultrasound followed by ovulation triggering. In the study group, endometrial scratching was performed during the follicular phase between days 3 and 8 of ovulation induction cycle. All patients were followed for three consecutive months with or without IU following randomisation. Primary outcome was clinical pregnancy rate at first trimester ultrasound. Secondary outcomes included live birth rate, ongoing pregnancy rate and miscarriage rate. Data were analysed as intention-to-treat. Two-sample t-test, Pearson’s Chi-Square test and Student T-distribution were used

RESULTS: Baseline patient demographic characteristics and fertility history were comparable in the two study groups. The mean age of the patients was 33.8 ±4.2 years. The mean AMH value was 2.8 ±2.1 ng/mL. Four hundred and ninety-nine intrauterine insemination cycles were completed with two hundred twenty-six in the intervention group and two hundred seventy-three in the control group. There were no significant differences in overall cumulative clinical pregnancy rate after three consecutive cycles between the scratching group 28% and the control group 25%; RR: 0.97 (95%CI: 0.87-1.08, p=0.73). Miscarriage rates were comparable between the two study groups. These results represent an interim analysis; the target sample size is three hundred ninety-four patients with 1-β=0.80 and analysis of the secondary outcomes.

CONCLUSIONS: Performing endometrial scratching in the early follicular phase was not found to be beneficial in this preliminary analysis of our randomized controlled trial prior to intrauterine insemination or spontaneous conception cycles with no impact on pregnancy rates. We will pursue recruitment to groups for the desired power.

IMPACT STATEMENT: Endometrial scratching performed during follicular phase was not found to be beneficial for patients undergoing intrauterine insemination. This study is the largest performed to date and more evidence based randomized controlled trial are needed before the use of an iatrogenic local endometrial injury can be recommended in routine clinical practice.
Surgical and Reproductive Outcomes in a Large Deceased Donor Uterus Program: Cleveland Clinic’s Six Year Report

Objective: To report the latest surgical and reproductive outcomes for the ongoing Cleveland Clinic Trial of Uterine Transplantation for the Treatment of Uterine Factor Infertility (ClinicalTrials.gov identifier NCT02573415), the oldest uterus transplant trial in the United States and to our knowledge the largest deceased donor trial. While use of deceased donors eliminates risk to a living donor, it is unclear whether outcomes are similar.

Materials and Methods: This is a prospective interventional trial of deceased donor uterus transplantation.

Results: Out of 8 transplants attempted, there have been 2 graft failures and 6 technically successful transplants. Of these, 6 first menses occurred within 34 days. Of the 2 experiencing graft failure, hysterectomy was performed within 12 days of transplant. Of 4 achieving livebirth, all became pregnant following 1-2 embryo transplant attempts. To date, in our trial there have been 4 livebirths, 1 ongoing second pregnancy, 1 planned second pregnancy, and 2 patients still awaiting pregnancy.

Conclusions: For all transplanted uteri that remained in situ for at least two weeks from transplant, there were no graft failures. Key success milestones in our trial (graft survival, time to menstruation, pregnancy rates, live birth rates) are comparable to other uterus transplant trials.

Impact Statement: Our data demonstrate that deceased donor uterus transplantation is a viable surgical treatment for patients with uterine factor infertility. We suggest that outcomes are the same in deceased donor as with living donor uterus transplantation.

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Endometrial Receptivity Analysis Testing: A Single Centre Experience

Objective: To review the clinical experience with the Endometrial Receptivity Analysis (ERA) at the Olive Fertility Centre (OFC), including the subgroup of patients who received ERA testing prior to first embryo transfer.

Materials and Methods: Retrospective descriptive chart review of patients who received ERA testing at OFC between January 1, 2014 and December 31, 2021 (n=403). Patients were stratified as those who had at least 1 prior failed transfer, and those who did not have a prior transfer. Final ERA results including receptivity in hours were collected. Pre- and post-ERA test implantation rate, biochemical pregnancy rate, ongoing pregnancy rate, and live birth rate were calculated.

Results: Amongst patients who underwent ERA (n=403), 81.9% of patients had a receptive result. For non-receptive results, pre-receptivity was noted in 15.6% (n=63), and post-receptivity was found in 2.5% (n=10). Amongst patients with at least 1 prior failed implantation who then underwent ERA (n=263), 81.7% (n=215) of patients had a receptive result. For non-receptive results, pre-receptivity was noted in 14.4% (n=38), and post-receptivity in 3.8% (n=10). The Pre-ERA implantation rates were 8.9% and 10.0% in the receptive and non-receptive groups respectively. The implantation rate after a receptive result was 55.2%, biochemical pregnancy rate was 8.5%, ongoing pregnancy rate (OPR) was 47.6%, and live birth rate (LBR) was 38.5%. For patients who had endometrial preparation modified by ERA results, implantation rate was 54.6%, biochemical pregnancy rate was 10.0%, OPR was 43.8%, LBR was 39.7%.

Amongst patients who underwent ERA prior to first transfer (n=127), 82.7% (n=105) of patients had a receptive result and 17.3% (n=22) had a non-receptive result, all of which were pre-receptive. The implantation rate after a receptive result was 63.6%, biochemical pregnancy rate was 11.7%, OPR was 57.7%, and LBR was 42.4%.

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Endometrial Receptivity Analysis Testing Table:

<table>
<thead>
<tr>
<th>#</th>
<th>Indication for transplant</th>
<th>Notable postoperative events</th>
<th>Time to graft failure (days)</th>
<th>Time to first menses (days)</th>
<th>Time to first ET (days)</th>
<th>Total number of ETs (including second pregnancy)</th>
<th>Pregnancy complications</th>
<th>Gestational age at delivery</th>
<th>Birthweight (g)</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MRKH</td>
<td>Graft failure</td>
<td>Yes (GH)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A Placenta accreta</td>
<td>N/A</td>
<td>N/A</td>
<td>GH</td>
</tr>
<tr>
<td>2</td>
<td>MRKH</td>
<td>Severe graft rejection</td>
<td>Pelvic hematoma, DVT, PE</td>
<td>No</td>
<td>34</td>
<td>183</td>
<td>1 cHTN, subchorionic hematoma</td>
<td>34w6d</td>
<td>2600</td>
<td>CH</td>
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<tr>
<td>3</td>
<td>MRKH</td>
<td>CMV infection, vaginal stricture</td>
<td>Yes (IVC filter, ex lap)</td>
<td>N/A</td>
<td>20</td>
<td>183</td>
<td>1 cHTN, subchorionic hematoma</td>
<td>34w6d</td>
<td>2600</td>
<td>CH</td>
</tr>
<tr>
<td>4</td>
<td>MRKH</td>
<td>Graft failure</td>
<td>No</td>
<td>N/A</td>
<td>10</td>
<td>274</td>
<td>12 N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>RIF</td>
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<tr>
<td>5</td>
<td>MRKH</td>
<td>Graft failure</td>
<td>Yes (GH)</td>
<td>N/A</td>
<td>6</td>
<td>185</td>
<td>N/A GDM, PPROM</td>
<td>N/A</td>
<td>2480</td>
<td>GH</td>
</tr>
<tr>
<td>6</td>
<td>MRKH</td>
<td>Tachycardia, vaginal stricture</td>
<td>Yes (ex lap)</td>
<td>N/A</td>
<td>20</td>
<td>185</td>
<td>N/A GDM, PPROM</td>
<td>N/A</td>
<td>2480</td>
<td>GH</td>
</tr>
<tr>
<td>7</td>
<td>MRKH</td>
<td>Incisional hematoma, vaginal stricture</td>
<td>No</td>
<td>N/A</td>
<td>23</td>
<td>191</td>
<td>4 N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>RIF</td>
</tr>
<tr>
<td>8</td>
<td>MRKH</td>
<td>Graft failure</td>
<td>No</td>
<td>N/A</td>
<td>26</td>
<td>189</td>
<td>1 None</td>
<td>37w1d</td>
<td>3022</td>
<td>Planning</td>
</tr>
</tbody>
</table>
CONCLUSIONS: The majority of patients undergoing ERA testing have a receptive result. In patients with a history of at least 1 prior implantation failure, nonreceptive findings were slightly higher than those who never had a prior transfer. 18.2% vs 17.3%. The implantation rates were highest amongst patients who never had a prior transfer and had endometrial preparation modified by ERA results at 70.3%. However, LBR in this group were different than those with no previous transfer and a receptive ERA result at 42.4%. Similarly, the LBR for patients with a prior failed transfer after a receptive or non-receptive ERA were similar at 38.5% and 39.7%, respectively. Further study is needed to compare clinical outcomes following ERA testing.

IMPACT STATEMENT: Data from this study will help clinicians understand the clinical application of ERA in a large volume fertility practice when applied to patients with or without implantation failure.

SUPPORT: none.

O-82 11:30 AM Monday, October 24, 2022

COVID-19 INFECTION IN UTERUS TRANSPLANT RECIPIENTS IN THE US. Margaret Rush, MD, Liza Johannesson, MD, PhD, Eileen Yee Yee Wang, MD, Nawar Latif, MD, MPH, MSCE, Emily Blumberg, MD, Kathleen O’Neill, MD Hospital of the University of Pennsylvania, Philadelphia, PA; Baylor University Medical Center, Dallas, TX; Hospital of the University of Pennsylvania; University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: The ongoing COVID-19 pandemic has been associated with greater risk of infection and severe complication in solid organ transplant recipients compared to the general population, yet sparse data exists on the effect of COVID-19 on uterus transplant (Utx) recipients. Though immunosuppressed individuals, including organ transplant recipients, experience higher rates of morbidity and mortality following COVID-19 infection, vaccination for COVID-19 has been shown to effectively reduce mortality for these patients. Despite these encouraging results, and statements from professional societies including ASRM recommending vaccination, vaccine hesitancy remains elevated in the infertility population. The goal of this report is to provide details regarding COVID-19 infection and vaccination rates in Utx recipients in the US.

MATERIALS AND METHODS: We performed a retrospective cohort analysis on individuals who have undergone Utx as of March 2021 in the US. Five Utx recipients at two centers (Baylor Scott and White, Dallas, Texas, and Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania) were diagnosed with COVID-19 infection as defined by the presence of a positive SARS-CoV-2 on reverse transcriptase-polymerase chain reaction (RT-PCR) testing from a nasopharyngeal swab. Data collected included demographic features, transplant history, transplant-related complications, vaccination status and pregnancy history.

RESULTS: The median time from transplant to diagnosis of COVID-19 was 22.8 months. Despite the availability of the COVID-19 vaccine, only one out of 5 Utx recipients was vaccinated at the time of diagnosis. Two recipients were pregnant at the time of diagnosis, one in the first trimester and one in the second trimester of pregnancy. One recipient experienced COVID reinfection three months following the first infection. All COVID positive Utx recipients experienced no or mild symptoms; one recipient was asymptomatic, 4 had nasal congestion, 2 had headaches, and one patient was febrile. Four recipients received Casirivimab-imdevimab. In 80% of patients, no changes were made to patients’ immunosuppression regimens.

CONCLUSIONS: All Utx recipients who were diagnosed with COVID-19 infection as of 3/2021 recovered without complications. As in other infertility patients, vaccine hesitancy remains a significant concern despite the Utx population having a higher risk of severe disease. Data continues to accrue demonstrating the safety of vaccination in pregnancy, and communication of these results to the Utx population is essential to promote maternal and child health.

IMPACT STATEMENT: This data provides reassuring information regarding outcomes for COVID-19 infection in Utx population; however, also demonstrate that similar to other pregnant patients or patients with infertility, vaccine hesitancy remains a significant issue.

O-83 11:45 AM Monday, October 24, 2022

EFFECTS OF FIBRIN SEALANT COMPARED WITH SUTURING OR NO HEMOSTATIC INTERVENTION ON OVARIAN RESERVE IN PATIENTS UNDERGOING OVARIAN CYSTECTOMY: A RETROSPECTIVE COHORT STUDY. Mary McKenna, MD, Paola Georgiev, MD, Maharat Singh, PhD, Rachel Yoon Kmetz, MD, Kirsten Sasaki, MD, Charles E. Miller, MD Chicago, IL; Advocate Lutheran General Hospital, Naperville, IL; Marquette University, Milwaukee; Mercy Clinic, Saint Louis, MO. OBJECTIVE: Determine the effect of Tisseel, a fibrin based hemostatic agent, versus no hemostatic interventions or suturing of the ovary on ovarian function after ovarian cystectomy measured by antir follicle count (AFC) and anti-Mullerian hormone (AMH).

MATERIALS AND METHODS: Retrospective review of prospectively maintained database of all women who underwent laparoscopic ovarian cystectomy from October 2017 through December 2021. Statistical analysis was done for variables such as age, intervention (Tisseel versus no hemostatic agent or suturing) AFC (left and right sides) and AMH before and after surgery. Average AFC (left and right) and AMH were compared for intervention and for suturing or no hemostatic method using repeated measure ANOVA. For all statistical tests an alpha of 0.05 was used and for all statistical tests SAS 9.4, SAS Institute, Cary, NC was used.

RESULTS: The study sample included 77 women with median age of 34 years (range 26-44). Tisseel was used for 43 (62.8%) women. No hemostatic intervention was used for 34 (44.2%) women. There were no complications in either group. The percentage of women with suturing was higher in no hemostatic intervention than in Tisseel group (37.2% vs 8.8%, p < 0.004). There was no statistical difference in average AFC (both left and right) after ovarian cystectomy between the Tisseel group and no hemostatic intervention or suturing group (p > 0.05). There was also no statistical difference in average AMH after ovarian cystectomy between the Tisseel group and no hemostatic intervention or suturing group (p > 0.05). Overall, average AFC and AMH were both higher after ovarian cystectomy compared to prior to both Tisseel group and no hemostatic intervention group and with and without suturing (p < 0.05).

CONCLUSIONS: It is well known that ovarian cystectomy leads to decreased ovarian function in women because of the procedure itself and the methods used to achieve hemostasis such as bipolar electrosurgical energy and hemostatic agents. The use of electrosurgical energy on ovarian tissue can lead to further decrease in ovarian function due to destruction of remaining ovarian tissue with thermal damage. The current preferred method to obtain hemostasis at the time of ovarian cystectomy is suture, as there have been no studies looking at hemostatic agents and their effect on ovarian function compared to the gold standard of suturing or no hemostatic intervention. Our study shows that there is no difference in subsequent AFC or AMH levels with the use of Tisseel compared to no hemostatic intervention or suturing of the ovary after ovarian cystectomy.

IMPACT STATEMENT: The use of Tisseel, a fibrin based hemostatic agent, does not negatively affect ovarian function after ovarian cystectomy compared to suturing or no hemostatic intervention.


O-84 12:00 PM Monday, October 24, 2022

SURVEYING ERGONOMIC RISK, OPTICS, AND TEACHING IN OPERATING SURGEONS WITH WEARABLE TECHNOLOGY: 4K-3D EXOSCOPE VS OPERATING MICROSCOPES IN MALE FERTILITY MICROSURGERY. Kevin Chu, MD, Rohit Reddy, B.S., Jesse Ory, MD, Maria Camila Suarez Arbelaez, MD, Ranjith Ramanathan, MD. 1Advanced Urology - Los Angeles, Miami Beach, FL; 2University of Miami, Miami, FL; 3University of Miami Miller School of Medicine, Miami, FL.
OBJECTIVE: Male fertility microsurgery presents ergonomic hazard due to the nature of lengthy surgeries. Historically, standard microscopes have predisposed surgeons to being in uncomfortable positions for prolonged periods starting in residency leading to cervical strain and chronic pain. This study aimed to perform ergonomic survey for optical differences and teaching value between the 4K-3D exoscope and operating microscope in male fertility microsurgery.

MATERIALS AND METHODS: Participating surgeons were fitted and calibrated with three wearable sensor inertial measurement units (IMUs) on the head, torso, and arms in the neutral position. Each IMU contained an accelerometer, magnetometer, and gyroscope to measure surgeon joint angle changes throughout all scope usage. Following 4K-3D and operating microscope usage, surgeons were surveyed by a 5-point Likert scale questionnaire covering ergonomic, optical, and teaching parameters.

RESULTS: Overall, surgeons spent 34% of procedure time in moderate to high-risk neck flexion positions. Standard microscope surgeons saw a 161% greater neck rotation when compared to 4K-3D exoscope users. Time of shoulder abduction in high to very high-risk positions was not significantly different between both scopes (p=0.25). 5-point Likert scale found surgeons to significantly favor 4K-3D exoscope in questionnaire topics of ergonomics, optics/clarity, lighting, and teaching.

CONCLUSIONS: Poor surgical ergonomics can predispose surgeons to chronic pain, discomfort, and ultimately shorten operating careers. The 4K-3D exoscope was associated with decreased neck flexion, rotation, and perceived surgical discomfort. Optic and teaching aid ratings were also found to be superior with the exoscope. While this study showed quantitative differences and clear male fertility surgeon/trainee preferences, further investigation is required to determine impacts in other urological specialties.

IMPACT STATEMENT: The 4K-3D exoscope technology shows great promise in improving surgical ergonomics and augmenting educational experience in the realm of male fertility surgery.

ORAL ABSTRACT SESSION: REGENERATIVE MEDICINE AND STEM CELLS

O-85 10:45 AM Monday, October 24, 2022

PERTURBATION OF DNA METHYLTRANSFERASES IN HUMAN TROPHOBLAST STEM CELLS LEADS TO A FAILURE OF TROPHOBLAST DIFFERENTIATION - A PUTATIVE CAUSE FOR HUMAN MISCARRIAGE. Yu Jin Jang, PhD,1 Philip Spinelli, BS,2 Martha Sussiaro, PhD,3 1Winifred Mak, MD, PhD4 UT Austin, Austin, TX; 2University of Rochester School of Medicine and Dentistry, Rochester, NY; 3University of Texas Dell Medical School, Women’s Health, Austin, TX.

OBJECTIVE: To investigate the role of DNA methyltransferase 1 (DNMT1) in the trophoblast of miscarriages using a novel human trophoblast stem cell (TSC) model. The DNMTs are an important family of proteins that catalyze the transfer of methyl groups to specific CpG structures in DNA (DNA methylation). DNMT1 has an essential function in development that catalyzes the transfer of methyl groups to specific CpG structures in DNA (DNA methylation). DNMT1 has an essential function in development.

RESULTS: Three DNMT1 KD TSC cell lines with the highest knockdown efficiency (>92% decrease in DNMT1 expression) were analyzed. All KD TSCs showed a significant reduction in DNMT1 protein. Two KD TSC cell lines showed a decrease in methylation of CpG in LINE1 elements and the imprinted genes H19/DIO1 (p<0.05). All DNMT1 KD TSC cell lines showed a change in cell morphology, a decrease in proliferation as well as a 50% decrease in expression of the TSC marker gene, GATA3 (p<0.05). Strikingly, all KD TSC lines were able to differentiate into ST lineage but failed to differentiate into EVT lineage. Moreover, the KD EVT cells showed down-regulation of EVT lineage genes and upregulation of ST lineage genes (p<0.05).

CONCLUSIONS: In summary, our results show that depletion of DNMT1 in the TSC cells results in DNA methylation changes which affect TSC proliferation and a failure of differentiation to EVT lineage. We conclude our preliminary data shows strong evidence that reduction in DNMT1 protein could be a putative cause for miscarriages by causing a defect in human placental development.

IMPACT STATEMENT: Our study provides new insights into an epigenetic etiology of human miscarriages.

SUPPORT: ASRM/SREI research grant.

O-86 11:00 AM Monday, October 24, 2022

A CELL THERAPY ASSISTED NOVEL MICROFLUIDIC DEVICE PROMOTES IN VITRO SPERMATOGENESIS IN NEONATAL MICE. Selin Onen, PhD, Candidate,1 Ali Can Atik, PhD, Student,2 Merve Gizer, PhD, Candidate,2 Sevil Kose Asst., Prof.,3 Onder Yaman, Prof, Haluk Kilah, Prof,2 Petek Korkusuz, MD, PhD4 Hacettepe University / Atilim University, Ankara, Turkey; 2Middle East Technical University, Faculty of Engineering, Ankara, Turkey; 3Hacettepe University, Graduate School of Health Sciences, Ankara, Turkey; 4Atilim University, Faculty of Health Sciences, Golbasi, Turkey; 5University of Ankara, School of Medicine, Ankara, Turkey; 6Hacettepe University, Faculty of Medicine, Ankara, Turkey.

OBJECTIVE: Chemo-radiotherapy applications result in permanent infertility in half of male pediatric cancer survivors1. Spermatogonial stem cells (SSCs) constitute the only option for fertility preservation since spermatogenesis is not initiated yet2. The rationale of study is that bone marrow derived mesenchymal stem cells (BMMSC) have similar embryonic origin and gene expression profile with Sertoli cells3, 4 that play crucial role in proliferation of SSCs, and microfluidic devices (MD) simulate microvascular flow in the body that could promote for in vitro spermatogenesis (IVS). We hypothesized that, syngeneic BMMSC-conditioned medium (BMMSC-CM) contributed monolayer pupiless MD leads to survival, expansion and differentiation of SSC pool in vitro.

In this study we combined MSC’s paracrine contribution with MDs’ amelioration. We aimed to design and validate a novel pupiless and monolayer MD in which syngeneic BM-MSC-CM supports spermatogenesis on-chip platform comparing to static hanging drop set up. Testicular strips were cultured for days 7-42. Epithelial thickness of seminiferous tubules and luminal diameter, number of SCSs, differentiating and total germ cells and testosterone level in culture media by flow cytometry, histology and LC-MS identified the efficiency of platform.

MATERIALS AND METHODS: Hacettepe University Ethical Board approved the study (#52338575-109). Dynamic PDMS-based MD with an insert for cellular secretome was designed to test BM-MSC-CM induced spermatogenesis-on-chip platform comparing to static hanging drop set up. Testicular strips were cultured for days 7-42. Epithelial thickness of seminiferous tubules and luminal diameter, number of SSCs, differentiating and total germ cells and testosterone level in culture media by flow cytometry, histology and LC-MS identified the efficiency of platform. One-way ANOVA and Kruskal Wallis tests analyzed parametric and nonparametric correlative outputs, respectively.

RESULTS: The novel pupiless monolayer MD has been successfully optimized for organ chamber size and vascular flow rate parameters and our group applied for patent (#8PT/ITR22022/050188). MD provided higher spermatogenic cell numbers in all time intervals comparing to static conditions (p<0.005). BMMSC-CM and MD induce tubular epithelial thickness, luminal diameter, number of spermatogonium, spermatocyte, spermatid and SALL4 immune labeled SSCs comparing to controls from day 7 to 42 (p<0.005). The correlated increase in PLZF, c-Kit and VASA immune labeled SSCs comparing to controls from day 7 to 42 (p<0.005). BMMSC-CM and MD induce tubular epithelial thickness, luminal diameter, and number of SSCs, differentiating and total germ cells and testosterone level in culture media by flow cytometry, histology and LC-MS identified the efficiency of platform.

CONCLUSIONS: In conclusion, the overall outputs revealed that syngeneic BMMSC derived cell therapy-assisted novel MD platform can promote survival, expansion of SSC pool and IVS up to round spermatids during 42 day-long culture.

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IMPACT STATEMENT: The syngeneic stem cell therapy assisted novel MD presents a promising personalized therapeutic tool for male oncofertility in terms of preserving and developing IVS on testicular strips being cryopreserved and transplanted back when the patient reaches adulthood following gonadotoxic cancer treatment. Obtaining round spermatids is also an advantage for getting offspring since round spermatid injection (ROSI) is a commonly used method included in assisted reproductive technology in the clinics.

SUPPORT: The Scientific and Technological Research Council of Turkey funded the study (2185421).

REFERENCES:
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O-87 11:15 AM Monday, October 24, 2022

EFFECT OF HUMAN UMBILICAL CORD BLOOD PLATELET-RICH PLASMA COMBINED WITH EXTRACELLULAR MATRIX HYDROGELS ON IMMUNOCOMPETENT ENDOMETRIAL DAMAGE MURINE MODELS. Adolfo Rodríguez Eguren, M.Sc.;1 Lucía De Miguel Gómez, Ph.D.;2 Emilio Francis Herrero, M.S.C.;3 María Gómez Álvarez, M.S.C.;3 Amparo Faus, B.Sc.;4 Inés Moret Tatuy, Ph.D.;4 Macarena Gómez, M.S.C.;2 Antonio Pellicer, MD, Ph.D.3 Irene Cervello, Ph.D.4 IVI Foundation- Health Research Institute La Fe, Valencia, Spain; 4IVI Foundation, Valencia, Spain; 3IVI Foundation - University of Valencia, Valencia, Spain; 5Health Research Institute La Fe; 4IVIRMA Rome - University of Valencia, Roma, Italy.

OBJECTIVE: Asherman syndrome or endometrial atrophy (AS/EA) are endometrial pathologies causing infertility. Human platelet-rich plasma (hPRP) contains growth factors (GF) and cytokines well-described in tissue regeneration. Adult peripheral blood hPRP has been used as therapy in different tissues, as well as for AS/EA women. Human umbilical cord blood hPRP (hUC-PRP) showed greater regenerative potential than other hPRP due to its younger source. Recently, we confirmed the use of endometrial extra-cellular matrix hydrogels (HG) as delivery system of GF in mice. Here, we aimed to investigate the efficacy of hUC-PRP alone or driven by HG (HG+hUC-PRP) to improve pathologic endometrium in a mouse model of AS/EA.

MATERIALS AND METHODS: hUC-PRP was obtained from healthy donors from Hospital La Fe. AS/E A murine model was induced by 70%-ethanol uterine injection. After four days, treatments were injected in the uterine horns (saline for the control group) of C57BL/6 mice, randomized as follows: saline (n=5), hUC-PRP (n=5), HG+hUC-PRP (n=5), and non-damaged sham (n=5). Two weeks later, mice were euthanized, and cava vein blood was collected to study the immunotolerance. Uterine horns were analyzed by Masson Trichrome (MT, Sigma), Ki67 (ab15580), lectin I (FL-1101) and a-sma (C6198). Multiplex Immunoassays (ThermoFisher) were used to characterize hUC-PRP and to study the immunocompetence. Kruskal-Wallis with Mann-Whitney U for 2-by-2 comparisons performed.

RESULTS: (1) Characterization of hUC-PRP: 1 million platelets/ml and 5-fold significant increase of platelets respect to total blood (p-value <0.05). From the 45 Cytokines/Chemokines/GF examined, to note the high amount of 8 GF (PDGFBB, EGF, HGF, SCE, VEGF-A, IP-10, MIP-1β, and SDF-1α, concentration >50pg/ml) related to processes as cell proliferation, angiogenesis, or immunomodulation. (2) Study of endometrial regeneration in AS/EA murine model: both treatments (hUC-PRP and HG+HUC-PRP) presented similar results to sham and significant differences compared to saline, with larger endometrial area (328582 ±90055, 875514±167455, 833284±474655, and 1082157±383220 μm² in saline, hUC-PRP, HG+HUC-PRP, and sham respectively), higher glands concentration (1.47±1.20, 4.54±1.36, 3.43±1.27, and 4.46±1.72 glands/mm³), increased cellular proliferation (11.34±2.25, 27.23±6.30, 26.61±1.42, and 27.71±4.00%), neovascularization (7.70±3.39, 19.69±2.64, 21.77±2.67, 19.14±3.55%), and lower incidence of fibrosis (86.88±2.27, 70.34±7.39, 57.45±10.80, and 58.34±14.52%) (p-value<0.05). (3) Immune response analysis: blood plasma from murine samples revealed lacked of immunological rejection to treatments, no differences in the expression of 26 Cytokines/Chemokines.

CONCLUSIONS: hUC-PRP alone or delivered by HG were compatible to immunocompetent mice and improved endometrial regeneration in AS/EA murine models.

IMPACT STATEMENT: These results reinforce the regenerative effect provided by HUC-PRP and HG+HUC-PRP supporting also the use of HG as vehicles for future treatments. This scenario opens up new applications in the field of reproductive medicine.

SUPPORT: This work was supported by the Carlos III Health Institute (IS-CIII) [ PI21/00305 and CPI19/00149], by the Spanish Ministry of Science, Innovation and Universities [FPU19/04850, FPU18/06327 and FPU20/00251] and by the Regional Valencian Ministry of Education [PROME-TEO/2018/137].

O-88 11:30 AM Monday, October 24, 2022

miRNA144-5p OVEREXPRESSION MENSECHYMAL STEM CELL-DERIVED SECRETOME REVERSES THE FUNCTION OF OGCS IN AN IN VITRO POI MODEL. Farzana Begum Liakath, PH.D.,1 Hang-Soo Park, Ph.D.,2 Jin Seok, Ph.D.,1 Mohammad M. Ghasraldost, Ph.D.,1 Ayman Al-Hendy, MD, PhD1 The University of Chicago, Chicago, IL;2University of Chicago, Chicago, IL.

OBJECTIVE: The clinical manifestation of Premature Ovarian Insufficiency (POI) is largely attributed due to the follicular atresia caused by excessive senescence, apoptosis, and loss of ovarian granulosa cells (OGC) resulting in the decreased number of follicles. miRNA144-5p has been reported to be downregulated in the plasma of POI patients and overexpression of miRNA can attenuate the damage in preclinical studies. This study aims to use a lentiviral-based transfection method to overexpress mir144-5p in human Bone Marrow Mesenchymal Stem Cells (hBM-MSCs) and evaluate the therapeutic effect of its secretome using an in vitro POI model.

MATERIALS AND METHODS: The hBM-MSCs were successfully transfected using a lentivirus construct carrying mir144-5p with Green fluorescent protein (GFP) tag with scramble control. The transfected clones were confirmed by fluorescent microscopy and sorted using Magnetic Assisted Cell Sorting (MACS). The overexpression of miR144-5p in MACS positive clones was confirmed by Q. RT-PCT. The stemness of the transfected MSCs was assessed for multilineage differentiation and immunophenotyping. We used the human granulosa cells (HGCr1) treated with 100 μg/ml of cyclophosphamide for 24 h as an in vitro POI model and treated these damaged HGCr1 cells with the secretome of miR144-5p overexpressing hBM-MSC for 24 hours post cytotoxicity. Cell proliferation and viability were studied using MIT and XTT assays respectively. Relative gene expression was studied using three sets of genes which include i) markers of cell proliferation and survival (AKT, Ki67 and TK1) ii) markers of apoptosis (Cas3, Bcl-2 and Bax) iii) makers of steroidogenesis (StAR, CYP19A1 and FSHR) with subsequent immunoblot analysis.

RESULTS: The secretome-treated HGrC1 group showed improved cell proliferation (p<0.05) compared to untreated damaged cells and increased cell viability in exosome treated group (95.72%) compared to the damaged cells (92.01%) respectively. Among the genes tested, the relative gene expression of cas-3, a major executor of apoptosis was downregulated (p=0.01) whereas Bcl-2, an anti-apoptotic marker in secretome treated group was significantly upregulated (p<0.001) compared to untreated damaged cells. The anti-apoptotic effect of miRNA144-5p was also observed with downstream apoptotic markers at the protein level. RNA sequencing is currently undertaken to understand the key regulatory pathways responsible for granulosa cell regeneration.

CONCLUSIONS: We showed that treatment of damaged HGCr1 cells with secretome of hBM-MSC overexpressing miRNA144-5p stimulates cellular proliferation and cell survival with the concurrent upregulation of Bcl-2. These preliminary findings encourage us to study the specific role of miRNA144-5p in regulating anti-apoptotic pathways which might be responsible for the regenerative potential.

IMPACT STATEMENT: As there is a constant search for novel cell-free therapeutic options for POI, miR144 expressing secretome/purified exosomes from the genetically modified BM-MSCs could potentially be an effective novel method in the near future.

SUPPORT: This study supported by a start-up fund of the University of Chicago to Dr. Ayman Al-Hendy.
ACTIVATION OF AKT, MAPK3/1 AND mTOR SIGNALING PATHWAYS IS ASSOCIATED WITH THE SUCCESS OF CAVITY FORMATION DURING HUMAN BLASTOID GENERATION. Asrafun Nahar, PhD,1 Toshihiko Ezashi, PhD, Heather Rogers, MSc, Leqian Yu, PhD, Yulei Wei, PhD, William B. Schoolcraft, MD,1 Mandy Katz-Jaffe, PhD, Jun Wu, PhD, Ye Yuan, PhD1 Colorado Center for Reproductive Medicine, Lone Tree, CO; UT Southwestern Medical Center, Dallas, TX.

OBJECTIVE: Cavitation is a crucial process during human blastocyst development that involves combined actions of ion gradient pumps, water channels, and intercellular junction complexes that assemble on the apical and basolateral membranes of trophectoderm cells, which are dependent on a series of metabolic signaling pathways that are poorly understood in human embryos. Here, we explored whether the blastoid model derived from human naive pluripotent stem cells to examine which metabolic signaling pathways are important for blastoid cavitation.

MATERIALS AND METHODS: Human blastoids with cavity were generated following the established protocol (Yu et al., Nature 2021). Stem cell aggregates that did not form a cavity from the same batch (aggregates), and surplus human blastocysts donated with patient consent for research, were used as negative and positive controls, respectively. The protein abundance of AKT, MAPK3/1, STAT3, AMPK and RPS6KB1 (a hallmark of activation of mTOR signaling pathway) and their phosphorylated forms were examined by capillary western blotting (JESS, ProteinSimple), and the metabolic pathway activities were assessed by the ratio of phosphor to total proteins. The experiments were performed in triplicate and data was analyzed by one or two way ANOVA with post hoc Tukey’s multiple comparison test to calculate the protein expression in human blastoids (with cavity), aggregates (without cavity) and human blastocysts.

RESULTS: We observed a significant increased ratio of Phosphor AKT (pAKT)/total AKT (P ≤ 0.001) in human blastocysts (1.13 ± 0.06) compared to both human blastoids (0.65 ± 0.04) and non-blastoid aggregates (0.18 ± 0.01), whereas human blastoids also showed higher pAKT/total AKT than the non-blastoid aggregates (P ≤ 0.001). Human blastocysts (0.55 ± 0.04) and blastoids (0.40 ± 0.08) had similar pMAPK3/1 / total MAPK3/1 and this ratio was significantly reduced in the non-blastoid aggregates (0.26 ± 0.01, P ≤ 0.05). We also found pRPS6KB1/total RPS6KB1 (P ≤ 0.001) significantly higher in human blastoids (0.45 ± 0.05) compared to the non-blastoid aggregates (0.21 ± 0.02), but lower than human blastocysts (0.77 ± 0.05). In contrast, there was no difference in pSTAT3/total STAT3 and pAMPK/total AMPK among human blastoids, non-blastoid aggregates and blastocysts.

CONCLUSIONS: Our results suggest that activation of AKT, MAPK3/1, and mTOR may be associated with the success of cavity formation during human blastoid generation. These signaling pathways may also play important roles during human blastocyst cavity formation.

IMPACT STATEMENT: Cavity formation during early embryo development is underpinned by specific metabolic pathways. The metabolic similarities between blastoids and human blastocysts suggest the utilization of human blastoids as the model to investigate human early embryo metabolism and improve in vitro culture conditions.


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O-90 12:00 PM Monday, October 24, 2022

OPTIMIZING EXTENDED CULTURE CONDITIONS OF STEM CELL DERIVED BLASTOIDS TO IMITATE HUMAN IMPLANTATION IN VITRO. Didi Logsdon, B.A., M.S.C.1 Toshihiko Ezashi, PhD, Leqian Yu, PhD, William B. Schoolcraft, MD, Jun Wu, PhD, Mandy Katz-Jaffe, PhD, Ye Yuan, PhD1 Colorado Center for Reproductive Medicine, Lone Tree, CO; UT Southwestern Medical Center, Dallas, TX.

OBJECTIVE: We compared different medium formulations, blastoid criteria, and feeder conditions to mimic implantation to optimize a model for human implantation.

MATERIALS AND METHODS: Naive human embryonic stem cells were differentiated into blastoids over 8 (D8) or 9 d (D9) (Yu et al., Nature 2021). In exp. 1, D8 blastoids between 150-250 μm diameter with a tight inner cell mass between 10-20% of total cells were selected and placed into IVC medium (with 20% FBS, 25 μM N-acetyl-cysteine, 8 mM estradiol, 200 ng/mL progesterone, 1X ITS-X) or EBC medium (with N2, B27, 55 mM 2-mercaptoethanol, 15% FBS, 8 mM estradiol, 200 ng/mL progesterone, 1 mM sodium pyruvate, 50 mM Chroman 1, 5 μM Emricasan, 1X polyamine supplement, and 0.7 μM Trans-ISRIB supplement) on fibronectin dishes for 3 d. In exp. 2, D8 or D9 blastoids were placed into EBC medium on fibronectin dishes for 3 d. In exp. 3, D8 blastoids were placed in EBC medium on either fibronectin, fetal fibroblast feeder cells, or immortalized endometrial stromal cells for 3 d. In exp. 4, D8 blastoids and donated human embryos were placed into EBC medium on fibronectin or on immortalized stromal feeder cells and cultured for 3 d. All embryos and blastoids were measured for tropheoblast outgrowth area and all culture was completed in 21% O2 and 6% CO2 at 37°C.

RESULTS: Blastoids grew significantly larger in EBC compared to IVC (EBC: 0.37±0.02, IVC: 0.12±0.13 mm2; p<0.0001) and attached to fibronectin dishes equally after 24 h. Both D8 and D9 blastoids attached to fibronectin dishes within 24 h equally, but trophodermctoderm outgrowth area of D8 blastoids was increased compared to D9 (D8: 0.37±0.03, D9: 0.18±0.02 mm2; p<0.001). The presence of fetal fibroblast feeder cells increased the area of trophodermectoderm outgrowth compared to fibronectin only (fibronectin: 0.28±0.03, fibroblast: 0.39±0.02 mm2; p<0.05). All blastoids attached to each feeder condition equally after 24 h. More blastoids were able to attach to stromal feeder cells (blastoids: 100%, embryos: 25%; p<0.001) or fibroblast only (blastoids: 75%; embryos: 25%; p<0.05) after 24 h compared to human embryos, but outgrowth areas were not different at the conclusion of culture.

CONCLUSIONS: D8 blastoids in EBC medium in the presence of fibroblast feeder cells exhibit significant improvements in trophoblast outgrowth in extended culture. Additionally, blastoids and human embryos exhibit similar peri-implantation development on day 3 of extended culture on fibronectin dishes and stromal feeder cells. These data suggest that D8 blastoids in EBC medium may be an appropriate model for human embryos during peri-implantation. Improvements to blastoid production and extended culture conditions may more closely mimic human embryo attachment during the peri-implantation period.

IMPACT STATEMENT: Refining culture conditions of stem cell derived blastoids will help to appropriately mimic human implantation in a way that has never been done before. Using this model, researchers can begin to tease apart mechanisms of early trophoblast differentiation and lineage segregation events during peri-implantation without the use of human embryos.

ORAL ABSTRACT SESSION: 2022 SCIENTIFIC CONGRESS PRIZE PAPER SESSION 2

O-91 10:45 AM Tuesday, October 25, 2022

FIBROID PREVALENCE AND BURDEN BY RACE IN AN ASYMPTOMATIC, DIVERSE COHORT OF REPRODUCTIVE-AGE WOMEN. David Huang, MD,1,2 Brady Magaaway, MD,1 Mitchell P. Rosen, MD, HCLD,1 Marcelle I. Cedars, MD1 University of California, San Francisco School of Medicine, San Francisco, CA;2University of California San Francisco, San Francisco, CA.

OBJECTIVE: Knowledge regarding the true prevalence of fibroids is limited, especially in non-White and non-Black women, as prior studies evaluated these groups primarily based on symptoms or hysterectomy specimen. It is important to further identify at-risk groups in an increasingly diverse U.S. population. We aim to determine the prevalence and burden of fibroids in a diverse cohort of asymptomatic women.

MATERIALS AND METHODS: Women aged 25-45 years old who were not seeking treatment for fertility or other medical conditions were prospectively recruited to join a community-based cohort designed to study reproductive aging. Effort was made to recruit an equal proportion of women from the four major racial groups in the U.S. (White, Black, Hispanic, and Asian-Chinese). All participants reported regular menses, had not used estrogen- or progestin-containing medications in the 3 months prior to enrollment, and denied history of ovarian or uterine surgery. All participants underwent a transvaginal ultrasound by two board-certified Reproductive Endocrinologists to evaluate for any ovarian or uterine lesions. Participant age, race, parity, body mass index (BMI) were compared among racial groups using analysis of variance (ANOVA). Fibroid prevalence by race was assessed using logistic regression, controlled for age and BMI. Parameters of fibroid burden were compared among racial groups using chi-square and ANOVA as appropriate. All analyses were performed using Stata v17.0.
RESULTS: A total of 996 women were included in the analysis, which consists of 281 White, 249 Black, 229 Asian, and 237 Hispanic women. Mean ages of the four racial groups were similar (p=0.50), but BMI differed significantly (p<0.01). The overall prevalence of fibroids was 19.9% in this cohort. Fibroid prevalence was 35.7% in Black, 21.8% in Asian, 12.7% in Hispanic, and 10.7% in White women. After controlling for age and BMI, Black and Asian women were more likely to have fibroids compared to White women (OR 4.10 [95% CI 2.46-6.85], p<0.01 and OR 2.61 [95% CI 1.57-4.31], p<0.01, respectively). In those with fibroids, there was a trend towards statistical significance for differences in proportion of women with multiple fibroids: 48.3% in Black, 34.5% in White, 33.3% in Hispanic, and 26.0% in Asian women (p=0.06). The largest diameter of fibroids (mean±SD) was 3.90±1.86cm in Black, 3.21±1.59cm in Asian, 3.16±1.65cm in White, and 2.97±1.36cm in Hispanic women (p=0.03).

CONCLUSIONS: Compared to White women, Black and Asian women are more likely to have fibroids. Black women tend to carry multiple fibroids and exhibit larger fibroid size. These findings are concordant with the increased morbidity and burden seen in Black women, and may contribute to the disparities seen in fertility treatment and pregnancy outcomes in Black and Asian women.

IMPACT STATEMENT: This is a large cross-sectional assessment of baseline fibroid prevalence in a diverse, asymptomatic cohort. Asian women of Chinese descent were found as an at-risk group, which has not previously been reported. Contribution of uterine fibroids to disparities in fertility treatment among racial groups should be examined.

SUPPORT: Supported by the National Institute of Aging Grant No. R01-AG05332-04.

REFERENCES:

O-92 11:00 AM Tuesday, October 25, 2022

THE IMPACT OF AN ADAPTED SPIKES PROTOCOL VERSUS STANDARD OF CARE IN DELIVERING NEGATIVE PREGNANCY TEST RESULTS TO IVF PATIENTS: A MULTICENTER, RANDOMIZED CONTROLLED TRIAL. Alice D. Domar, Ph.D.,1 Ann Korkidakis, M.D., M.P.H.,2 Pietro Bortoletto, MD, MSc,3 Natalie B. Gulrajani, BS,4 Darya D. Khodakhah, BA,5 Kristin L. Rooney, B.A.,6 Annika D. Gompers, Ph.D.,7 Michele R. Hacker, Sc.D., M.S.P.H.,8 Elizabeth A. Grill, PsyD9 Boston IVF, Waltham, MA; 1, 4, 5 New York- Presbyterian Hospital/Weill Cornell Medical Center, New York, NY; 2, 6 Beth Israel Lahey Health, Boston, MA; 3 Harvard Medical School/Beth Israel Deaconess Medical Center, Boston, MA; 8 Weill Cornell Medical Center, New York, NY.

OBJECTIVE: To determine if the SPIKES protocol for delivering bad news is a more compassionate and effective communication method than the current standard of care for patients receiving negative pregnancy test results after an IVF cycle. SPIKES is a widely cited framework for presenting bad news to patients undergoing IVF.

MATERIALS AND METHODS: The SPIKES protocol was compared with a control group to determine the impact of using the SPIKES framework. The study included 163 patients from five IVF centers in the United States. Patients were randomized to receive bad news using either the SPIKES protocol or the standard of care. The SPIKES protocol includes the following components: Setting, Perception, Information, Empathy, Summary, and K-E-S (Knowledge, Empathy, Summary). The control group received bad news using the standard of care.

RESULTS: A total of 34 patients were randomized to the SPIKES group and 127 to the control group. The nurses were experienced, with a median length of 48 months (IQR 12-162) working in healthcare, and none had previously received SPIKES training. A total of 465 patients were invited to participate; 70 responded in the SPIKES group and 66 in the control group, yielding response rates of 30% and 29%, respectively. Baseline characteristics, including age, prior children, prior infertility treatment, and insurance coverage were similar between the groups. Thirty-three percent of the SPIKES patients reported that they felt “extremely sad” compared to 15% of the control patients. Of the 22 parameters of the CBR scale, SPIKES patients reported significantly more negative results than the control patients in eight categories. For example, 50% of respondents in the SPIKES group felt the “The nurse paced the information well” compared with 73% in the control group, (p=0.02). There were no categories where the SPIKES patients reported significantly more positive results. Compassion Scores were not significantly different between the SPIKES and control groups (34.7±13.7 vs. 37.8±12.5, p=0.25).

CONCLUSIONS: The use of the adapted SPIKES protocol when delivering negative pregnancy test results by phone to patients who underwent IVF did not provide any advantage to patients and, in fact, may lead to more distress.

IMPACT STATEMENT: Despite its effectiveness with other patient populations, the SPIKES protocol may not be a compassionate mode of delivering bad news to patients undergoing IVF.

O-93 11:15 AM Tuesday, October 25, 2022

UBIQUITIN C-TERMINAL HYDROLASE L1 (UCHL1) AND THE TERRIBLE, NO GOOD OVARIAN FOLLICLE. Alexis K. Gadson, MD,1 Morgan F. Woodman, BS,2 Kathryn J. Grive, PhD3 Warren Alpert Medical School of Brown University; Women & Infants Hospital, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Providence, RI; 1 Women & Infants Hospital of Rhode Island, Providence, RI; 2 Warren Alpert Medical School of Brown University; Women & Infants Hospital of Rhode Island, Providence, RI.

OBJECTIVE: Ubiquitin C-Terminus Hydrolase L1 (UCHL1) is a de-ubiquitinating enzyme enriched in human and mouse oocytes. Studies of UCHL1 post that it modulates activity of the epidermal growth factor receptor and overexpression leads to down-regulation of the estrogen receptor. UCHL1 also directly regulates protein stabilization and turnover in developing germ cells. Our lab has demonstrated that mice that are heterozygous or homozygous for UCHL1 deletion exhibit severe subfertility and aberrant ovulation, however the mechanism of these changes is not clear. Our objective is to explore the role of UCHL1 in the function of the murine ovarian follicle, as we hypothesize that UCHL1 loss of function results in reduced viability of granulosa cells, altered expression of steroidogenic enzymes, and ovarian and endocrine dysfunction.

MATERIALS AND METHODS: Animal protocols were approved by Brown University IACUC (#19-07-0001). Wild-type (WT), heterozygous (HET) and knockout (KO) mice from the B6.C-Uch1+/−/− line were sacrificed at 1 month and ovaries collected. Immunofluorescence of zona pellucida Protein 3 (ZP3) and Connexin 37 (CX37) was then performed by standard protocols and ovary sections imaged. TUNEL staining (Roche) was performed on sections from the same ovaries to assess cell death and different expression of ZP3. Additional studies included immunofluorescence for the zona pellucida which directly affects granulosa cell function. Future studies to elucidate the mechanistic role of UCHL1 in the zona pellucida which directly affects granulosa cell function. Our results suggest that UCHL1 KO mice demonstrate abnormal formation of the zona pellucida, qPCR analysis of Zp3 showed no significant change in mRNA expression despite increased ZP3 protein expression in KO oocytes. The secondary follies of KO mice also demonstrated less organized expression of CX37 molecules that regulate communication between the oocyte and the granulosa cells. TUNEL staining demonstrated a higher proportion of oocytes arrested in the secondary follicle stage in KO mice with increased rates of granulosa cell apoptosis in comparison to WT (p<0.001). This apoptosis coincides with altered expression of steroidogenic enzymes in isolated KO mural granulosa cells compared to WT. AqPCR of Cypr9a1, Hsd17b1, and Zp3 in technical replicates. Relative gene expression levels were compared by Student’s t-test.

RESULTS: UCHL1 KO mice demonstrate abnormal formation of the zona pellucida. qPCR analysis of Zp3 showed no significant change in mRNA expression despite increased ZP3 protein expression in KO oocytes. The secondary follicies of KO mice also demonstrate less organized expression of CX37 molecules that regulate communication between the oocyte and the granulosa cells. TUNEL staining demonstrated a higher proportion of oocytes arrested in the secondary follicle stage in KO mice with increased rates of granulosa cell apoptosis in comparison to WT (p<0.001). This apoptosis coincides with altered expression of steroidogenic enzymes in isolated KO mural granulosa cells compared to WT.

CONCLUSIONS: UCHL1 plays a crucial role in regulation of follicular function. Without it, the ovarian follicle fails to function properly leading to subfertility. Our results suggest that UCHL1 is required for the proper formation of the zona pellucida which directly affects granulosa cell function. Future studies to elucidate the mechanistic role of UCHL1 in the murine ovary are ongoing, including comprehensive assessment of the gene expression in WT and KO mural granulosa cells, with a focus on down-stream targets of UCHL1.

IMPACT STATEMENT: UCHL1 is a de-ubiquitinating enzyme that has a role in regulation of the expression of the estrogen receptor and ovarian steroidogenic enzymes. Abnormal expression of UCHL1 leads to poor formation of the zona pellucida and arrested development of ovarian follicles in mice.
OBJECTIVE: To determine whether the scope of coverage afforded by state infertility mandates and the proportion of the population eligible for mandated coverage are associated with a reduction in racial/ethnic inequities in assisted reproductive technology (ART) utilization.

MATERIALS AND METHODS: Cross-sectional ecological study of reproductive-aged women (20–44 years) living in the U.S. in 2018 based on Census Bureau estimates who initiated an ART cycle reported to the Centers for Disease Control and Prevention. States were classified as: Comprehensive, Limited, and No ART Mandate coverage. ART utilization was defined as the number undergoing ≥1 ART cycles per 10,000 reproductive-aged women. Differences in ART utilization were evaluated in two ways: 1) rates within each racial/ethnic group were compared across mandate categories using the Comprehensive Mandate group as reference; and 2) rates within each mandate category were compared across racial/ethnic groups using Non-Hispanic (NH) Asian as the reference group as they had the highest Comprehensive Mandate utilization rate. Rate ratios (RR) with 95% confidence intervals (CI) were calculated. Only fully-insured private insurance plan subscribers are eligible for coverage under state infertility mandates. Race-specific estimated proportions of populations eligible for coverage were used to correct denominators in the Comprehensive Mandate group.

RESULTS: In 2018, 147,803 women underwent ≥1 ART cycle with an overall utilization rate of 27.5 cycles/10,000 women. Across all mandate categories (Comprehensive, Limited, No Mandate, respectively), NH Asian (78.4, 69.0, 44.3 cycles/10,000 women) and NH White (57.3, 53.7, 32.3) populations had higher ART utilization than Hispanic (18.3, 10.2, 11.1), NH Black (25.8, 16.9, 10.1), and NH Other/Multiple Races (17.4, 19.0, 24.7) populations. The NH Other/Multiple Races and NH Black populations had the largest disparities in ART utilization rates when comparing the No Mandate to Comprehensive Mandate groups (RR 0.33 95% CI 0.28-0.38 and RR 0.39 95% CI 0.37-0.41, respectively). Within the Comprehensive Mandate group, utilization RRs moved towards the null after correcting for mandated coverage eligibility in Hispanic (from RR 0.23 95% CI 0.22-0.25 to RR 0.35 95% CI 0.33-0.37) and NH Black populations (from RR 0.33 95% CI 0.31-0.35 to RR 0.45 95% CI 0.42-0.47); demonstrating an attenuation in racial/ethnic differences in ART utilization.

CONCLUSIONS: The disparity in ART utilization between Comprehensive mandate and No Mandate groups was greatest for NH Black and NH Other/multiple populations. Differences in ART utilization in Hispanic and NH Black populations compared to the NH Asian population in Comprehensive Mandate states were attenuated when considering coverage eligibility. Despite these findings, inequities in ART utilization persist even in comprehensive mandate states.

IMPACT STATEMENT: Racial/ethnic inequities in ART utilization were smaller in states with comprehensive infertility coverage mandates; inequities were further attenuated after correcting for mandate eligibility.

SUPPORT: Financial disclosure: Support for this research was provided by Open Philanthropy through a grant to the CDC Foundation. Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC Foundation or the Centers for Disease Control and Prevention.
RESULTS: A total of 120,815 cycles (median = 10 cycles per participant; interquartile range: 4-21) from 9,295 women (8,129 vaccinated; 1,160 unvaccinated) were included. Forty-eight percent of participants received the Pfizer-BioNTech vaccine, 32% received Moderna, and 7% received Johnson & Johnson/Janssen. We found no evidence of a difference between mean menstrual cycle length in the unvaccinated and vaccinated participants prior to vaccination (0.16 days, 95% CI: -0.44, 0.75). Among vaccinated women, COVID-19 vaccination was associated with a small increase in cycle length for cycles containing the first dose (0.47, 95% CI: 0.17, 0.76) and cycles containing the second dose (0.36, 95% CI: 0.06, 0.65) of Pfizer-BioNTech or Moderna vaccines compared with pre-vaccination cycles. Cycles containing the single dose of Johnson & Johnson/Janssen were, on average, 1.22 days longer (95% CI: 0.41, 2.03) than pre-vaccination cycles. Post-vaccination cycles returned to average pre-vaccination length, with a 0.11 (95% CI: -0.17, 0.38) day increase in mean cycle length in the first cycle following vaccination, 0.12 (95% CI: -0.15, 0.40) in the second, -0.22 (95% CI: -0.50, 0.05) in the third, and -0.25 (95% CI: -0.52, 0.02) in the fourth cycle post-vaccination.

CONCLUSIONS: COVID-19 vaccination was associated with an immediate short-term increase in menstrual cycle length. However, the magnitude of this increase diminished in cycles following vaccination, and no association with cycle length persisted over time.

IMPACT STATEMENT: Menstrual cycle change following COVID-19 vaccination appears temporary and should not discourage women from becoming vaccinated.

ORAL ABSTRACT SESSION: ACCESS TO CARE

O-97 10:45 AM Tuesday, October 25, 2022

WHEN STATES REQUIRE FULLY-INSURED EMPLOYERS TO PROVIDE INSURANCE COVERAGE FOR IN-VITRO FERTILIZATION (IVF), DO SELF-INSURED EMPLOYERS FOLLOW SUIT? James M. Dupree, M.D., M.P.H., Jane Kitaevich, BA, AM, Sitara Murali, BS, Luca Borah, BA, SA, Kate Castle, BA, Anna Kirkland, PhD, JD University of Michigan, Ann Arbor, MI.

OBJECTIVE: In the United States, access to fertility care is mediated by health insurance coverage, and most reproductive-age adults receive insurance from their employers. Employers can be “fully-insured” and beholden to state insurance mandates or can be “self-insured” and exempt from state insurance mandates. Thirteen states mandate that fully-insured employers provide insurance coverage for IVF(1). However, 65% of adults with employer-sponsored insurance work for self-insured employers(2). Our objective was to evaluate the fertility coverage offered by self-insured employers in these 13 states, even though they are exempt from the state mandates.

MATERIALS AND METHODS: We obtained access to Leverage Global Consulting’s repository of employer-sponsored health insurance benefits documents, which is the largest known such repository. We identified benefits documents from self-insured employers operating in the 13 states with insurance mandates for IVF coverage. Then, we performed a content analysis of the benefits documents to systematically extract features of fertility coverage. All documents were independently coded by two trained reviewers using a coding protocol; conflicts were adjudicated by a third reviewer. We used Cohen’s Kappa to measure inter-reviewer agreement. Finally, we produced descriptive statistics detailing how many self-insured employers offer coverage for fertility care, including diagnostic testing, treatment for underlying conditions causing infertility, fertility preservation before cancer treatment, fertility medications, intrauterine insemination (IUI), and IVF.

RESULTS: We analyzed 189 health insurance benefits documents from self-insured employers in nine states (AR, CO, CT, IL, MA, MD, NJ, NY, UT) from 2019-2021. The Cohen’s Kappa was 85%, which is a very high level of coding agreement. Overall, 59.0% of employers offer coverage for fertility care. However, the spectrum of coverage varies widely, with some employers only covering diagnostic testing and excluding all treatments. Specifically, 29.1% of employers cover treatments for underlying conditions. 32.1% of employers cover fertility preservation. 46.8% of employers cover fertility medications. 57.9% of employers cover IUI and 42.1% cover IVF. Employees’ lifetime fertility spending limits range from $5,000 to $100,000.

CONCLUSIONS: 42% of self-insured employers operating in states with insurance mandates for IVF provide IVF coverage for their employees. In addition, there is significant variation in what types of other fertility treatments are covered, with most employers covering IUI but few covering fertility preservation.

IMPACT STATEMENT: For most Americans, limitations in their health insurance benefits remain significant barriers for accessing fertility care. State mandates are important targets for improving access to advanced fertility treatments like IVF. However, since 65% of adults with employer-sponsored health insurance work for self-insurance employers, which are exempt from state mandates, our data highlights a need for increased advocacy to self-insured employers.

SUPPORT: The University of Michigan Institute for Research on Women & Gender and Institute for Healthcare Policy and Innovation.

REFERENCES:
CHARACTERISTICS OF PATIENTS SEEKING FERTILITY CARE IN A LOW-INCOME SETTING. Miriam Tarrash, MD,1 Olutunmike Kuyoro, M.D.,1 M.D.,1 Randi H. Goldman, M.D.,2 Christine Mullin, M.D.1
1Northwell Health Fertility, Zucker School of Medicine at Hofstra Northwell, Manhasset, NY; 2Northwell Health Fertility, Northwell Health, Manhasset, NY.

OBJECTIVE: Patients face challenges accessing ART due to barriers such as financial burdens, delayed referral to reproductive endocrinologists (REI), low medical literacy, language barriers and numerous other health disparities. Women seeking fertility care from low resource, predominantly immigrant communities have greater disparities in fertility knowledge and overall lower health literacy compared to women from high resource clinical settings. Furthermore, studies show that education level and household income are associated with the total amount of money spent on fertility care affecting their chance of a live birth. Medicaid in New York offers coverage for office visits, blood tests, HSGs, and pelvic ultrasounds for infertility. Our uninsured and underinsured patients are referred to a resident/fellow REI clinic with limited available diagnostic and treatment options. The aim of this study is to delineate the characteristics of the underserved patient population and determine their ability to complete the initial fertility workup.

MATERIALS AND METHODS: This was a retrospective study of all patients seeking fertility care at a single resident/fellow REI clinic in New York from September 2020 – January 2022.

RESULTS: During the study period, 87 patients (avg age = 35.2 y) sought care at the resident/fellow clinic within 126 appointments. Of these, 66.7% of patients canceled the scheduled appointment, 80.5% of patients had Medicaid, 12.2% used Sliding Scale Health Center, and 2.3% had no health insurance. Most primary languages spoken included English (70.1%), Spanish (21.8%), and Bengali (3.4%). Documented Race was comprised of Other (46%), African American (21.8%), Asian (17.2%), White (11.5%), Native Hawaiian (1.1%), and Unknown (2.3%). Approximately 35% of the population identified as Hispanic or Latino. The majority of patients completed a lab workup (70-80% obtained AMH, which was typically drawn at the time of the initial visit, and day 3 labs). Fewer patients underwent a scheduled hysterosalpingogram (59.8%, of which 40.4% had abnormal findings). A smaller proportion of patients’ partners completed a semen analysis (27.6%, of which 50% had abnormal findings).

CONCLUSIONS: Patients have an easier time obtaining labs than imaging studies and partner workup, despite the majority of patients having insurance coverage for these tests. This suggests that the financial barrier may not be the greatest factor preventing completion of the fertility workup in this population. As such, understanding what factors govern and predict this default from care is undoubtedly an area requiring further exploration and ultimately may help to improve access to ART for underserved communities.

IMPACT STATEMENT: Completing the fertility workup, particularly the male partner workup and imaging studies, can present challenges for underserved patients with infertility.

SUPPORT: None.

REFERENCES:

O-100 11:30 AM Tuesday, October 25, 2022
FERTILITY PRESERVATION INSURANCE COVERAGE IN PROFESSIONAL SCHOOLS. Sonali Gupta, MD,1 Jawaria Amir, MD,1 Anna Petersen, BS,1 Sarala Prabhu, MA,1 Sadia Haider, MD, MPH,1 Slouve L. York, MD MPH,2 Chicago, IL; 2Yale University, Chicago, IL.

OBJECTIVE: To evaluate professional schools’ provision of elective fertility preservation (FP) coverage and determine if there are patterns in FP coverage by professional school type (medical, business, law), geographic region, or by presence/absence of mandated coverage laws in states.

MATERIALS AND METHODS: Using the U.S. News & World Report 2022, the top 100 medical, law, and business schools in the country were identified. A thorough review of schools’ websites was conducted to determine availability of student health insurance and policy documents. If information was not available online, up to 3 phone calls and 3 emails were sent to student affairs offices requesting coverage information.

RESULTS: Data was obtained for 96 medical, 95 law, and 93 business schools. 99% of master policies were found online and 1% were acquired via email. No schools offered coverage for elective FP. 79 schools (28%) provided FP coverage for iatrogenic (IA) infertility— 29 medical (30%), 21 business (42%), and 25 business (27%). Within these, 16 schools also explicitly covered FP in cases of gender-affirming (GA) surgery. Western and northeastern schools were significantly more likely to cover IA or GA FP [60% western, 48% northeastern, 17% midwestern, 6% southwestern, and 1% southeastern (p<0.00001)]. Western and northeastern schools were also significantly more likely to offer infertility diagnosis or treatment coverage (p<0.00001). Of 152 schools in the 19 states with some infertility coverage mandate, 49% covered IA or GA FP versus 3% of schools in states without infertility mandates (p<0.00001). Of 97 schools in the 11 states with an FP-specific coverage mandate, 73% covered IA or GA FP compared to 4% of schools in states without an FP mandate (p<0.00001).

CONCLUSIONS: As more women attend professional schools and prefer to delay childbearing, many will have an increased risk of infertility. Studies show that female physicians have a higher-than-average rate of infertility and some express regret about not proceeding with FP in the past. One solution would be improved FP coverage in professional women’s 20s and 30s. We explored insurance plans for professional students and remarkably found very little coverage for FP. Of the 284 schools surveyed, none covered elective FP and less than one-third covered medically necessary FP. Our findings indicate a large gap in coverage for this population for whom FP is critical for when fertility healthcare needs. There is a clear difference in coverage based on region and presence of state mandated coverage laws, which is important for both students and policy makers to consider.

IMPACT STATEMENT: Given the impact of future infertility on female professionals, school administration needs to understand the importance of providing FP coverage. Presence of mandated legislation in states may be an incentive for schools to provide coverage.

SUPPORT: None.

O-99 11:15 AM Tuesday, October 25, 2022
STATE MANDATED INSURANCE IS ASSOCIATED WITH REDUCED RACIAL DISPARITIES IN ACCESS AND LIVE BIRTH RATES FOR EGG RECIPIENTS - AN ANALYSIS OF 44,033 CYCLES FROM THE SART CORS DATABASE FOR 2014-2016. Caiyun Liao, M.D., M.P.H, 1 Alexander Kotlyar, M.D., 2 David B. Seifer, MD 3 1Yale School of Medicine, 2Yale University, New Haven, CT.

OBJECTIVE: To determine the impact of state insurance mandates on donor oocyte assisted reproductive technology (ART) outcomes in relation to recipient’s race/ethnicity.

MATERIALS AND METHODS: This is a retrospective cohort study of ART cycles utilizing donor oocytes 2014-2016, as reported to the Society for Assisted Reproductive Technologies Clinic Outcome Reporting System (SART CORS). Race/ ethnicity distribution among oocyte recipients was compared to that in the 2016 United States (US) census. The probability of ever achieving a live birth through one or more donor ART cycles 2014-2016 was compared across racial/ethnic groups using multivariable Poisson regression and stratified by state insurance mandate for donor oocyte ART coverage.

RESULTS: We analyzed 44,033 donor ART cycles performed for 28,157 oocyte recipients, 98% of whom ranged 26-53 in age. Race and ethnicity were reported for 17,281 recipients, 66.2% of whom identified as non-Hispanic White (NHW), while 58.9% reported to be NHW among women aged 25-54 in the 2016 US census. The probability of ever achieving a live birth through one or more donor ART cycles 2014-2016 was compared across racial/ethnic groups using multivariable Poisson regression and stratified by state insurance mandate for donor oocyte ART coverage.

SUPPORT: None.

O-101 11:45 AM Tuesday, October 25, 2022
embryos, and polycystic ovary syndrome demonstrated that NHB recipients were less likely to achieve a live birth compared with their NHW counterparts. In non-mandated states (incidence rate ratio (IRR) 0.82, 95% confidence interval (CI) 0.77-0.87), as were Asian recipients (IRR 0.96, 95% CI 0.93-0.99). However, live birth rates were comparable across all races/ethnicities in mandated states and oocyte recipients were more likely to achieve a live birth if they lived in a mandated state, regardless of race/ethnicity (IRR 1.11, 95% CI 1.05-1.17).

CONCLUSIONS: Women of color were underrepresented among donor oocyte recipients in the US. Although racial disparities existed in live births following donor ART in non-mandated states, states with insurance mandates were associated with narrowed disparities in outcomes and improved live birth rates in donor ART cycles regardless of race/ethnicity.

IMPACT STATEMENT: These data suggest that by expanding access through state insurance mandates, live birth rates after donor ART may be improved and racial disparities in donor ART outcomes may be mitigated.

O-102 12:00 PM Tuesday, October 25, 2022

EARLY ATRAITION AFTER ACCESS TO FERTILITY CARE: RACIAL DISPARITIES IN COMPLETION RATES OF FERTILITY WORK-UP. Alexandra Acker, MD,1 Nathan C. Koelper, MPH,2 Anuja Dokras, MD, PhD,3 Suneeta Senapati, MD, MSCE1 1University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; 2UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, Philadelphia, PA; 3University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: To identify risk factors for attrition after initial consultation to fertility care.

MATERIALS AND METHODS: All patients who presented to an academic center for a new fertility patient visit from September 2020 to June 2021 were identified. Patients who identified as Black or White and had 3 or more components included in the fertility work-up (labs tests, ultrasound cavity/tubal evaluation, semen analysis, and genetic screening) were included. Standard statistical tests were used to determine differences by race. Logistic regression was used to determine the association between patient characteristic and work-up completion.

<table>
<thead>
<tr>
<th></th>
<th>Black (n=125)</th>
<th>White (n=209)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>32.9 ± 5.21</td>
<td>34.9 ± 4.19</td>
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</tr>
<tr>
<td>Marital Status</td>
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<tr>
<td>Married</td>
<td>48 (38.4)</td>
<td>163 (78.0)</td>
<td>0.001</td>
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<tr>
<td>Single</td>
<td>66 (52.8)</td>
<td>33 (15.9)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>11 (8.8)</td>
<td>13 (6.2)</td>
<td></td>
</tr>
<tr>
<td>Duration of infertility**</td>
<td>24 [12-43.5]</td>
<td>12 [7-24]</td>
<td>0.001</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Public</td>
<td>36 (28.8)</td>
<td>14 (6.70)</td>
<td>0.001</td>
</tr>
<tr>
<td>Private</td>
<td>87 (69.6)</td>
<td>194 (92.8)</td>
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</tr>
<tr>
<td>No insurance</td>
<td>2 (1.6)</td>
<td>1 (0.5)</td>
<td></td>
</tr>
<tr>
<td>Insurance coverage for diagnostic testing</td>
<td>93 (74.4)</td>
<td>200 (95.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Insurance coverage for treatment</td>
<td>65 (52.0)</td>
<td>162 (77.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Work-up in 90 days</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>54 (43.2)</td>
<td>146 (69.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Incomplete</td>
<td>44 (35.2)</td>
<td>46 (22.1)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>27 (21.6)</td>
<td>17 (8.1)</td>
<td></td>
</tr>
<tr>
<td>Length of time to work-up completion &lt; 90 days**</td>
<td>27 [16-36]</td>
<td>30 [22-44]</td>
<td>0.118</td>
</tr>
</tbody>
</table>

*Mean ± SD
**Median [IQR]

RESULTS: Of the 334 patients (Black n=125, White n=209), Black patients were more likely to be younger (p=0.001), single (p=0.001), and experience infertility for a longer duration (p=0.02) than White patients. Black patients were also more likely to have public insurance (p=0.001) and less likely to have insurance coverage for diagnostic testing (p=0.001) or subsequent infertility treatment (p=0.001). Despite longer duration of reported infertility prior to first consult, more Black patients did not complete any work-up tests compared to White patients (21.6% vs 8.1%, p=0.001). After adjusting for marital status, infertility duration, insurance, and diagnostic testing, Black women were less likely to complete the fertility work-up within 90 days of first consult (aOR 0.41, 95% CI, 0.23-0.74, p=0.003) when compared with white women.

CONCLUSIONS: Significant racial disparities identified in completing fertility diagnostic work-up may contribute to reported disparities in access to assisted reproductive technologies. Further studies are needed to identify barriers specific to the Black race.

IMPACT STATEMENT: In order to offer equitable fertility care, it is critical to dismantle barriers and disparities along the entire fertility journey.

SUPPORT: None.

ORAL ABSTRACT SESSION: ANDROGEN EXCESS AND POLYCYSTIC OVARY SYNDROME

O-103 10:45 AM Tuesday, October 25, 2022

THE PROINFLAMMATORY CYTOKINE RESPONSE TO SATURATED FAT INGESTION IS INDEPENDENT OF ABDOMINAL ADIPOSITY (AA) IN POLYCYSTIC OVARY SYNDROME (PCOS). Frank Gonzalez, M.D.,1 Robert V. Considine, Ph.D.,2 Ola A. Abdelhadi, M.D., Ph.D.,3 Anthony J. Acton, Jr., B.S.3 University of Illinois at Chicago College of Medicine, Chicago, IL; 1Indiana University School of Medicine, Indianapolis, IN; 3University of California at Berkeley School of Public Health, Berkeley, CA.

OBJECTIVE: Lipid-stimulated inflammation is increased in PCOS independent of obesity.1 We evaluated the effect of saturated fat ingestion on tumor necrosis factor-alpha (TNFα) and interleukin-6 (IL-6) secretion from mononuclear cells (MNC) of women with PCOS who were either normal weight with and without AA or who were obese, compared with body composition-matched ovulatory controls; and its relationship with insulin sensitivity and HCG-stimulated ovarian androgen secretion.

MATERIALS AND METHODS: We studied 30 women with PCOS (7 normal weight [NW] with AA, 7 NW without AA, 8 obese) diagnosed on the basis of oligo-amenorrhea and hyperandrogenemia and 30 ovulatory controls (7 NW with AA, 7 NW without AA, 8 obese) ages 18-40. AA was defined as the % ratio of truncal fat to total body fat measured by DEXA that was >2SD above the mean of NW controls without AA. MNC were isolated from blood samples drawn while fasting and 3 hours after dairy cream ingestion (100 ml). TNFα and IL-6 were measured by ELISA in MNC culture supernatants. Androgens were measured by RIA from blood samples drawn fasting and 24, 48 and 96 hours after HCG administration (5000 IU). Insulin sensitivity was derived by ISOGTT.

RESULTS: In response to saturated fat ingestion, the absolute change in MNC-derived cytokine secretion increased in both NW PCOS groups, and was significantly different compared with either NW control group which decreased (TNFα – NW with AA: 24.1±11.1 vs. -11.2±3.9, p<0.02; NW without AA: 19.0±8.3 vs. -18.2±7.4, p<0.01; IL-6 – NW with AA: 17.2±5.0 vs. -12.1±5.1, p=0.004; NW without AA: 14.3±5.6 vs. -19.2±4.1, p<0.002). In contrast, the lipid-stimulated cytokine response increased in both obese groups (TNFα – PCOS: 38.9±11.0; controls, 30.9±11.2; IL-6 – PCOS: 26.3±9.0; controls, 21.8±6.7) and was significantly (p<0.004) different compared with the response of either NW control group. Compared with controls, all 3 PCOS groups exhibited greater (p<0.05) HCG-stimulated area under the curve (AUC) for testosterone (T) (NW with AA: 6466±775 vs. 3858±531, NW without AA: 6157±1026 vs. 3064±587, obese: 82.7±1357 vs. 361±158) and androstenedione (A) (NW with AA: 501±35 vs. 307±24, NW without AA: 516±38 vs. 300±36, obese: 573±60 vs. 288±20). For the combined groups, the lipid-stimulated cytokine response was positively correlated with HCG-stimulated androgen AUC (TNFα – T: r=0.32, p<0.04; A: r=0.35, p<0.03; IL-6 – A: r=0.40, p<0.009), and negatively correlated with ISOGTT (TNFα: r=-0.51, p<0.0006; IL-6: r=-0.55, p<0.0002).
CONCLUSIONS: Lipid-stimulated cytokine secretion is increased in PCOS independent of adiposity. We speculate that this proinflammatory phenomenon in PCOS promotes hyperandrogenism and insulin resistance, and is further perpetuated by AA.

IMPACT STATEMENT: Inflammation triggered by saturated fat ingestion is inherent to PCOS and may underpin the endocrine and metabolic features of the disorder.

SUPPORT: NIH grant R01 DK-107605 to F.G.

REFERENCES:

O-104 11:00 AM Tuesday, October 25, 2022

CARDIOVASCULAR AND METABOLIC OUTCOMES AMONG PCOS PARTICIPANTS IN THE CARDIA COHORT. Ange Wang, MD,1 Cora Elizabeth Lewis, MD, MSPH,1 Stephen Sidney, MD, MPH,1 Heather Gibson Huddleston, MD1 (University of California, San Francisco, San Francisco, CA;2 University of Alabama at Birmingham;3 Kaiser Permanente Division of Research, Piedmont, CA;4 University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: To investigate the incidence of and time to development of cardiovascular events and multiple metabolic outcomes (hypertension, hyperlipidemia, diabetes) by polycystic ovary syndrome (PCOS) status among participants in the Coronary Artery Risk Development in Young Adults (CARDIA) cohort.

MATERIALS AND METHODS: We utilized a population-based sample of Black and White women across the United States enrolled in CARDIA, a 30-year prospective, multicenter, observational study. Participants were enrolled in 1985 and 1986, at ages 18-32, and have been followed for up to 30 years (mean age 25.2 years at baseline). PCOS was defined as meeting U.S. National Institutes of Health (NIH) criteria based on androgen levels at year 2 and symptoms of oligomenorrhea and hirsutism, ascertained at Year 16. Our primary outcomes were adjudicated cardiovascular events (obtained annually); and hypertension, hyperlipidemia, and diabetes (ascertained at years 5, 7, 10, 16, 20, 25, and 30). We used multivariate logistic regression models to estimate the association between PCOS and incidence of outcomes through year 30 with adjustment for founders. We also used Cox proportional hazards models to investigate time to development of outcomes in both the PCOS and non-PCOS subjects.

RESULTS: Of 1,112 participants in the CARDIA cohort with PCOS status available, 81 (7.8%) met criteria for PCOS; while remaining 1,031 (92.3%) did not. The groups were similar for characteristics measured at baseline, including age, BMI, smoking/drinking status, and income. There were a total of 69 cardiovascular events (66 non-PCOS – 6.4%, 3 PCOS – 3.7%), 460 hypertension cases (425 non-PCOS – 41.2%, 35 PCOS – 43.2%), 393 hyperlipidemia cases (347 non-PCOS – 34.7%, 35 PCOS – 43.2%), and 250 diabetes cases (228 non-PCOS 22.1%, 27 PCOS – 33.3%). On multivariable logistic regression, PCOS was significantly associated with incident diabetes (OR for PCOS 2.07 95% CI 1.23-3.46 p = 0.006), but not cardiovascular events (OR 0.68 95% CI 0.21-2.28, p = 0.54), hypertension (OR 1.40, 95% CI 0.85-2.29, p = 0.19), or hyperlipidemia (OR 1.52 95% CI 0.95-2.41, p = 0.08). On Cox proportional hazards analysis, PCOS was significantly associated with time to development of diabetes (HR for PCOS 1.74, 95% CI 1.16-2.59 p = 0.007), hypertension (HR 1.66 95% CI 1.17-2.35, p = 0.004), and hyperlipidemia (HR 1.46, 95% CI 1.03-2.08, p = 0.03) but not cardiovascular outcomes. CONCLUSIONS: Incidence of diabetes, but not other metabolic conditions, was associated with PCOS in the CARDIA cohort. PCOS was also associated with faster time to development of diabetes, hypertension, and hyperlipidemia. We did not observe an increased number of cardiovascular events, although the number of events was small in these mid-life participants. In addition, the mean baseline BMI in our cohort was in the non-obese range; further investigation of the impact of PCOS status in other BMI classes is warranted.

IMPACT STATEMENT: Our CARDIA study extends prior literature that PCOS is associated with increased risk of diabetes and earlier time to develop hypertension, diabetes and hyperlipidemia, independent of BMI.

O-105 11:15 AM Tuesday, October 25, 2022

IDENTIFICATION OF NOVEL PCOS-RISK ALLELES BY LARGE-SCALE GENOME WIDE META-ANALYSIS PROVIDES NEW INSIGHTS INTO BIOLOGICAL MECHANISMS AND CLINICAL HEALTH OUTCOMES. Loes Moolhuysen, MSc,1 Felix R. Day, PhD,2 Tugce Karaderi, PhD,1 Benjamin H. Mullin, PhD,1 Jia Zhu, MD,1 Natalia Pujol Gualdo,2 Ky Era V. Actkins, PhD,2 Corinne K. Welt, MD,2 Yvonne Louwers, MD, PhD,1 Jenny A. Visser, Ph.D.,11 Joop Laven, MD, PhD1 (Erasmus Medical Center, Rotterdam, Netherlands; 2MRC Epidemiology Unit, Cambridge Biomedical Campus, University of Cambridge School of Clinical Medicine, Cambridge, United Kingdom; 3Center for Health Data Science, Faculty of Health and Medical Sciences, University of Copenhagen, 2200 N Copenhagen, Denmark; 4School of Biomedical Sciences, University of Western Australia, Perth, Western Australia, Australia; 5Division of Endocrinology, Boston Children’s Hospital, Boston, MA 02115, USA; 6Estonian Genome Centre, Institute of Genomics, University of Tartu 51010, Tartu, Estonia; 7National Institute of Environmental Health Sciences, Durham, NC; 8University of Utah, Salt Lake City, UT; 9Erasmus University Medical Center, Rotterdam, Netherlands; 10Erasmus MC, Rotterdam, Netherlands.

OBJECTIVE: To perform the largest genome-wide association study (GWAS) meta-analysis in women with polycystic ovary syndrome (PCOS) to identify novel genetic associations, and hence, biological pathways involved in the etiology of the syndrome, and to understand the clinical implications of the genes involved in PCOS.

MATERIALS AND METHODS: A large fixed-effect, inverse-variance weighted meta-analysis was performed by the PCOS Consortium in 11,653 PCOS cases and 423,614 controls from 13 cohorts of European (86.5%), Hispanic (1.3%), African American (2.2%) and East Asian (10%). We performed an all ancestries combined and European only meta-analysis, using age-adjusted and age- and BMI-adjusted models. These results were then combined with previously published European GWAS meta-analysis summary statistics reaching a total of 21,570 PCOS cases and 523,971 controls. Secondary analysis included annotation of the identified variants and Summary-data-based Mendelian Randomization (SMR) in relevant traits to link PCOS-risk alleles to genes of interest. Furthermore, potential associations between identified loci and other metabolic and endocrine phenotypes within PCOS were explored through additional polygenic risk score (PRS) analysis and MR-based analysis were performed to study the links between PCOS and other traits of interest.

RESULTS: In total, 19 loci were identified in the all-ancestries meta-analysis, of which 7 loci were novel, and 12 loci replicated previously reported risk-alleles. The newly identified variants included for the first time the FTO gene, supporting the reported association between PCOS and BMI. No heterogeneity was observed between the different criteria that have been used to identify PCOS cases. Using SMR analysis we identified several potential effector genes acting through PCOS-relevant tissues, including the NEIL2 gene located at 8q23.1. Similar to the previous GWAS even more risk alleles could be linked to genes known play a role in reproductive hormonal pathways, including FSHβ, SHBG, INHBB and TEX41. Interestingly, several identified variants are in or near genes that play a role in DNA-repair mechanisms, such as NEIL2, MSH6, CHEK2 and RAD50, implicating the importance of these pathways in the pathophysiology of PCOS. Annotation of the identified PCOS loci with the publicly available GWAS results showed multiple associations with age at menopause, which was confirmed by additional post-GWAS analyses showing a causal association between PCOS and later age at menopause. Also, other PRS associated traits demonstrated an impact of PCOS-risk alleles on cardiovascular, metabolic and mental health outcomes in both men and women.

CONCLUSIONS: The current study identified novel PCOS-risk alleles, providing new insights into biological mechanisms involved in PCOS etiology and disease implications for women with PCOS.

ACKNOWLEDGEMENTS: Abstract is presented on behalf of the PCOS Consortium.
OBESITY PCOS DISPLAED COMPROMISED GLUCOSE METABOLISM ALONG WITH ALTERED FEEDING, SLEEPING, AND ACTIVITY PATTERNs. Alexandra Gannon, M.D., Janet Bruno-Gaston, M.D., Vinip A. Vidyadharan, Ph.D., Shaji Chacko, Ph.D., Marta L. Fiorotto, Ph.D., Juan Marini, Ph.D., Amy K. Schutt, M.D., M.S.C.I., William Gibbons, M.D., Chellakkan Selvanesan Blesson, B.S.C., M.P.H.I., M.C.S., Ph.D., Inka Dideijiu, M.S., Baylor College of Medicine, Houston, TX; Baylor College of Medicine; Dept. of Obstetrics & Gynecology, Houston, TX.

OBJECTIVE: Metabolic characterization of obese polycystic ovary syndrome (PCOS) using a dihydrotestosterone induced obese PCOS mouse model. MATERIALS AND METHODS: An obese PCOS mouse model was made by post-pubertal placement of controlled release of a dihydrotestosterone (DHT) or a placebo pellet in the control group. We compared baseline characteristics of obese PCOS mice to controls by measuring body weight over time, body mass index (BMI), body composition and estrous cycles. We compared total glucose production rate (GPR) with their respective controls in both fasting and glucose-rich/simulated-fed states by measuring the pentactenatinate derivative of deuterium-enriched glucose using isotopic ratio mass spectrometry. We compared expression of signaling molecules involved in insulin signaling by performing qPCR and Western blot on liver and ovary. We evaluated differences in feeding and activity patterns, total energy expenditure and body composition using Comprehensive Laboratory Animal Monitoring System.

RESULTS: There was significant increase in body weight in the PCOS group when compared to controls starting one week after DHT pellet insertion until the termination of the experiment at 3 months of age (p<0.0001). Obese PCOS mice had increased BMI at 3 months (0.34 g/cm² in Obese PCOS vs 0.29 g/cm² in controls; p<0.0001) with increased in body fat (3.3g in PCOS vs. in controls; 2.5g; p<0.05) and lean mass (20.3g in PCOS vs. in controls; 17.4g; p<0.0001). All obese PCOS mice were acyclic and were persistently in diestrus phase. Suppression of GPR was greater in obese PCOS mice (54±5% in PCOS vs 40±5% in controls; p<0.05). Multiple metabolic pathways, including the glycolytic pathway were affected in the obese PCOS ovary and liver as measured by mRNA and protein expression. Although, there was no difference in the overall feed intake, obese PCOS mice ate more than controls during the daytime (1.5g in PCOS vs. 1.3g in controls; p<0.05). Obese PCOS mice had a higher resting metabolic rate and total energy expenditure (9.9 kcal/d vs 9.2 kcal/d in controls; p<0.0001). The PCOS group had decreased ambulatory and fidgeting activities, increased maximum sleep bout length and extended sleep time during day but had decreased maximum sleep bout length during night. CONCLUSIONS: Obese PCOS mice demonstrate increased suppression of GPR and altered expression of RNA and protein in multiple metabolic pathways in liver and ovary. Obese PCOS mice ate more during day and had decreased activity patterns along with dysregulated sleep pattern when compared to controls. IMPACT STATEMENT: Androgen driven obesity in classical PCOS is due to increased in both lean and fat mass along with changes in feeding, sleep, and activity patterns. Further, they also have defective glycolytic pathway and dysregulated sleep pattern when compared to controls.

SUPPORT: None.

O-107 11:45 AM Tuesday, October 25, 2022

POLYCYSTIC OVARY SYNDROME (PCOS) IS ASSOCIATED WITH AN INCREASED RISK OF EUPLOID PREGNANCY LOSS: A SART CORS ANALYSIS OF 56,564 FROZEN EMBRYO TRANSFERS. Jennifer B. Bakkenes, MD, Christina E. Boots, MD, MSCI Northwestern University Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: Prior studies have suggested that an increased risk of pregnancy loss among patients with polycystic ovary syndrome (PCOS) may be attributable to embryonic aneuploidy. The objective of this study was to evaluate the association of PCOS with pregnancy outcomes following euploid frozen embryo transfer (FET).

MATERIALS AND METHODS: First single autologous euploid FETs from SART CORS 2016-2019 were included. Cycles from patients with recurrent pregnancy loss or uterine factor were excluded. Cycle characteristics were compared between cycles with and without PCOS using ANOVA or chi-square. Multiple logistic regression was used to determine odds ratios (OR) with 95% confidence intervals (CI) for cycle outcomes adjusting for age at transfer, race, parity, prior pregnancy loss, smoking, BMI, PGT indication, and PGT methodology (p < 0.05 = significant).

RESULTS: Characteristics and outcomes of cycles with and without PCOS (N = 56,564 cycles). CONCLUSIONS: PCOS is associated with increased odds of pregnancy loss and decreased odds of live birth following euploid FET.

POLYCYSTIC OVARY SYNDROME AND DIFFERENCES IN BRAIN HEALTH AT MID-LIFE: RESULTS FROM THE CARDIA COHORT. Heather Gibson Haddleton, MD, Eleni Jasua, Kaitlin Casalotto, PhD, John Neuhaus, PhD, Kristine Yaffe, MD University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; UCSF, San Francisco, CA; University of California, San Francisco; University of California San Francisco, San Francisco, CA.

O-108 12:00 PM Tuesday, October 25, 2022

ASRM Abstracts
OBJECTIVE: Increasing evidence links metabolic disorders, such as diabetes, to accelerated cognitive aging. Our objective was to use the Coronary Artery Risk Development in Young Adults (CARDIA) cohort to investigate the association between polycystic ovary syndrome (PCOS) and key indicators of mid-life brain health, including cognitive performance and brain MRI features.

MATERIALS AND METHODS: CARDIA recruited black and white individuals from the US for a prospective observational study. Participants enrolled in 1985, at ages 18-30, and have been followed for over 30 years. We identified subjects with PCOS as those with elevated androgen levels (year 2) and symptoms of oligomenorrhea and hirsutism (year 16 as part of the CARDIA Women's Study). At year 30, participants completed a cognitive testing, including Rey Auditory Verbal Learning Test (RAVLT) (verbal learning/memory); Digit Symbol Substitution Test (DSST) (processing speed/executive function); Stroop (attention/cognitive control); and category and letter fluency tests (semantics/attention); lower scores indicate lower performance. A subset also completed brain MRI studies. Multivariate regression models estimated associations between PCOS and outcomes. Models were adjusted using propensity score analyses, considering age, race, education, study center, year of MRI, and intracerebral volume (structural measures only).

RESULTS: Of 910 participants with cognitive testing, 65 (7.1%) met criteria for PCOS. At baseline both groups were similar for age, BMI, smoking/drinking status, and income. At year 30 (mean age 55.2), PCOS participants had lower performance on several measures, including Stroop (attention), RAVLT (memory) and category fluency (semantics). Of 291 subjects with MRI’s, 25 (8.5%) had PCOS. There was no difference in gray or white matter volume between groups, however PCOS participants demonstrated decreased total white matter fractional anisotropy, a measure of white matter integrity (Coef (95% CI): -0.01(-0.021, -0.005); p=.003).

Table Coefficient (95% CI) p
Stroop -4.0 (-0.69, -7.37) .018
DSST -0.55 (-4.5, 3.4) NS
RAVLT -1.14 (-0.45, 0.17) .043
Category Fluency -1.13 (-2.6, -0.003) .049
Letter Fluency -0.01 (.1, 1.6) NS

CONCLUSIONS: Our results suggest that PCOS status associates with lower cognitive performance and decreased white matter integrity at mid-life. Additional research is needed to confirm these findings and to determine potential mechanistic pathways.

IMPACT STATEMENT: PCOS is known for its reproductive and metabolic manifestations. Our study now raises the possibility of adverse cognitive aging in individuals with this highly prevalent disorder.

SUPPORT: UCSF Intramural RAP Grant.

ORAL ABSTRACT SESSION: CONTRACEPTION AND COMPLEX FAMILY PLANNING

O-109 11:30 AM Tuesday, October 25, 2022
THE EFFECT OF HORMONAL CONTRACEPTION USE ON OVARIAN RESERVE MARKERS IN THOSE SEEKING INFERTILITY EVALUATION. Dana R. Siegel, MD,1 Joelien Friesa, BA,2 Angela Fought, MS,2 Jeanelle Sheeder, PhD,2 Karen Hampanda, PhD, MPH,2 Leslie Coker Appiah, MD,2 University of Colorado Anschutz Medical Campus, Aurora, CO;1 The University of Colorado School of Medicine - Anschutz Medical Campus, Aurora, CO.

OBJECTIVE: To determine if women seeking evaluation for infertility who used long-term (>2 years) hormonal contraception (HC) have lower ovarian reserve (OR) markers and higher uptake of assisted reproductive technology (ART) than short-term (<2 years) or non-HC users.

MATERIALS AND METHODS: A cross-sectional survey was disseminated to adult patients seen at the University of Colorado Advanced Reproductive Medicine (CU ARM). The survey consisted of 29 items that explored contraceptive, reproductive, and medical history. A retrospective chart review was then performed to gather data including anti-Müllerian hormone (AMH), follicle stimulating hormone (FSH), antral follicle count (AFC), hysterosalpingogram (HSG) and/or saline-infusion sonohystogram (SIS). Analysis included descriptive statistics and bivariate comparison (Chi Squared, t-test, or Mann-Whitney Wilcoxon test), followed by linear regression models to compare OR markers by HC use.

RESULTS: OR markers were available for 166/198 eligible participants who completed the survey. Of those, 123 had documented discontinuation of HC prior to OR assessment. Mean age was 33.4 years (SD=4.5) and 79.7% (98/123) reported a history of long-term HC use. The majority of those (84.7%: 83/98) stopped using for >12 months prior to infertility evaluation. The most used HC was oral contraceptive pills (48.6%). Median OR markers did not significantly differ (p>0.05) between long-term and short-term/no HC users (AMH: 2.4 vs 3.2; AFC: 18 vs. 26; FSH: 7.6 vs. 6.3) even after adjusting for age and history of polycystic ovarian syndrome (PCOS) in the linear regression models. However, for each additional year that a patient stopped using long-term HC, there was, on average, a 0.05 increase in AMH (p=0.05). There was also a marginally significant (p=0.06) difference in the uptake of ART between long-term (64.3%) and short-term/no HC users (44.0%), specifically in the use of in vitro fertilization (IVF) (60.7% vs 18.2%, p=0.01). Ovulation induction was more likely to result in conception (p=0.01) and live birth (p=0.01) among short-term/no HC users (24.0% and 20.0%) versus long-term users (7.1% and 4.1%) but no other differences in conception or pregnancy outcomes were found.

CONCLUSIONS: OR markers may be artificially decreased in recent long-term HC users, resulting in an increased use of ART.

IMPACT STATEMENT: The findings from this study suggest that the length of time a patient has discontinued long-term HC may affect certain OR markers, but overall, long-term HC use should not impact fertility outcomes.

SUPPORT: None.

O-110 11:00 AM Tuesday, October 25, 2022
RECENT TREND OF SURGICAL STERILIZATION AND LONG-ACTING REVERSIBLE CONTRACEPTION USE AT VAGINAL DELIVERY. Alexandra M. McGough, BA, Heather E. Sweeney, MD, Rachel S. Mandelbaum, MD, Joseph G. Ouzounian, MD, MBA, Koji Matsuo, MD, PhD University of Southern California, Los Angeles, CA.

OBJECTIVE: To examine national-level trends of patients who received surgical sterilization (SS) or long-acting reverse contraceptives (LARC) immediately following vaginal delivery in the United States.

MATERIALS AND METHODS: The National Inpatient Sample was queried retrospectively and vaginal deliveries from 10/2016-12/2019 were analyzed (n=8,013,785). Exposure allocation was per SS (bilateral tubal ligation [BTL] or bilateral salpingectomy [BS]) or LARC use (intrauterine device [IUD] or subdermal contraceptive implant [SCI]). The primary outcome measure studied was the utilization of SS or LARC over time, assessed with linear segmented regression with log transformation (year-quarter increments).

RESULTS: The number of patients undergoing SS decreased from 1.90% to 1.55% (18.4% relative-decrease, P<0.001) and those receiving LARC increased from 0.35% to 1.02% (191% relative-increase, P<0.001) during the study period. Among the SS types, BTL cases decreased from 0.66% to 0.18% (72.7% relative-decrease, P<0.001) whereas BS cases were unchanged from 1.24% to 1.37% (P=0.298). Among LARC types, both IUD (0.22% to 0.52%, P<0.001) and SCI (0.12% to 0.50%, P<0.001) increased during the study period, but the interval increase was higher for SCI compared to IUD (relative-increase 31% versus 136%). Across the four exposure groups, the most frequent procedure in the last quarter of 2019 was BS (1.37%) followed by IUD (0.52%), SCI (0.50%), and BTL (0.18%).

FERTILITY & STERILITY®
CONCLUSIONS: There appears to be a national-level shift from SS to LARC in recent years in the United States. This shift is mainly due to the decrease in BTL and increase in SCI.

IMPACT STATEMENT: Decreasing utilization of SS in favor of LARC may signify improved education regarding the excellent efficacy of LARC as well as greater access to non-permanent contraceptive methods in the immediate postpartum period. Understanding these trends will not only allow for improved patient counseling but also hopefully fuel further research on additional LARC methods giving increasing national interest and uptake.

O-111 11:15 AM Tuesday, October 25, 2022
DELADED FAMILY BUILDING AND INFERTILITY AMONG WOMEN IN MEDICINE: KNOWLEDGE IS NOT ENOUGH. Jennifer B. Bakkensen, MD,1 Angela K. Lawson, Ph.D.,1 Karishma Desai, BA,1 Lia A. Bernardi, M.D.,1 Elaine O. Cheung, Ph.D.,2 Patricia I. Moreno, Ph.D.,2 Kara N. Goldman, MD,2 Eve C. Feinberg, MD2 Northwestern University Feinberg School of Medicine, Chicago, IL; 3Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL.; 4Northwestern University Feinberg School of Medicine, Department of Medical Social Sciences, Chicago, IL; 4University of Miami Miller School of Medicine, Department of Public Health Sciences, Miami, FL.

OBJECTIVE: Women in medicine experience unique challenges regarding fertility and family building. The objective of this study was to characterize patterns of delayed family building and prevalence of infertility among female physicians, and to assess the association with fertility knowledge.

MATERIALS AND METHODS: An electronic survey assessing demographics, family building, and fertility was distributed to female physicians via a national social media campaign from March-April 2022. Multiple choice questions were asked assessing age-related fertility decline and monthly chance of conception. Chi square analyses were used to test the association between fertility knowledge, delayed family building, and infertility as well as the association between infertility and family building regret.

RESULTS: 741 female physicians including 512 attendings, 66 fellows, and 89 residents from academic, private, and community practice settings completed the survey (mean age = 38.8 years, SD = 7.69). The majority of respondents were heterosexual (n = 670, 90.4%), married/partnered (n = 632, 85.5%), and had children (n = 496, 66.9%).

Fertility knowledge was high, with 75.6% of respondents correctly identifying the age of precipitous fertility decline, and the majority identifying the approximate monthly chance of conception by age. Despite this, 78.9% reported delaying family building due to medical training or specialty choice and 38.6% had experienced infertility. Among those with infertility, 54.9% had used IVF to conceive.

Women who intentionally delayed family building for 3 or more years were more likely to experience infertility than those who delayed 0-3 years (p < 0.001). High fertility knowledge did not prevent postponement of family building; there was no relationship between fertility knowledge and years of delayed fertility.

When asked in retrospect what they would do differently, respondents who experienced infertility were more likely to strongly agree that they would have tried to conceive earlier (77.6% vs. 22.4%, p < 0.001) or pursued oocyte vitrification (78.2% vs. 21.8%, p < 0.001).

CONCLUSIONS: In this large national survey of female physicians from diverse specialties and practice locations, the majority of respondents reported delaying childbearing due to medical training and/or choice of specialty. While this delay was associated with infertility and family planning regret, it was not due to lack of fertility knowledge.

IMPACT STATEMENT: This national survey of female physicians is the largest to date and highlights rates of delayed family building and infertility which exceed those previously reported. The persistence of these findings despite high fertility awareness within this population suggests a need for ongoing research into reasons underlying delayed family building and potential opportunities for targeted support and policy reform.

SUPPORT: Research supported by a grant from the ASRM Research Institute.

O-112 10:45 AM Tuesday, October 25, 2022
FREQUENCY OF CONTRACEPTIVE COUNSELING AND USE OF BIRTH CONTROL IN ADOLESCENTS AND YOUNG ADULTS WITH SICKLE CELL DISEASE. Jenna Reich, MD,1 Charis Stanek, MA2 Charleen I. Theroux, BA,1 Asha K. Dahiya, MS,3 Lindsay Martay, BS,4 Lulu Peng, BS,5 Madeleine Walsh, BSN, RN1 Susan E. Creary, MD, MSc1, Leena Nahata, M.D.,1 Gwendolyn P. Quinn, Ph.D.1 NYU Grossman School of Medicine, New York, NY; 2Nationwide Children’s Hospital, Columbus, OH; 3Nationwide Children’s Hospital, Columbus, OH; 4NYU School of Medicine, New York; 5NYU Grossman School of Medicine; 6New York University School of Medicine, Department of Obstetrics and Gynecology, New York, NY.

OBJECTIVE: Females with Sickle Cell Disease (SCD) are at an increased risk of pregnancy related morbidity and mortality, as well as higher rates of unintended pregnancies. Comparatively, little is known about the sexual health of males with SCD. We aimed to examine documented discussions between both male and female adolescents and young adults (AYAs) with SCD and their providers regarding sexual history and contraception, in addition to contraceptive use among AYAs.

MATERIALS AND METHODS: Medical records were reviewed of all patients aged 14-21 seen at pediatric hematology clinics in Ohio and New York from 1/1/2015 – 12/31/2019. Demographics and documentation of discussions of sexual activity and contraceptive history during routine SCD visits were abstracted. Patients with hemoglobin SS and Sβ-thal were considered to have severe disease and other genotypes were considered to have mild disease. The primary outcome was the frequency of documentation of contraceptive counseling and use among AYAs with SCD. The secondary aim was to analyze these metrics by patient sex and disease severity. Analyses included t-tests and chi-squares, with p < 0.05 considered significant.

RESULTS: The final sample (N =167) included 90 (53.9%) females and 77 (46.1%) males with no significant difference in age (M_age =18.10; SD 3.0 vs. M_age =18.21; SD 3.23; p =0.143). Overall, 65 (38.9%) patients had previous sexual activity and 96 (57.5%) had contraceptive counseling documented. 72 (43.1%) patients had documented use of birth control, the most common method being condoms among males and females in comparable amounts (Male: n =24, 100% vs. Female: n =23, 25.6%, p =0.42). Other contraception methods (among females only) included depo-provera (n=22, 24%), hormonal implants (n=11, 12%) and progesterone only pills (n=11, 12%). 26 (28.9%) females had documented discussions of birth control complications.

When comparing females and males, females reported history of sexual activity more frequently (n=37, 41% vs. n=28, 36.3%, p =0.003). In addition, more females had documented use of birth control at some point (n=48, 53.3% vs. n=24, 31.2%, p =0.014). Although a greater proportion of male patients had documented contraceptive counseling, the difference was not statistically significant (n=47, 61.0% vs. n=49, 54.4%, p =0.390). Disease severity was also not significantly associated with contraceptive counseling (Severe: n=57, 60%, Mild: n=39, 54.2%, p =0.450).

CONCLUSIONS: In our cohort of AYAs with SCD that included many who were previously sexually active, contraception discussions were documented in over half of patients, though fewer had recorded birth control use. When comparing females and males, sexual activity and use of birth control was more frequently documented among female AYAs. Contraceptive counseling was similar between groups, though it occurred in less than two-thirds of patients.

IMPACT STATEMENT: This is one of the first studies to examine discussions surrounding sexual activity and contraception in AYAs with SCD and suggests that these high risk AYAs are not being sufficiently counseled regarding these important topics.

SUPPORT: None.

O-113 11:45 AM Tuesday, October 25, 2022
IMPACT OF QUANTITATIVE POST-VASECTOMY SEMEN ANALYSIS REPORTING ON PATIENT COMPLIANCE AND NEED FOR REPEAT SEMEN ANALYSIS. John Ermendorf, BA,1 Catherine Gu, M.D.,2 Martin Kathrins, MD,3 Harvard Medical School, Boston, MA; 2Brigham and Women’s Hospital, Boston, MA.

MATERIALS AND METHODS: Medical records were reviewed of all patients aged 14-21 seen at pediatric hematology clinics in Ohio and New York from 1/1/2015 – 12/31/2019. Demographics and documentation of discussions of sexual activity and contraceptive history during routine SCD visits were abstracted. Patients with hemoglobin SS and Sβ-thal were considered to have severe disease and other genotypes were considered to have mild disease. The primary outcome was the frequency of documentation of contraceptive counseling and use among AYAs with SCD. The secondary aim was to analyze these metrics by patient sex and disease severity. Analyses included t-tests and chi-squares, with p < 0.05 considered significant.

RESULTS: The final sample (N =167) included 90 (53.9%) females and 77 (46.1%) males with no significant difference in age (M_age =18.10; SD 3.0 vs. M_age =18.21; SD 3.23; p =0.143). Overall, 65 (38.9%) patients had previous sexual activity and 96 (57.5%) had contraceptive counseling documented. 72 (43.1%) patients had documented use of birth control, the most common method being condoms among males and females in comparable amounts (Male: n =24, 100% vs. Female: n =23, 25.6%, p =0.42). Other contraception methods (among females only) included depo-provera (n=22, 24%), hormonal implants (n=11, 12%) and progesterone only pills (n=11, 12%). 26 (28.9%) females had documented discussions of birth control complications.

When comparing females and males, females reported history of sexual activity more frequently (n=37, 41% vs. n=28, 36.3%, p =0.003). In addition, more females had documented use of birth control at some point (n=48, 53.3% vs. n=24, 31.2%, p =0.014). Although a greater proportion of male patients had documented contraceptive counseling, the difference was not statistically significant (n=47, 61.0% vs. n=49, 54.4%, p =0.390). Disease severity was also not significantly associated with contraceptive counseling (Severe: n=57, 60%, Mild: n=39, 54.2%, p =0.450).

CONCLUSIONS: In our cohort of AYAs with SCD that included many who were previously sexually active, contraception discussions were documented in over half of patients, though fewer had recorded birth control use. When comparing females and males, sexual activity and use of birth control was more frequently documented among female AYAs. Contraceptive counseling was similar between groups, though it occurred in less than two-thirds of patients.

IMPACT STATEMENT: This is one of the first studies to examine discussions surrounding sexual activity and contraception in AYAs with SCD and suggests that these high risk AYAs are not being sufficiently counseled regarding these important topics.

SUPPORT: None.
OBJECTIVE: The American Urological Association (AUA) recommends a single PVSA demonstrating azoospermia, rare non-motile sperm (RNMS), or ≤100,000 non-motile sperm per mL prior to cessation of contraception. Previously, our institution’s andrology laboratory reported PVSA qualitatively, indicating only the number of sperm per high-powered field (HPF) and motility. Recently, our laboratory began performing quantitative sperm concentration assessments for any result greater than rare sperm, allowing for application of AUA guidelines. Herein, we analyze the extent to which quantitative PVSA impacted compliance rates and need for repeat PVSA at a multi-surgeon, single institution.

MATERIALS AND METHODS: We performed a retrospective review of patients undergoing vasectomy from January 2013 to June 2018 (Cohort 1) and from November 2020 to April 2022 (Cohort 2), during which our institution began performing quantitative PVSA. Demographic information was obtained from our institution’s Research Patient Data Registry. The primary outcomes were compliance, defined as patient completion of necessary number of PVSA’s, and number of PVSA’s required to confirm sterility. Descriptive statistics were used to characterize demographics. Continuous and categorical variables were compared using t-tests and chi-squared tests, respectively, with \( p < 0.05 \) as significant.

RESULTS: Baseline characteristics are listed in Table. There were no significant differences between cohorts, other than a greater proportion of men in Cohort 2 with no children. In cohort 1, 59% returned for ≥1 PVSA at a median of 103 days, with 13% having > RNMS requiring repeat PVSA. In cohort 2, 58% returned for ≥1 PVSA at a median of 114 days, with 36% having > RNMS. Among those with > RNMS, more men were approved for cessation of contraception after PVSA #1 within cohort 2 (77 versus 60%, \( p < 0.0001 \)). Men in cohort 2 were more compliant with repeat PVSA’s (100 versus 48%, \( p = 0.09 \)) and required fewer repeat PVSA’s.

CONCLUSIONS: Quantifying the concentration of > RNMS on PVSA allowed for greater compliance with repeat PVSA’s compared to qualitative assessment. Additionally, more men were approved for cessation of contraception after a single PVSA, requiring fewer repeat PVSA’s.

IMPACT STATEMENT: Quantitative sperm concentration assessments on PVSA may save patients and practitioners repeat PVSA’s to confirm sterility.

<table>
<thead>
<tr>
<th></th>
<th>Cohort 1</th>
<th>Cohort 2</th>
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<tbody>
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\(* p < 0.0001\)

SUPPORT: N/A

REFERENCES:
CONCLUSIONS: The time to next ET following a miscarriage is 43 days longer compared to those who do not conceive following an ET. Transfers that result in biochemical pregnancies had the shortest time to next transfer out of all miscarriages. Following a clinical miscarriage, surgical management had an approximately 2 month longer duration to next ET compared to medical management.

IMPACT STATEMENT: Miscarriage is a devastating, yet relatively common outcome of infertility treatment cycles. Findings from this study allow us to counsel patients about their expectation of average time to next ET cycle. Following a clinical miscarriage, time to next transfer is approximately 4 months with medical management, 6 months with surgical management, and over 9 months with expectant management.

O-116 11:00 AM Tuesday, October 25, 2022

DOES VAGINAL BLEEDING BEFORE 20 WEEKS GESTATION RESULT IN ADVERSE PERINATAL OUTCOMES FOR WOMEN WITH SINGLETON IVF PREGNANCIES IN BRITISH COLUMBIA? Ruth Habte, MD, 1 Arianne Y. K. Albert, PhD, 1 Mohamed Ali Bedaiwy, MD, PhD 2 University of British Columbia, Vancouver, BC, Canada; 3Women’s Health Research Institute, Vancouver, BC, Canada.

OBJECTIVE: To determine if a relationship exists between vaginal bleeding at <20 weeks gestational age (GA) and stillbirth, antepartum hemorrhage >20 weeks GA, preterm delivery, and pregnancy induced hypertension (PIH) in patients with IVF pregnancies.

MATERIALS AND METHODS: A population-based retrospective cohort study of singleton IVF pregnancies in British Columbia between April 1, 2004 and March 31, 2020 (n=12,940) was undertaken. Data was obtained from the British Columbia Perinatal Data Registry (BCPDR) and was statistically modelled utilizing chi-squared analyses.

RESULTS: Amongst 12,940 singleton IVF pregnancies, 507 patients experienced vaginal bleeding prior to 20 weeks GA, while 12,433 did not. Vaginal bleeding at <20 weeks GA was significantly associated with stillbirth (1.4% compared to 0.6%), Fisher’s p<0.029. Vaginal bleeding at <20 weeks GA was also associated with significantly higher rates of antepartum hemorrhage >20 weeks GA (8.3% vs 2.2%) and preterm delivery (21.9% vs 11.5%). These relationships remained significant when adjustments for age, previous preterm birth, previous low birth weight infant, and substance use were made. The rates of PIH were not significantly different (10.1% vs 9.1%), p=0.531.

CONCLUSIONS: Vaginal bleeding at <20 weeks GA in singleton IVF pregnancies is associated with higher rates of stillbirth, antepartum hemorrhage >20 weeks GA, and preterm delivery.

IMPACT STATEMENT: Vaginal bleeding at <20 weeks in singleton IVF pregnancies carries an increased risk of stillbirth, antepartum hemorrhage >20 weeks GA, and preterm delivery.

O-117 11:15 AM Tuesday, October 25, 2022

HOW LONG TO CONCEPTION? AN EXAMINATION OF THE INTERVAL PATIENTS ARE COUNSELED TO WAIT AFTER RECEIVING METHOTREXATE FOR AN ECTOPIC PREGNANCY BEFORE ATTEMPTING CONCEPTION. Katherine Koniares, MD, 1 Michelle Dellalana, BA, 2 John Nulsen, MD 1 University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT; 2UCConn School of Medicine, Farmington, CT; 3Center for Advanced Reproductive Services, University of Connecticut School of Medicine, Farmington, CT.

OBJECTIVE: With more than 100,000 ectopic pregnancies annually in the United States, ectopic pregnancies pose a prevalent and potentially life-threatening risk during the first trimester. Ectopic pregnancies may be treated medically or surgically, with methotrexate (MTX) being the medical management. ACOG and ASRM have published guidelines on the management of ectopic pregnancies. However, there remains a dearth of evidence regarding the minimal period of time between the administration of MTX and the safe conception of a subsequent pregnancy. The objectives of this study were to investigate the practice patterns of MTX utilization for the treatment of ectopic pregnancies at REI Programs and to gain an understanding of how and why patients are counseled to wait a particular time interval before attempting conception following the administration of MTX.

MATERIALS AND METHODS: A 16-question survey with branching logic was approved by the University of Connecticut Institutional Review Board and administered via REDCap to first year reproductive endocrinology and infertility (REI) fellows.

RESULTS: Of the 46 first year REI fellows emailed the REDCap link, 21 completed the survey (45.7%), 17/21 (80.1%) and 4/21 (19.0%) survey respondents were from academic and academic-affiliated private practice infertility clinics, respectively. The annual number of in vitro fertilization cycles at each clinic was as follows: <250 (9.5%), 251-500 (28.6%), 501-750 (4.8%), 751-1000 (14.3%), and >1000 (42.9%). The number of ectopic pregnancies treated per month at a single clinic was reported as: <1 (19.0%), 1-3 (57.1%), 4-6 (19.0%), and >6 (4.8%). 100% of survey respondents reported utilizing MTX for the treatment of ectopic pregnancies. The time interval clinics counsel patients to wait prior to attempting conception after receiving MTX was reported as: 1 month (14.3%), 2 months (9.5%), 3 months (66.7%), 1 ovariary cycle (4.8%), or 1-3 months depending on the provider (4.8%). When asked to select all the reasons why providers counsel patients to wait a particular period of time prior to attempting a subsequent conception, 19.0% of respondents reported “This is what the evidence shows,” 61.9% selected “I was taught,” and 28.6% chose “This is what ASRM/ACOG recommends.”

CONCLUSIONS: Despite the universal utilization of MTX for the medical management of ectopic pregnancies, there is wide variation in the time period patients are counseled to wait before attempting conception. Further research is needed to determine the shortest safe time interval between receiving MTX for treatment of an ectopic pregnancy and conception to avoid an unnecessary delay between MTX administration and subsequent attempts at conception.

IMPACT STATEMENT: There are discrepancies in the counseling of patients with regard to how long they must wait to attempt conception following MTX treatment. There is an urgent need to standardize counseling of patients on the minimal safe time interval to attempt conception following MTX treatment in order to avoid unnecessary delays in infertility treatment.

O-118 11:30 AM Tuesday, October 25, 2022

LACK OF ACCESS TO MIFEPRISTONE LEADS TO SUBOPTIMAL MANAGEMENT OF EARLY PREGNANCY LOSS: SURVEY OF PROVIDERS. Zachary Anderson, MD, Ravi Agarwal, MD, Rachel S. Mandelbaum, MD, James Patrick Toner, MD, Brian T. Nguyen, MD MPH 1University of Southern California, Los Angeles, CA; 2Keck School of Medicine of USC; 3Keck School of Medicine, University of Southern California; 4Emory School of Medicine, GA; 5University of Southern California.

OBJECTIVE: To describe patterns and variations in the medical and surgical management of early pregnancy loss (EPL) among Reproductive Endocrinology and Infertility (REI) specialists, with attention to mifepristone use.

MATERIALS AND METHODS: An online survey was distributed to 826 members of the Society for Reproductive Endocrinology and Infertility (SREI) listserve. Survey questions assessed physician demographics and practice patterns/preferences for the management of EPL. Primary outcomes were the use of expectant, surgical, and medical management with either misoprostol alone or misoprostol in combination with mifepristone. The chi-squared test was applied for bivariate statistics.

RESULTS: In total, 98 surveys were completed (response rate=11.9%). Of respondents, 51% were female, and 51% were in private practice compared to 49% in hospital/university-affiliated practices. Nearly all (97.9%) agreed on the importance of considering how different treatment modalities can impact future assisted reproductive outcomes. 70.4% of respondents diagnosed EPL at least once per week. 85.7% of respondents offer both expectant, medical, and surgical management options for patients, however 49% of respondents preferred medical management as compared to 27.6% who preferred surgical management and 15.3% who preferred expectant management. Avoiding surgical risk and ease of use were the most common reasons respondents preferred medical management. Only 27.6% of providers offer mifepristone for medical management of EPL; 10.2% of all respondents identified this combination as their preferred management. Respondents who were hospital/university-affiliated were over 7-times more likely to prescribe mifepristone compared to those in private practice (odds ratio 7.22, 95% confidence interval [2.42-21.55], P<0.001). There was no significance for mifepristone use with respect to respondent age, gender, years in practice, prior abortion training, or practice region. The most commonly cited reason for not using mifepristone was a lack of access to the drug.
CONCLUSIONS: While medical management is the most popular method of EPL management among REI providers, less than 30% of those surveyed have adopted the most effective regimen that includes mifepristone. These results suggest that this may be due to a lack of access to the medication.

IMPACT STATEMENT: Mifepristone with misoprostol is the most effective regimen for the medical management of EPL. However, the majority of REI physicians surveyed are not routinely offering this regimen in practice.

SUPPORT: None.

O-119 11:45 AM Tuesday, October 25, 2022
CANNABIS USE AND PREGNANCY LOSS: A SYSTEMATIC REVIEW AND META-ANALYSIS. Camille Zeitouni, B.Sc., Amanda Forsyth-Greig, B.Sc., M.D., M.Sc., Daniel Corsi, Ph.D., M.Sc., B.A., Doron Shumorgun, M.D., Clara Q. Wu, M.D., 1University of Ottawa, Ottawa, ON, Canada; 2Ottawa Hospital Research Institute, Ottawa, ON, Canada.

OBJECTIVE: To investigate the effect of cannabis use on the risk of pregnancy loss.

MATERIALS AND METHODS: A systematic search across the Medline, Embase, Cochrane library and Google Scholar databases was performed including papers from the inception dates of respective databases until January 2022. Observational studies examining cannabis use with pregnancy loss as an outcome were included. Pregnancy loss was defined as a positive h-HCG without a live birth. Two reviewers independently assessed studies for inclusion and performed the data extraction. Quality assessment was performed using the Ottawa Newcastle Scale. The meta-analysis was conducted using DerSimonian and Laird random effect models. When available, Adjusted odds ratios (OR) were used and effect estimates for studies that reported outcomes on more than one cannabis group were pooled separately. Subgroup analyses comparing odds of pregnancy loss between cannabis users and non-users were performed to based on the sex of cannabis users and the timing of pregnancy loss. Inverse variance study weights were used, and study results were presented as ORs with their respective 95% confidence intervals (CI).

RESULTS: Eight prospective and retrospective observational studies examined the association between cannabis use and pregnancy losses. In total, 1571 patients with a history of cannabis use and 5744 patients without a history of cannabis use were included in the systematic review. Across all studies, the pooled OR of cannabis use and associated pregnancy loss of any gestation was 1.28 (95% CI, 1.03-1.59; I² = 37.4%). For earlier pregnancy losses (under 22 weeks gestation), even higher odds of pregnancy loss were observed in cannabis users than non-users (pooled OR, 1.39; 95% CI, 1.10-1.76; I² = 23.7%). The increased odds of pregnancy loss were not specific to the sex of cannabis users. In the subgroup analysis by sex, non-significant change in pregnancy loss rates were found in male (pooled OR, 1.49; 95% CI, 0.83-2.68) and female cannabis use (pooled OR, 1.21; 95% CI, 0.96-1.53).

CONCLUSIONS: The odds of pregnancy loss before 22 weeks of gestation among cannabis users was nearly 1.4 times that of non-users. Emphasis should be placed on educating patients and partners in the pre-conception and early pregnancy period about the risk of miscarriage associated with the use of cannabis.

IMPACT STATEMENT: Since its legalization in Canada and many states in the United States, cannabis use has increased drastically along with the perception of its presumed safety. Due to conflicting past data, the link between cannabis use and pregnancy loss has been controversial. Our review demonstrates a significant association between cannabis use and pregnancy loss. Disseminating the results of our study will be critical in promoting the safer use of this substance.

SUPPORT: N/A.

O-120 12:00 PM Tuesday, October 25, 2022
ROLE OF EMBRYO IGF2 IN THE ETIOLOGY OF THE LONG-TERM CONSEQUENCES OF ART IN OFFSPRING. Rossella Cannarella, MD, PhD,1 Oliver J. Rando, MD, PhD,2 Fengyun Sun, PhD,2 Ebru Kaymak, PhD,2 Pablo Bora, PhD,2 Qiangzong Yin, PhD,2 Aldo E. Calogero, MD1 1Cleveland Clinic, Cleveland, OH; 2Department of Biochemistry and Molecular Pharmacology, University of Massachusetts Medical School, Worcester, MA, USA; 3University of Catania, Catania, CT, Italy.

OBJECTIVE: A higher prevalence of myocardial dysfunction, blood hypertension, asthma, allergies, autism spectrum disorder, hypospadias, cryptorchidism, and cancer has been described in children conceived with assisted reproductive technology (ART) compared to those conceived spontaneously. The reasons are still unclear. Hypermethylation of the insulin-like growth factor 2/H19 differently methylated region (IGF2-H19 DMR) occurs in spermatogonia of infertile patients and can be transmitted on to offspring. In turn, this can lead to lower IGF2 expression in early-stage embryos. Therefore, this study aimed to evaluate the effects, if any, of IGF2 on the expression of target genes in early embryos.

MATERIALS AND METHODS: The oocytes were collected from twelve-week-old superovulated mice. They were activated by incubation in an activating medium and then incubated with recombinant human IGF2 (rhIGF2) protein or vehicle for 92 hours. Those that reached the blastocyst stage were sequenced using the Smart3-Seq protocol.

RESULTS: A total of 80 blastocysts (40 incubated with rhIGF2 and 40 incubated with the vehicle) were collected and sequenced. The incubation of murine parthenotes with rhIGF2 seemed to influence the expression of genes involved in cardiovascular diseases (e.g. Lhb, Adra2b, Btkrb1), autism (e.g. Mag, CunkA, Hoxa1), immunity (e.g. Fcgrt), gametogenesis (e.g. Tdrd12, Sobhi2, Slc25a41, Ankrd51, M1ap, Lemd1), and cancer (e.g. Cea-cant2, Egln3, Cd27, Fatri1).

CONCLUSIONS: The results of this study indicate that IGF2 can modulate the expression of genes involved in diseases similar to those seen in offspring conceived with ART.

IMPACT STATEMENT: Experiments in mouse models with a selective knockout for the ifg2 gene in gonocytes will be useful to evaluate cardiovascular health, fertility, and cancer in the ART-conceived progeny. This may help in understanding why children conceived with ART have a higher prevalence of these diseases.

SUPPORT: None.
ORAL ABSTRACT SESSION: FIBROIDS

O-121 10:45 AM Tuesday, October 25, 2022

FIBROID BURDEN DOES NOT AFFECT THE RISK PROFILE OF SAME-DAY DISCHARGE AFTER MINIMALLY INVASIVE MYOMECTOMY: A COMPARISON OF POST-OPERATIVE COMPLICATION RATES BY LENGTH OF STAY. Jeremy Applebaum, MD, 1 Edward Kim, MD, MPH, 1 Margaret Rush, MD, 2 Divya Kelath Shah, MD, MME 1 Hospital of the University of Pennsylvania, Philadelphia, PA; 2Philadelphia, PA.

OBJECTIVE: To compare postoperative complication rates between same-day discharge (SDD) and admitted patients after minimally invasive myomectomy (MIM) based on fibroid burden.

MATERIALS AND METHODS: Demographics, perioperative variables, and 30-day postoperative complications were extracted from the National Surgical Quality Improvement Program database on patients undergoing MIM between 2015-2019, stratified by low fibroid burden (1-4 fibroids and ≤250 grams, CPT 58545) and high fibroid burden (>5 fibroids or >250 grams, CPT 58546). Chi Square, Fisher’s exact, univariable and multivariable logistic regression were performed.

RESULTS: Of 8100 patients who underwent MIM, 5656 had a low fibroid burden and 2444 had a high fibroid burden. SDD rate was 64.6% of those with low fibroid burden and 56.8% for high fibroid burden. Overall rate of SDD rose from 57.2% in 2015 to 65.0% in 2019. Unadjusted postoperative complication rates are shown in Table 1. Age, race, ASA classification 3 or 4, preoperative hematocrit <36%, hypertension, diabetes, bleeding disorder, and operative time were associated with admission. After adjusting for these variables, composite postoperative complication rates were similar between SDD and admission regardless of fibroid burden (adjusted OR 0.66; 95% CI 0.18-2.47 for low fibroid burden and aOR 0.91; 95% CI 0.18-4.63 for high fibroid burden). Odds of urinary tract infection was higher among admitted patients with both low (aOR 9.1; 95% CI 2.27-37.04) and high (aOR 8.24; 95% CI 1.59-42.49) fibroid burdens.

CONCLUSIONS: The rate of SDD after MIM has increased over time. Though blood transfusions were more common among admitted patients, composite postoperative complication rates were similar between SDD and admitted cohorts regardless of fibroid burden.

IMPACT STATEMENT: SDD after MIM appears to be low-risk and fibroid burden does not seem to affect its risk profile.

SUPPORT: N/A

REFERENCES: N/A

O-122 11:00 AM Tuesday, October 25, 2022

INTERIM RESULTS OF A PHASE 3B, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL EVALUATING 24-MONTH SAFETY OF ELAGOLIX WITH ADD-BACK FOR HEAVY MENSTRUAL BLEEDING ASSOCIATED WITH UTERINE FIBROIDS. Yvette M. Poindexter, MD, 1 Juki W. Ng, PharmD, PhD, 1 Eric L. Brown, MD, 1 Jose Rodriguez, MD, 1 Liesl K. Breddesen, MD, 2 Brenda Hinnan McIlroy, DO, MPH, 3 Hong Li, PhD, 4 Michael C. Snabes, MD, PhD 5 Community Health Network – Advances in Health, Inc., Pearland, TX; 2AbbVie Inc., North Chicago, IL; 3Medi-Sense, Inc., GA; 4GCP Clinical Research, Tampa, FL; 5HCA Medical City Dallas, Dallas, TX; 6AbbVie Inc.

OBJECTIVE: To evaluate the long-term safety of oral gonadotropin-releasing hormone receptor elagolix (ELA) with hormonal add-back therapy (AB) in women with heavy menstrual bleeding (HMB) associated with uterine fibroids (UF).

MATERIALS AND METHODS: This is a multicenter, phase 3b, sequential, randomized, 12-month (M) double-blind, placebo-controlled, 36M open-label study to evaluate the safety of ELA 300 mg twice a day (BID) with estradiol 1 mg/norethindrone acetate 0.5 mg (E2/NETA) one a day AB (NCT03271489) in women with HMB associated with UF. For the first 12M of the study, the study group received ELA+AB and the control group received placebo (PBO) in a 2:1 ratio. After 12M, patients in both groups entered the open-label treatment period, whereby all patients in the study received ELA+AB. This study is ongoing. Herein, we report safety data at 12M and 24M.

RESULTS: A total of 478 women were randomly assigned to receive ELA+AB (n = 319) or PBO (n = 159). Patient demographics were balanced between groups with a study mean (SD) age of 42.3 (3.3) years, mean (SD) BMI 32.8 (7.2) kg/m², and the majority of participants (57%) were Black. At the end of 12M, overall adverse events (AEs) were slightly higher with ELA+AB compared with PBO (63% versus 52%, respectively). Serious AEs occurred in 3.1% of women taking ELA+AB compared with 1.3% taking PBO. The most common AEs (≥5%) were hot flush (ELA+AB, 9.4%; PBO, 3.8%), headache (ELA+AB, 5.6%; PBO, 3.8%), and back pain (ELA+AB, 3.8%; PBO, 5.0%); key AEs of special interest (AESI) included bone mineral density decrease (ELA+AB, 5.0%; PBO, 1.3%) and intermenstrual bleeding (ELA+AB, 3.8%; PBO, 0.0%). A total of 278 patients entered the open-label treatment period. AE frequency was similar to the placebo control period (ELA+AB/ELA+AB, 54.1%; PBO/ELA+AB, 66.7%). The serious AE rate was ELA+AB/ELA+AB, n = 7 (3.6%); PBO/ELA+AB, n = 4 (4.8%). The most common AEs during the open-label treatment period were COVID-19 (ELA+AB/ELA+AB, 3.1%; PBO/ELA+AB, 8.3%), decreased bone density (ELA+AB/ELA+AB, 6.0%; PBO/ELA+AB, 6.0%), heavy menstrual bleeding (ELA+AB/ELA+AB, 1.5%; PBO/ELA+AB, 7.1%), hot flush (ELA+AB/ELA+AB, 1.0%; PBO/ELA+AB, 6.0%) and hypotension (ELA+AB/ELA+AB, 3.6%; PBO/ELA+AB, 6.0%). In general, the AESI rates observed at 24M were consistent with those observed at 12M.

CONCLUSIONS: The overall safety profile of ELA 300 mg BID with E2/NETA is consistent with its profile established from the previous Elagolix Uterine Fibroid Phase 3 studies in terms of overall AE rates and most frequent AEs. Safety findings at 24M were similar and consistent to those observed at the end of 12M with no new safety signals identified.

IMPACT STATEMENT: The safety results from this study represent the longest duration of exposure to a GnRH agonist with E2/NETA add-back. Results show that treatment up to 24M with ELA plus E2/NETA is well-tolerated in women with HMB associated with UF.

SUPPORT: AbbVie Inc. participated in the study design; study research; collection, analysis, and interpretation of data and writing, reviewing, and approving this abstract for submission. All authors had access to the data; participated in the development, review, and approval of the abstract; and agreed in the decision to submit this abstract to ASRM for consideration as a poster or oral presentation. AbbVie funded the research for this study.

Table 1: Unadjusted comparison of postoperative complications between SDD and admitted patients, stratified by fibroid burden

<table>
<thead>
<tr>
<th>Complication</th>
<th>SDD (n = 3,654)</th>
<th>Admitted (n = 2,002)</th>
<th>SDD (n = 1,388)</th>
<th>Admitted (n = 1,056)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite complications</td>
<td>111 (3.0%)</td>
<td>178 (8.9%)</td>
<td>49 (3.5%)</td>
<td>150 (14.2%)</td>
</tr>
<tr>
<td>Surgical site infection</td>
<td>50 (1.4%)</td>
<td>42 (2.1%)</td>
<td>11 (0.8%)</td>
<td>24 (2.3%)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2 (0.05%)</td>
<td>11 (0.6%)</td>
<td>0</td>
<td>4 (0.4%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0</td>
<td>4 (0.2%)</td>
<td>2 (0.1%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>UTI</td>
<td>16 (0.4%)</td>
<td>25 (1.3%)</td>
<td>6 (0.4%)</td>
<td>12 (1.1%)</td>
</tr>
<tr>
<td>DVT</td>
<td>2 (0.05%)</td>
<td>2 (0.1%)</td>
<td>0</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>2 (0.05%)</td>
<td>4 (0.2%)</td>
<td>2 (0.1%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>15 (0.4%)</td>
<td>85 (4.2%)</td>
<td>15 (1.1%)</td>
<td>105 (9.9%)</td>
</tr>
<tr>
<td>Unplanned reoperation</td>
<td>6 (0.2%)</td>
<td>16 (0.8%)</td>
<td>6 (0.4%)</td>
<td>13 (1.2%)</td>
</tr>
<tr>
<td>Readmission</td>
<td>33 (0.9%)</td>
<td>42 (2.1%)</td>
<td>14 (1.0%)</td>
<td>23 (2.2%)</td>
</tr>
</tbody>
</table>

Vol. 118, No. 4, Supplement, October 2022
and provided writing support for this abstract. No honoraria or payments were made for authorship. Medical writing assistance, funded by AbbVie, was provided by Mayoni Ranasinghe, MBBS, MPH and Kersten Reich, MPH, CMPP, of JB Ashin.

O-123 11:15 AM Tuesday, October 25, 2022

IMPACT OF ELAGOLIX WITH ADD-ON-BACK ON BONE MINERAL DENSITY AT 24 MONTHS: INTERIM RESULTS OF A RANDOMIZED, PLACEBO-CONTROLLED TRIAL IN WOMEN WITH HEAVY MENSTRUAL BLEEDING ASSOCIATED WITH UTERINE FIBROIDS. Yvette M. Poin Dexter, MD,1 Juki W. Ng, PharmD, PhD,2 Eric L. Brown, MD,1 Jose Rodriguez, MD,1 Liesl K. Bredeson, MD,1 Nelson Watts, MD,1 Brenda Himmin McClroy, DO, MPH,1 Hong Li, PhD,1 Michael C. Snabes, MD, PhD3 Community Health Network – Advances in Health, Inc., Pearl land, TX; 2AbbVie Inc., North Chicago, IL; 3Medi-Sense, Inc., Atlanta, GA; 4GCP Clinical Research, Tampa, FL; 5HCA Medical City Dallas, Dallas, TX; 6Mercy Health Osteoporosis and Bone Health Services; 7AbbVie Inc.

OBJECTIVE: To evaluate the effect of oral gonadotropin-releasing hormone receptor elagolix (ELA) with hormonal add-back therapy (AB) on bone mineral density (BMD) in women with heavy menstrual bleeding (HMB) associated with uterine fibroids (UF).

MATERIALS AND METHODS: This is a multi-center, phase 3b, sequential, randomized, 12-month (M), double-blind, placebo-controlled, and 36M open-label trial to evaluate the effect of ELA 300 mg twice a day (BID) with estradiol 1 mg/norethindrone acetate 0.5 mg everyday AB (ELA+AB) on the BMD of women with HMB associated with UF (NCT03271489). For the first 12M, the study group received ELA+AB and the control group received placebo (PBO) in a 2:1 ratio. At the end of 12M, patients in both groups entered the open-label treatment period, whereby all patients in the study received ELA+AB. BMD was measured via dual-energy X-ray absorptiometry of the lumbar spine, femoral neck, and total hip at 6M intervals beginning at baseline. A total of 478 women were randomly assigned to receive ELA+AB (n = 319) or PBO (n = 159). Baseline BMD was similar between groups. At the end of the 12M double-blind treatment period, ELA+AB showed no statistically significant difference (LS mean [SE]) compared with PBO in %CFB in BMD for any of the measured sites: lumbar spine (ELA+AB, -1.26% [0.24]; PBO, -0.47% [0.56]), total hip (ELA+AB, -0.57% [0.20]; PBO, -0.57% [0.31]), and femoral neck (ELA+AB, -0.77% [0.35]; PBO, -0.60% [0.53]).

O-124 11:30 AM Tuesday, October 25, 2022

MECHANICAL AUGMENTATION OF PROGESTERONE ACTION IN UTERINE FIBROID CELLS REQUIRES PROGESTERONE RECEPTOR B (PRB) AND IS ASSOCIATED WITH PRB PHOSPHORYLATION. Lena W. Chen, M.D., Md, Soriful Islam, PhD, Kamaria C. Cayton Vaught, M.D., Joshua T. Brennan, MS, MPH, Briana Winer, B.S., James H. Segars, MD Johns Hopkins University School of Medicine, Baltimore, MD.

OBJECTIVE: Progesterone responsive genes are implicated in fibroid growth, but the mechanisms that integrate mechanical signaling with progesterone receptor activation are not fully understood. We previously reported that a mechanically stiff substrate promoted progesterone-dependent, progesterone receptor-mediated gene activation in fibroid cells. Here we investigated whether altered mechanical stiffnesses directly influenced phosphorylation of progesterone receptor B (PRB), and used siRNA directed against PRB to test whether this isoform was required to transduce mechanical signals in fibroid cells.

MATERIALS AND METHODS: Patient-derived immortalized human leiomyoma (P57F) and patient-matched myometrial (P57M) cell lines were plated on collagen coated stiff polystyrene (30GPa) or soft silicone (930 kPa) plates. After overnight serum starvation, complete growth media was added and cells were incubated for 24 hours. Western blot was used to determine levels of phosphorylated PRB (anti-Ser345) in stiff versus soft plates. Band intensity was quantified with ImageJ 1.52a software and normalized with anti-ß-actin. In knockdown experiments, PRB mRNA was measured following knockdown using 1M or 10M of two PRB siRNAs, or 10M of negative control siRNA. P57F and P57M cells were co-transfected with a progesterone responsive luciferase reporter (PRE-luc) and 5mg of an expression construct encoding PRB, and treated with 40nM progesterone (P4) or vehicle control for 24 hours. Analyses were performed using Student's t-test with an alpha of p<0.05.

RESULTS: PRE-luc activity was greater in P4-treated fibroid cells, compared to myometrial cells grown on stiff plates (fibroid 18.0-fold vs. myometrial 8.6-fold; p<0.01). Upon investigating the impact of mechanical stiffness on PRB phosphorylation, PRE-luc activity was 15.9-fold greater in fibroid cells grown on stiff compared to soft plates, and was also increased albeit to a lesser degree (7.6-fold) in myometrial cells (both p<0.01). PRB knockdown with siRNA at 10M significantly reduced PRE-luc activity in P4-treated cells compared to negative control in both cell types (fibroid 16.2-fold difference, myometrial 6.7-fold difference; both p<0.01). Western blot analysis demonstrated 41% greater levels of phosphorylated PRB in fibroid cells grown on stiff compared to soft plates (p<0.01), and 51% greater levels of phosphorylated PRB in fibroid compared to myometrial cells grown on stiff plate (p<0.01).

CONCLUSIONS: These data support the conclusion that a mechanically stiff tissue environment increased PRB phosphorylation in fibroid cells. Further, the mechanical augmentation of ligand-dependent progesterone receptor activity specifically required PRB, and did not appear to be mediated by other progesterone receptor isoforms.

IMPACT STATEMENT: These results provide an additional support for the central role of PRB in the mechanotransduction pathways that influence activity of progesterone-responsive genes involved in fibroid growth.

O-125 11:45 AM Tuesday, October 25, 2022

TRANSCRIPTOME ANALYSIS REVEALS THAT VITAMIN D LOW-DOSE TARGETS EXTRACELLULAR MATRIX AND WNT/B-CATENIN PATHWAY IN A XENO-GRAFT MOUSE MODEL HARBOURING UTERINE FIBROIDS FROM AFRICAN AMERICAN PATIENTS. Ana Corachan, Ph.D.,1 Maria Victoria Victoria Bariani, PhD,1 Qiwei Yang, Ph.D.,2 Tao Bai, PhD,2 Hortensia Ferrero, PhD,1 Ayman Al-Hendy, MD, PhD3 University of Chicago - Universidad de Valencia, Chicago, Illinois, 3JIV Foundation - Instituto de Investigación Sanitaria INCLIVA, Valencia, Spain.

OBJECTIVE: To determine the effect of Vitamin D (Vit D) low-dose treatment on uterine fibroids (UF) gene expression in a patient-derived xenograft (PDX) mouse model.

MATERIALS AND METHODS: Human uterine fibroids obtained from African American (AA) patients (n=3) were xenografted to NOD/SCID mice. Mice were treated for 6 weeks with Vehicle (0.08% EtOH, Control) or Vit D 0.1 µg/kg/day (n=3/group). Total RNA was extracted from UF
The downregulation of MMP significantly increased the expression of POPULATION.

THE ASSOCIATION BETWEEN FIBROIDS, OBESITY AND ADIPOSITY IN A LATINA/LATINX POPULATION. Ali A. Bazzi, MD, Samantha B. Schon, M.D., M.S., Charley Jiang, MS, Felix Valbuena, Jr., MD, Donna D. Baird, Ph.D., Erica E. Marsh, MD, MSC, FACOG, Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI; 2MD/MSCR candidate, Ann Arbor, MI; 3Community Health and Social Services (CHASS) Center, Detroit, MI; 4National Institute of Environmental Health Sciences, NIH, Durham, NC.

OBJECTIVE: Previous studies suggest that BMI is positively associated with the risk/prevalence of fibroids. Furthermore, case control studies demonstrate that waist-hip ratio can be used as screening tool to identify groups at high risk for uterine fibroids. This and similar studies conclude that an increase in body mass index (BMI), waist-hip ratio (w/h) and visceral fat, increase the risk of uterine fibroids. However, few studies have assessed this relationship in the Latina/LatinX population. The objective of this study was to assess the relationship between obesity/adiposity (utilizing a multi-parametric approach) and fibroid incidence in a large cohort of Latina/LatinX women.

MATERIALS AND METHODS: This is a cross-sectional analysis of data collected as part of a prospective longitudinal cohort study. The Environment, Epidemiology, Latinas, and Adiposity Study (ELLAS) follows 603 Latina/LatinX women over a 5-year period. All participants in this study were between the ages of 21-50 at the time of consent. Participants underwent a baseline pelvic ultrasound to assess for the presence of fibroids. Bioelectrical impedance analysis was performed to assess adiposity via several measurements. The association between fibroids and BMI, w/h, percent body fat and percent visceral fat, were assessed as both continuous and categorical variables. Statistical associations were determined using Chi-squared test, Wilcoxon rank-sum test and Linear or Logistic regression analysis as appropriate.

RESULTS: Data from 603 participants was available for analysis. A total of 68 participants were noted to have fibroids (11.3%), while 535 participants did not have fibroids at time of the initial study visit (88.7%). The mean age of the participants was 37.4 ± 6.95 years. There was no difference in BMI between participants with and without fibroids (30.9 kg/m2 vs 30.0 kg/m2, respectively, (p=0.125). Similarly, there was no difference in w/h ratio or percent body fat between the women with or without fibroids (0.9 for both groups, p=0.768). The percentage of visceral fat was significantly higher in women with fibroids compared to those without fibroids (7.9% vs 6.8%, p<0.009); however, this association was no longer significant when adjusted for age.

CONCLUSIONS: Among a large cohort of Latina/LatinX women, body weight and adiposity were not associated with fibroid prevalence. IMPACT STATEMENT: This stresses the importance of utilizing diverse study populations and the need for future research among minority populations that are often not represented in research studies.

ORAL ABSTRACT SESSION: GENETICS (NON-PGT)

O-127 10:45 AM Tuesday, October 25, 2022

RESCUED BY PARAFFIN: WHEN FRESH PRODUCTS OF CONCEPTION (POC) ANALYSIS DOES NOT PROVIDE A RESULT: Katherine L. Howard, MS, Melissa K. Maisenbacher, M.S., Melda Balcicoglu, BS, Karine Hovanes, PhD, Carrie Chou, MS Natera Inc., San Carlos, CA.

OBJECTIVE: Examine success rate of genetic testing on formalin fixed paraffin embedded (FFPE) POC after unsuccessful testing on fresh tissue analysis and report potential factors related to obtaining results from FFPE POC testing.

MATERIALS AND METHODS: Reviewed cases from a reference lab tested over the last 10 years to identify those with no fetal results on fresh tissue POC analysis with FFPE POC analysis on the same pregnancy loss.

RESULTS: 243 singleton cases met criteria; mean maternal age was 33.4 yrs and mean gestational age (GA) was 8 wks 6 days.
122/243 (50.2%) cases received a fetal result with a mean GA of 9 wks 3 days. Pathology reports stated: absence of villi/fetal tissue or degenerative tissue (AV/FT) or DT in 21/87 (24.1%) cases. 104/243 (42.8%) of cases received results on the first dissection.

For 121/243 (49.8%) cases with non-fetal results after multiple dissections (range 1-8), mean GA was 8 wks 3 days. Pathology report stated: AV/FT or DT in 22/90 (24.4%) cases.

CONCLUSIONS: ~50% of cases had a fetal result showing the utility of analysis on FFPE POC when fresh tissue testing fails to provide a fetal result. GA stratification showed higher euploid (66.7% vs. 21.8%) and lower MCC/ineffective rates (16.7% vs. 44.1%) in losses after first trimester. Comparison of result types and pathology reports showed no correlation between villi/fetal tissue identification and fetal results. SNP array analysis differentiated normal female and MCC results, impacting ~50% of results. Additional dissections gave information on 18/243 (7.4%) cases. Selecting a lab that offers array-based testing on FFPE POC with multiple dissections can add information for pregnancy loss management.

IMPACT STATEMENT: ~50% of cases that did not receive a genetic test result via fresh POC analysis obtained a result after analysis on FFPE POC, showing the benefit of pursuing genetic testing on another sample type.

O-128 11:00 AM Tuesday, October 25, 2022

“MINING” VUS’S FOR PATHOGENICITY: CAN INTER-LAB CONFLICTS RENDER VARIANTS OF UNCERTAIN SIGNIFICANCE (VUS’S) PATHOGENIC AND THEREFORE, ACTIONABLE? Alexandra Peyser, M.D.,1 Kenan Onel, M.D., Ph.D.,2 Avner Hershlag, MD 1Northwell Health Fertility, Zucker School of Medicine at Hofstra Northwell, Manhasset, NY; 2Sema4, New York, CT; 3Island Fertility, Stony Brook University, Commack, NY.

OBJECTIVE: The increasing availability of genomic testing has been associated with an ever-increasing by-product: the VUS (Variant of Uncertain Significance). Indeed, frustration is how physicians perceive VUS in patients who are symptomatic or with an impressive family history. Current guidelines recommend that physicians disregard VUS and not pursue PGT-M for the variant. Laboratories will occasionally reclassify VUS as “upgraded” to pathogenic (P) or likely pathogenic (LP), both of which are considered clinically actionable. How should patients be counseled when a variant is reported a VUS by one laboratory and pathogenic by another? This study aims to explore the extent of VUS reporting over a 3-year period, and to specifically determine how many VUS’s are in conflict between labs, making them potentially actionable.

MATERIALS AND METHODS: Utilizing the American College of Medical Genetics (ACMG) recommended 113 gene pre-conception panel consisting of 97 autosomal recessive and 16 X-linked conditions, we assessed the number of VUS’s in conflict over time with more variants considered to be in conflict, thus creating a dilemma for genetic counselors and REI physicians as to whether PGT-M should be recommended.


O-129 11:15 AM Tuesday, October 25, 2022

PROFILING THE MALE GERMLINE GENOME TO UNRAVEL ITS REPRODUCTIVE POTENTIAL. Stephanie Cheung, M.S., Philippe Xie, B.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To use ancillary sperm testing and whole exome sequencing (WES) to assess the ability of the male gamete to sustain fertilization and full pre-post-implantation development, as well as analyze the presence of specific germline mutations related to various reproductive processes.

MATERIALS AND METHODS: Over 6 years, 31 couples with negative infertility workups and normal semen parameters were included in this study and divided according to whether they had successful ART outcomes (fertile, n=10) or not (infertile, n=21). Ancillary sperm assays were carried out on the ejaculated specimens to assess sperm function, and WES was performed on spermatozoal DNA. Sperm aneuploidy by copy number variant (CNV) analysis and gene mutation profiles were compared between the two study cohorts as well as according to the specific reasons for reproductive failure.

RESULTS: All couples had normal peripheral karyotypes. CNV analysis indicated lower sperm aneuploidy in the fertile (4.0% vs. 8.4%) cohort (P<0.00001). Spermatozoa from both cohorts displayed mutations associated with sperm-egg fusion (ADAM5A) and acrosomal development (SPACA4), justifying the use of ICSI. The infertile cohort was then categorized according to reasons for reproductive failure: absent fertilization, poor early embryo development, implantation failure, or pregnancy loss.

Spermatozoa from the fertilization failure subgroup (n=4) had negligible PLCε presence (10±9%) as well as gene mutations (PLCZI, PIWIL1, and ADAM5A) indicating a sperm-related oocyte-activating deficiency. These couples were successfully treated by assisted gamete treatment in their subsequent cycles.

Spermatozoa from the poor early embryo development subgroup (n=5) had abnormal centrosomes (45.9±5.5%), and displayed mutations impacting centrosome integrity (HAUS1) and microtubular stabilization (KIF4A, XRN1). Microfluidic sperm processing was subsequently used to yield a term pregnancy.

Spermatozoa from the implantation failure subgroup (n=7) also had abnormal centrosomes (53.1±13.9%), and were characterized by ultrastructural abnormalities. We also identified mutations affecting embryonic implantation (IL9R) and microtubule/centrosomal integrity (MAP1S, SUP57H, PLK4), whereas those from the pregnancy loss subgroup (n=5) displayed mutations on genes involved in trophoblast development (NLRP7), cell cycle regulation (MARK4, TRIP13, DAB2IP, KIF1C), and recurrent miscarriage (TP53).

CONCLUSIONS: By assessing the male gamete’s genome, we identified specific germline mutations related to various reproductive processes. Our findings can be used to generate a targeted gene panel for diagnostic purposes to effectively identify elusive factors responsible for male gamete reproductive competence and guide treatment for the best approach for couples with unexplained infertility.

IMPACT STATEMENT: Screening spermatozoa for these specific mutations is an example of using precision medicine approaches to enhance the diagnosis, treatment, as well as predicting clinical outcomes in couples with unexplained infertility.

O-130 11:30 AM Tuesday, October 25, 2022

IDENTIFYING TYPES OF AZOOSPERMIA AND REPRODUCTIVE POTENTIAL BY SCREENING FOR GERMLINE MUTATIONS. Stephanie Cheung, M.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

IMPACT STATEMENT: Variants of unknown significance are increasing over time with more variants considered to be in conflict, thus creating a dilemma for genetic counselors and REI physicians as to whether PGT-M should be recommended.


O-129 11:15 AM Tuesday, October 25, 2022

PROFILE THE MALE GERMLINE GENOME TO UNRAVEL ITS REPRODUCTIVE POTENTIAL. Stephanie Cheung, M.S., Philippe Xie, B.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To use ancillary sperm testing and whole exome sequencing (WES) to assess the ability of the male gamete to sustain fertilization and full pre-post-implantation development, as well as analyze the presence of specific germline mutations related to various reproductive processes.

MATERIALS AND METHODS: Over 6 years, 31 couples with negative infertility workups and normal semen parameters were included in this study and divided according to whether they had successful ART outcomes (fertile, n=10) or not (infertile, n=21). Ancillary sperm assays were carried out on the ejaculated specimens to assess sperm function, and WES was performed on spermatozoal DNA. Sperm aneuploidy by copy number variant (CNV) analysis and gene mutation profiles were compared between the two study cohorts as well as according to the specific reasons for reproductive failure.

RESULTS: All couples had normal peripheral karyotypes. CNV analysis indicated lower sperm aneuploidy in the fertile (4.0% vs. 8.4%) cohort (P<0.00001). Spermatozoa from both cohorts displayed mutations associated with sperm-egg fusion (ADAM5A) and acrosomal development (SPACA4), justifying the use of ICSI. The infertile cohort was then categorized according to reasons for reproductive failure: absent fertilization, poor early embryo development, implantation failure, or pregnancy loss.

Spermatozoa from the fertilization failure subgroup (n=4) had negligible PLCε presence (10±9%) as well as gene mutations (PLCZI, PIWIL1, and ADAM5A) indicating a sperm-related oocyte-activating deficiency. These couples were successfully treated by assisted gamete treatment in their subsequent cycles.

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CONCLUSIONS: By assessing the male gamete’s genome, we identified specific germline mutations related to various reproductive processes. Our findings can be used to generate a targeted gene panel for diagnostic purposes to effectively identify elusive factors responsible for male gamete reproductive competence and guide treatment for the best approach for couples with unexplained infertility.

IMPACT STATEMENT: Screening spermatozoa for these specific mutations is an example of using precision medicine approaches to enhance the diagnosis, treatment, as well as predicting clinical outcomes in couples with unexplained infertility.

O-130 11:30 AM Tuesday, October 25, 2022

IDENTIFYING TYPES OF AZOOSPERMIA AND REPRODUCTIVE POTENTIAL BY SCREENING FOR GERMLINE MUTATIONS. Stephanie Cheung, M.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.
OBJECTIVE: To determine whether whole exome sequencing (WES) of surgically retrieved spermatozoa from azospermic men can pinpoint mutations related to the etiology of their infertility and ability to support pregnancy.

MATERIALS AND METHODS: Over 3 years, we recruited men undergoing epididymal sperm aspiration for acquired obstructive azoospermia (OA; n=19) or testicular biopsy for nonobstructive azoospermia (NOA; n=11). Eight men were included as fertile controls. Sperm DNA was extracted and amplified from surgically retrieved specimens. Copy number variants and gene mutation profiles were obtained by WES and compared between the OA and NOA cohorts, followed by sub-analyses within those two categories according to whether they generated a clinical pregnancy (fertile) or not (infertile), while controlling for maternal age.

RESULTS: Of 30 men (paternal age, 42.3±7.3yrs), 19 OA men underwent epididymal sperm retrievals (concentration 1.1±4x10^6/ml, motility 9.1±12%), while 11 NOA men underwent testicular biopsies (concentration 0.03±0.4x10^6/ml, motility 0.5±1%). WES did not detect a significant difference in karyotypes between these two etiologies (OA, 1.7%; NOA, 1.8%) compared with controls (1.1%).

When assessing the origin of azoospermia, we found that the OA group had only 3 housekeeping genes deleted, while the NOA cohort carried deletions on 5 genes involved in RNA transcription (POLR2L1, apoptosis (APSM1), and spermogenic function (API12, APIG2, and APOE).

We then assessed the reproductive potential of these men. The OA group underwent 19 ICSI cycles with their partners (maternal age, 36.8±4.5yrs), resulting in a delivery rate of 72.7% (8/11). Of the couples who delivered (n=9), all of the men shared only a mutation in ZNF749, a transcriptional regulation gene. OA men who remained infertile (n=10) all carried a common deletion on PRB1, which is associated with controlling essential DNA replication.

When we assessed the NOA men who underwent 11 ICSI cycles with their female partners (maternal age, 32.2±2.2yrs), yielding a delivery rate of 72.7% (8/11). All had deletions on MIPG6B, which is involved in stem cell lineage differentiation. Their infertile counterparts (n=3) all had deleted genes involved in spermatogenesis-genesis (n=6) as expected, but most importantly, mutations on genes encoding for early embryo development (MBD5, CCAR1, PMP1A, POLK, RECS, REPIN1, MAPRE3, ARL1C).

CONCLUSIONS: Sperm DNAseq can distinguish germline mutations responsible and help delineate the types of azoospermia. For men who achieved a successful pregnancy, we identified mutations on genes limited to spermatogenesis-genic function. However, for azospermic men unable to sustain a pregnancy, particularly in the NOA cohort, we identified mutations on genes related to impaired embryo development.

IMPACT STATEMENT: The identification of key germline mutations explains reproductive failure regardless of azoospermic etiology and provides valuable information on the ability of azoospermic men to reproduce, laying the foundation for predicting their reproductive potential.

O-132 11:45 AM Tuesday, October 25, 2022
THE INFLUENCE OF MATERNAL AGE ON THE PREVALENCE OF FOUR DISTINCT MOSAIC RESULT CLASSIFICATIONS.
Sarah Rutzick, BS, Retik Kalliyil, PhD, Vi Nguyen, BA, Alyssa Snider, MS, PhD, CGC, IgenomiX, Torrance, CA.

OBJECTIVE: To determine whether maternal age influences the prevalence of four distinct mosaic result classifications observed in preimplantation genetic diagnosis for aneuploidy (PGT-A) testing of isolated low mosaic, isolated high mosaic, complex low mosaic, and complex high mosaic.

MATERIALS AND METHODS: Data from a single PGT-A laboratory for 92,696 embryo biopsies tested with next generation sequencing (NGS) between 2019 and 2021 was compiled. 6,691 of these samples were classified as mosaic. Samples were classified as mosaic if there was at least one chromosomal present with a full copy number change. The percentages of each mosaic result classification, while controlling for maternal age, were calculated for maternal ages 25-42. Linear regression models and ANOVA statistics were generated.

RESULTS: The prevalence of isolated and complex low mosaic results displayed a statistically significant decrease with maternal age. In contrast, the prevalence of isolated and complex high mosaic results exhibited no statistically significant relationship with maternal age.

<table>
<thead>
<tr>
<th>% All Mosaic</th>
<th>% Low Mosaic</th>
<th>% High Mosaic</th>
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<tbody>
<tr>
<td></td>
<td>N 6,691</td>
<td>4,114 0.01</td>
</tr>
<tr>
<td></td>
<td>R² -0.81</td>
<td>0.99E-10 0.01</td>
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<tr>
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<td>P 3.57%E-07</td>
<td>9.95E-10 0.01</td>
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</table>

CONCLUSIONS: Although it is understood that the frequency of mitotic errors does not increase with maternal age (2), it is reasonable that fewer embryos are classified as mosaic as more embryos are classified as aneuploid due to mitotic errors. Interestingly, when broken down into low and high mosaic classifications, this phenomenon is observed only for the low mosaic classification, while the incidence of embryos classified as high mosaic remains constant with increasing maternal age.

IMPACT STATEMENT: Mosaicism is a burgeoning topic in PGT-A and the assisted reproductive community at large. While previous studies aimed to determine whether a significant relationship exists between maternal age and mosaicism, this study delves deeper to reveal that a significant relationship exists depending upon low or high mosaic result classification. Considering recent studies supporting the developmental potential of embryos classified as low mosaic (1), this finding will allow physicians and genetic counselors to better counsel patients when questions regarding mosaic results inevitably arise.

REFERENCES:

O-133 12:00 PM Tuesday, October 25, 2022
BEYOND CHROMOSOMAL ABERRATIONS – TRANSCRIPTOMIC PROFILES OF ANEUPLOID, MOSAIC, AND EUPLOID EMBRYOS FROM TROPHOECTODERM BIOPSY.
Svetlana Madjunkova, MD, PhD,1 Brandon Wyse, B.S.C., M.S.C.,2 Noga Fuchs Weizman, MD, Rima Kharsany, B.S.C.,2 Amy Harmon, PhD,3 Aashi Aggarwal, M.S.C.,2 Rina Abramov, M.S.C.,2 Clifford Lawrence Librach, MD,4 ON, Canada;3 CREATE fertility Centre, Toronto, ON, Canada;1 CREAtfe fertility centre, Toronto, ON, Canada.

OBJECTIVE: The effects of aberrant chromosome dosage on gene expression and the mechanisms that regulate the transcriptional processes in preimplantation embryos are poorly understood. We pioneered low-input parallel whole genome and transcriptome sequencing from a clinical trophectoderm biopsy (TE). Our objective was to profile unique transcriptional landscapes of aneuploid-A, euploid-E, and mosaic-M embryos and to identify the impact of abnormal chromosomal content on global gene expression.

MATERIALS AND METHODS: Single centre prospective clinical study (IRB#16447) of 49 TE from embryos undergoing clinical PGT-A. DNA and RNA were sequenced from good grade E (n=24); which were matched by morphology and cycle characteristics with A:T trisomy (T), S monosomy (M); and 7-M. PGT-A was performed on the Illumina platform (resolution 10Mb; 30% mosaicism). cDNA and RNAseq was performed using SMART-seqv4 and Illumina sequencing platform. Differential gene expression (DE) was performed using DESeq2 and pathway analysis with GSEA comparing Avs E, M vs. A, Evs M and T vs. M. Genes were considered DE with FDR<0.05 and fold change (FC)>2.

RESULTS: The RNAseq quality metrics were uniform across all samples (av. Phred 36.2; av. alignment of 65%; median 25 M reads/sample). There was no difference in the number of uniquely expressed genes among E, A, and M embryos (av. 10,000/sample). Principal component analysis (PCA) revealed tight clustering of A samples along principal component one (PC1), accounting for 6% of the variability in the dataset. The E and M samples were scattered along PC2, which accounted for 3.5% of the variability. DE between A and E embryos showed 203 down and 99 upregulated genes.
A embryos had pathways enriched in mitochondrial respiration (eg. STOML2), metabolism and oxidative phosphorylation, centromere assembly and cell cycle control and division (eg. APC/CDC20, PTTG1). A-embryos had 4 FC higher expression of ATP8 than E and M embryos. In contrast, E had pathways enriched in response to chemokines and transmembrane transport. There were 101 down and 53 upregulated genes in T vs. M embryos with evidence of global dysregulation of transcription.

CONCLUSIONS: Our data presents the first multi-omic assessment of TE in a clinical setting and shows that in addition to whole genome analysis, we can investigate the full transcriptome of preimplantation embryos. Aneuploid embryos exhibit global dysregulation of transcription, and enhanced expression of genes involved in cell cycle control, metabolism and respiration. In line with the quiet embryo theory, E embryos downregulate the above-mentioned pathways. Further studies are needed to map the transcriptional signature of M as they segregate from A and are transcriptionally like E.

IMPACT STATEMENT: Our pioneering approach for clinical multi-omic assessment of preimplantation embryos allows for accurate identification of transcripts affected by aneuploidy and could enhance our understanding of the embryo-endometrial cross talk. This could in turn aid in identifying biomarkers of successful implantation and development.

SUPPORT: CREAte Fertility Centre


ORAL ABSTRACT SESSION: IMAGING AND REPRODUCTIVE MEDICINE

O-133 10:45 AM Tuesday, October 25, 2022

UTERINE CONTRACTILE FUNCTION ACROSS THE MENSTRUAL CYCLE IN HEALTHY WOMEN: AN EXPLORATION OF REFERENCE VALUES USING THE WAVES METHOD. Connie Odette Rees, MD, MSc,1 Yizhou Huang, MSc, PdEng,2 Anna De Boer, BSc,3 Blijke Wessels, BSc,3 Aleida G. Huppelschoten, MD, PhD,1 Brunella Zizolfi, MD,3 Attilio DI. Spiezio Sardo, M.D., PhD,1 Virginia Foreste, MD,1 Nicholas Christoforidis, M.D.,1 Huib Van Vliet, MD, PhD,4 Massimo Miscihi, PhD,3 Benedictus Christiaan Schoot, MD, PhD1 Catharina Hospital, Eindhoven, Netherlands; 2Eindhoven University of Technology, Eindhoven, Netherlands; 3University of Naples Federico II, Naples, Italy; 4Embryolab Fertility Center, Thessaloniki, Greece; 5Department of Gynaecology and Obstetrics, Catharina Hospital Eindhoven, Eindhoven, Netherlands; 6Department of Electrical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands; 7Department of Reproductive Medicine, University Hospital Ghent, Ghent, Belgium.

OBJECTIVE: To explore the characteristics of normal uterine contractile function across the menstrual cycle in healthy women using a novel quantitative ultrasound method.

MATERIALS AND METHODS: Multi-centre observational prospective cohort study carried out in the outpatient gynaecology department of the Catharina Hospital in Eindhoven, the Netherlands, the University of Naples, Federico II, Naples, Italy and Embryolab Fertility centre in Thessaloniki, Greece. Patients were included from September 2014 up to January 2022. Primary outcomes were the contraction frequency (contractions/minute), amplitude, direction (Cervix-to-fundus, Fundus-to-cervix), and coordination. 93 women were included from the gynaecological department of participating centres. Women were included if they were ≥18 years of age, premenopausal and had a normal, natural menstrual cycle. A normal cycle was defined as having a duration ± 28 days, no dysmenorrhea, no menometrorrhagia. Transvaginal ultrasounds were performed during the menstrual phase (M), late follicular (periovulatory) phase (LF), early luteal phase (EL, ovulation + 3 days) and/or late luteal phase (LL, ovulation + 7 days).

RESULTS: Uterine contractility features were extracted from the gathered ultrasound recordings using a quantitative dedicated speckle tracking algorithm previously developed by our group. Each patient underwent a transvaginal ultrasound in the mid-secretory section. Patients had a mean age of 32 years, cycle duration of 27.8 days, and BMI of 23.0. The majority of women were nulliparous. The majority of uterine contraction features differed significantly between menstrual cycle phases. Contraction frequency was highest in the LF phase and lowest in the M and LL phases (1.55 vs. 1.28/min, p = 0.001). A trend was found for contractions during the periovulatory and early luteal phases contractions to travel mainly from anterior to posterior direction, whilst the menstrual phase showed contractions mainly from the fundus to cervix (p = 0.05). No significant difference between phases was found for contraction amplitude. Contraction coordination (simultaneous contraction of the anterior and posterior walls in the same direction) was highest in the periovulatory phase (p = 0.002). Our results are in line with previous published studies using subjective visual inspection.

CONCLUSIONS: This is the first study which investigates contraction coordination as a specific feature of uterine peristalsis. Not all patients were available for multiple ultrasounds, thereby a within-subjects comparison of the uterine contractions was not possible. We confirm differences in uterine contractility across the menstrual cycle, with highest activity seen in the periovulatory phase, and lowest in the late luteal phase.

IMPACT STATEMENT: We explored further implementation of a quantitative method of uterine peristalsis measurement including a novel contraction coordination: characteristic: coordination. Further research using this method and suggested reference values will provide insight into contraction characteristics in abnormal uteri.

SUPPORT: Unrestricted grant GE Healthcare Austria

O-134 11:00 AM Tuesday, October 25, 2022

MONITORING WITH ULTRASOUND AND HUMAN CHORIONIC GONADOTROPIN TRIGGER VERSUS LUTEINIZING HORMONE SURGE TO TIME INTRAUTERINE INSEMINATION: A SYSTEMATIC REVIEW AND META-ANALYSIS. Nivedita Potapragada, BA1, Elnur Babayev, MD, MSc,1 Danielle E. Strom, MD, Molly Beestrum, MLIS,1 Jacob Michael Schauer, Ph.D.,1 Emily S. Junghiem, MD, MSCI1 Northwestern University, Chicago, IL; 2Northwestern Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: To compare odds of pregnancy following intrauterine insemination (IUI) timed by frequent ultrasound monitoring and hCG administration versus monitoring LH levels.

MATERIALS AND METHODS: The protocol of this study was prospectively registered in PROSPERO. Registration number: CRD42021230520. PubMed (MEDLINE), Embase (Elsevier), Scopus (Elsevier), Web of Science (Clarivate Analytics), and the Cochrane Library (Wiley) were searched from the inception till Dec/31/2020. No language limitations were applied. Following de-duplication, 3607 unique citations were subject to independent review by 3 investigators. Thirteen studies (five retrospective cohort, four cross-sectional, two randomized controlled trials and two randomized crossover studies) which enrolled women undergoing natural cycle and/or oral medication (clomid or letrozole) IUI were included in the final random effects model meta-analysis.

RESULTS: No significant difference odds of pregnancy between endogenous LH monitoring and hCG administration was observed (log odds ratio -0.08, 95% CI [-0.37, 0.20], p = 0.53). Significant statistical heterogeneity (I² = 46.6%) was noted between studies. There was no evidence of publication bias by Egger’s test (p = 0.828). Subgroup analysis of the five studies that included natural cycle/IUI outcomes also showed no significant difference in odds of pregnancy between ultrasound/hCG and LH-timed IUI (log odds ratio -0.13, 95% CI [-0.78, 0.52], p = 0.61). Again, significant statistical heterogeneity was noted (I² = 69%), but there was no evidence of publication bias. Lastly, subgroup analysis of 10 studies that included women who underwent ovarian stimulation using oral medications (clomid or letrozole) did not demonstrate a difference in odds of pregnancy between ultrasound/hCG trigger and LH-timed IUI (log odds ratio -0.13, 95% CI [-0.41, 0.15], p=0.32). Statistical heterogeneity between these studies was not significant (I² = 0%). Funnel plot demonstrated asymmetry suggesting possible publication bias. Although Egger’s test was not conclusive (p = 0.18) for this, we fit a model with a trim-and-fill to adjust for publication bias and found no difference in odds of pregnancy between these groups.

CONCLUSIONS: Ultrasound/hCG injection timing for IUI is not superior to LH-timed IUI.

IMPACT STATEMENT: Uterine monitoring with hCG trigger to timed IUI can be costly and time consuming. Patients should be ensured that at-home LH monitoring to timed IUI offers similar success rates.
The influence of hormonal stimulation during IVF/ICSI treatment on uterine peristalsis measured by ultrasound speckle tracking.

**OBJECTIVE:** To study the effect of exogenous hormones on uterine contraction features using a validated new automated quantitative method which objectively analyses uterine strain with speckle tracking.

**MATERIALS AND METHODS:** This multicentre prospective observational cohort study was performed between 2014 and 2022 in the Catharina Hospital in Eindhoven, the Netherlands, Embryolab Fertility Centre in Thessaloniki, Greece; 1Department of Mechanical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands; 2University of Naples Federico II, Naples, Italy; 3Embryolab Fertility Center, Thessaloniki, Greece; 4Department of Reproductive Medicine, University Hospital Ghent, Ghent, Belgium.

**RESULTS:** Patient characteristics of the IVF/ICSI patients and healthy volunteers whose recordings were included in analysis showed no statistically significant differences. Both groups predominantly consisted of multiparous women. In IVF/ICSI patients, the contraction amplitude was significantly higher compared to controls (0.053 vs. 0.040, p < 0.001). No statistically significant differences were found in contraction direction, frequency and coordination (p > 0.05). IVF/ICSI indications, treatment protocols and the number of produced follicles have no statistically significant differences. Both groups predominantly consisted of nulliparous women. In IVF/ICSI patients the contraction amplitude was statistically significantly higher than in controls with spontaneous regular cycles served as controls. All included patients presented with sonographic normal uteri. Each participant underwent a 4-minute transvaginal ultrasound of the uterus in mid-sagittal plane. Ultrasound recordings were acquired at least 24 hours prior to the day of follicle aspiration. Uterine contractions were compared with naturally ovulating controls on day 9 – 14. The contraction features frequency, amplitude, direction and coordination were extracted from the ultrasound recordings with an automated quantitative method which objectively analyses uterine strain with speckle tracking.

**CONCLUSIONS:** Excepting contraction amplitude, all uterine peristalsis features are similar in IVF/ICSI patients with normal uteri and patients with regular menstrual cycles. This suggests that a uterus behaves similarly in IVF/ICSI treatment and during the natural cycle, regardless of hormonal stimulation. Thus, the presence of abnormal uterine peristalsis in IVF/ICSI patients most likely indicates the presence of underlying uterine pathology.

**IMPACT STATEMENT:** If future studies can concretely correlate uterine peristalsis in IVF/ICSI patients with embryo transfer is preferred during the natural or stimulated cycle. The aim would be to significantly reduce ICSI failures caused by the male gamete, as well as the need for couples to undergo several attempts to finally obtain a healthy newborn.

**SUPPORT:** Unrestricted supportive grant by GE Healthcare Austria.

**O-137 11:45 AM Tuesday, October 25, 2022**

**SINGLE-SPERM MOTILITY ANALYSIS DURING ICSI USING AN ARTIFICIAL INTELLIGENCE SPERM IDENTIFICATION SOFTWARE (SID) AND CORRELATION WITH MORPHOLOGY.** Adolfo Flores Saffie Farias, M.Sc, Ph.D.; Denny Sakkas, Ph.D.; Alejandro Chavez-Badia, M.D. Olcay Ocali, B.Sc. Gerardo Mendiabal, Ph.D. Roberto Valencia, M.Sc, Ph.D. Aleska Valadez, B.S. Mitzy I. Hernandez, B.S. Andrew J. Drakeley, MD FRCOG. Jacques Cohen, B.SC., M.SC., PH.D. 3 IVF 2.0 Limited, London, London, United Kingdom; 4Boston IVF - The Eugin Group, Waltham, MA; 1IVF 2.0 LTD, Maghull, United Kingdom; 5Boston IVF, Waltham, MA; 1IVF 2.0 Limited; 6New Hope Fertility Center, Guadalajara, JA, Mexico; 7Liver- pool Women’s Hospital, Liverpool, United Kingdom; 8IVFqc, Hudson, NY.

**OBJECTIVE:** To describe the association between operator-assessed single sperm morphology and kinetic patterns obtained using a computer vision based software (SID) during single sperm pickup for ICSI.

**MATERIALS AND METHODS:** 2154 individual sperm were video-recorded (resolution of 200 X 200 pix) during sperm selection in a 7% PVP solution. Sperm samples were prepared using a density gradient prior to ICSI. Sperm morphology was retrospectively evaluated by embryologists from individual sperm high resolution images captured from the same videos. Sperm morphology was classified as 1. normal, 2. head defects, 3. neck / midpiece defects, 4. tail defects, or 5. excess residual cytoplasm. Multiple defects were classified when present. 12 sperm motility variables* (i.e., VSL, VCL, LIN, VAP, ALH, WOB, STR, MAD) from the population of spermatozoa, were obtained from each video using the software SID1 (IVF2.0 Ltd., UK). To compare the magnitudes of the motility variables of morphological groups with respect to each variable we used a one-tailed Mann-Whitney U test*.

**O-136 11:30 AM Tuesday, October 25, 2022**

**HYERSPECTRAL IMAGING OF SINGLE SPERMATOZOA AS A PROMISING NON-DESTRUCTIVE OBJECTIVE TOOL FOR SPERM SELECTION PRIOR TO ICSI - DETERMINATION OF REPRODUCIBILITY, SENSITIVITY AND SPECIFICITY.** Maria Gil Julià, MSc, MRes, Jose Maria de los Santos, PhD, Irene Hervás Herrero, MSc, Ana Navarro Gomez-Lechon, MSc; Laura Mossetti, MSc; Rocio Rivero-Egea, PhD; Maria J. De Los Santos, PhD; Nicolas Garrido Puchalt, PhD 1IVI Foundation - IIS La Fe Biomedical Research Institute, Valencia, Spain; 2IVIRMA Valencia, Valencia, Spain; 3IVIRMA Roma, Rome, Italy; 4IVI Foundation, Valencia, Spain.

**OBJECTIVE:** This study aims to evaluate the reproducibility, sensitivity and specificity of hyperspectral imaging of individual spermatozoa immobilized prior to intracytoplasmic sperm injection (ICSI) to establish a unique fingerprint that unequivocally identifies each cell.

**MATERIALS AND METHODS:** This was a pilot study performed in IVIRMA Valencia. The HinaLea 4200M Microscope System hyperspectral camera was coupled to an Olympus IX73 inverted microscope. TruScope 1.1.17 was used to obtain the hyperspec. MATLAB 2016a was used to select the informative wavelengths that allowed for the definition of the borders of each spermatozoon. A mask was generated in python and applied to each hypercube in MATLAB, to retrieve only the spectra for that specific sperm cell avoiding interference from other cells or debris in the image. The masks were focused on the head and mid-section of the spermatozoa. To determine the reproducibility, the intraclass correlation coefficient was calculated using values of intensity recorded for all spermatozoa repetitions at once (global) and for the 10 repetitions of each of the 12 spermatozoa separately (individual sperm). A partial least squares regression with discriminant analysis was performed to create a model to classify the 12 spermatozoa in 12 classes. Sensitivity and specificity were computed according to the accuracy of the model when classifying an image to the sperm from which it belongs and not a different one.

**RESULTS:** An automatic image processing and sperm segmentation system was developed. Every region of interest resulting from the application of the mask to define each spermatozoon in a hypercube retrieved information from 299 wavelengths. Global reproducibility resulted in 0.999 (0.999, 0.999), and individual sperm reproducibility averaged at 0.997 (0.994, 1.000). The classification made by the model was sensitive at 93.84% and specific at 96.76%.

**CONCLUSIONS:** Despite this being a pilot study performed to ensure the feasibility and accuracy of the technique, hyperspectral imaging of immobilized single spermatozoa has been proven to be highly reproducible, sensitive and specific.

**IMPACT STATEMENT:** Artificial intelligence (AI) has been previously used to identify patterns in sperm motility and morphology but not their biochemical information. This can only be obtained using destructive techniques. Hyperspectral imaging is an innocuous technique that combines the information provided by a conventional optical image and the chemical information given by the spectra recorded at a vast number of wavelengths, creating a unique signature for each sample – each spermatozoon. Given the reproducibility, sensitivity and specificity of our setup when recognizing each individual immobilized sperm and differentiating them from the rest, hyperspectral imaging could be used to develop AI predictive algorithms to select the selection of a given sperm cell for ICSI with the outcome of the cycle. The aim would be to significantly reduce ICSI failures caused by the male gamete, as well as the need for couples to undergo several attempts to finally obtain a healthy newborn.

**e56 ASRM Abstracts Vol. 118, No. 4, Supplement, October 2022**
RESULTS: We found statistical evidence that normal sperm have higher Linearity (LIN) than those with head defects, higher LIN and Straight Line Velocity (VSL) than those with neck and midpiece defects, higher VSL, Curvilinear Velocity (VCL), Average Path Velocity (VAP), and Amplitude of the Lateral displacement of the Head (ALH) than those with tail defects, and higher VSL than those with excess of residual cytoplasm, and higher VSL and LIN than those with any defect (Table 1).

CONCLUSIONS: The findings suggest that individual sperm morphology is linked significantly to motility patterns in samples ready for ICSI. Sperm classified as morphologically normal tend to display better motility variables than sperm with single, or multiple defects. From all morphology defects, tail defects had the most significant impact on motility variables.

IMPACT STATEMENT: A high correlation between sperm morphology and its kinetic patterns suggests that sperm motility might suffice to determine an individual sperm’s health during selection for ICSI. However, its evaluation requires objective quantification, perhaps only possible with the aid of computer vision and AI software.

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SUPPORT: Support by the company IVF 2.0 limited.

REFERENCES:

ORAL ABSTRACT SESSION: IVF OUTCOME PREDICTORS 2

O-139 10:45 AM Tuesday, October 25, 2022

A THREE-DOSE GNRH AGONIST TRIGGERING PROTOCOL TO IMPROVE LIVE BIRTHS IN HYPER-RESPONDERS UNDERGOING FRESH EMBRYO TRANSFER AND INTENSIVE LUTEAL SUPPORT: A PROSPECTIVE RANDOMIZED CLINICAL TRIAL.

Johnny T. Awwad, M.D., HCLD/TS(ABB),1 Sarah Faour, MD,2 Elie Moubarak, MD,3 Dalia Khalife, M.D.,4 Anastasia Salame, M.D.,4 Suleiman Samer Ghunaim, MBBS MRCOG,5 Lina El Taha, MD,6 Fadi Choucair, Ph.D.,7 Ghina Said Ghazeer, M.D,8 1Sidra Medical & Research Center, OPC-3, Office 302, Doha, Qatar; 2American University of Beirut Medical Center; 3American University of Beirut Medical Center, Beirut, Lebanon; 4American University of Beirut Medical Center, Lebanon; 5AUBMC, Beirut, Lebanon.

OBJECTIVE: The use of GnRH agonists to trigger final follicle matura-
tion in fresh IVF/ICSI cycles is associated with suboptimal reproductive out-
comes due to a short LH surge duration. Few studies have reported on the use of repeat GnRH agonist triggering for the purpose of enhancing the efficiency of LH-dependent events during IVF/ICSI cycles. The purpose of this study is to address an existing knowledge gap by investigating whether the use of a three-dose GnRH agonist strategy improves IVF/ICSI outcomes in hyper-re-
sonders undergoing fresh embryo transfer.

MATERIALS AND METHODS: This is a randomized controlled open-la-
bel study conducted at a university-affiliated fertility center between 2018 and 2022. Eligible women, ages 18-40 undergoing IVF/ICSI with 15 or more follicles (≥12 mm in diameter) on trigger day, were randomized to receive either a three-dose triptorelin trigger at 12 hour-intervals (0.3/0.2/
0.2mg) or a single-dose trigger (0.3 mg) for final follicle maturation. For fresh embryo transfers, intensive luteal phase supplementation was continued until 12 weeks of gestation and included daily oral estradiol (8 mg), oral dydrogesterone (40 mg), micronized vaginal progesterone (300 mg), and daily oral estradiol (8 mg), oral dydrogesterone (40 mg), micronized vaginal progesterone (300 mg) until 12 weeks of gestation. Therefore, the conception cycle lasted 21-27 days in women with their highest pregnancy rate (mean global maturation rate 75.9%). Three of the cases with no MII formation were compared between the 5 groups. In patients with a Null/Poor maturation rate (76.4%, n=44), Optimal (84.8%, n=44), Acceptable (51-75% MII, n=44), Low (26-50% MII, n=45), and Null/Poor (0% MII, n=46) maturation rate, the outcomes were comparable. In patients with a Null/Poor maturation rate, the ongoing pregnancy rate per thaw cycle for oocytes age 29 (41.0%) was comparable to all other oocyte ages (range: 5.5% to 5.9%, p = 0.540). In a multivariate analysis after adjusting for confounders, an inverse association was confirmed to be the utilization of the three-dose triptorelin trigger and clinical pregnancy loss (OR 0.33; CI 95% 0.12-0.93).

CONCLUSIONS: Our findings indicate that while a three-dose triptorelin trigger did not improve live births in women hyper responders undergoing fresh ET, the intervention was associated with a significant reduction in pregnancy losses.

IMPACT STATEMENT: Repeat GnRH agonist trigger does not appear to enhance LH-dependent final follicle maturation events. A favorable impact on sustained embryo implantation was nonetheless observed and deserves further investigation.

SUPPORT: None

O-141 11:15 AM Tuesday, October 25, 2022

THE ASSOCIATION BETWEEN OOCYTE AGE AND REPRODUCTIVE POTENTIAL IN DONOR OOCYTES BETWEEN 21 TO 32 YEARS. Phillip A. Romanski, MD, MSc,1 Wayne Caswell, MS,2 Melissa O. Stratton, BA,2 Kathleen Devine, MD1 Shady Grove Fertility, New York, NY; 2Donor Egg Bank USA, Rockville, MD; 3Shady Grove Fertility, Washington D.C., DC.

OBJECTIVE: Evidence supports that chromosome errors in oocytes occur in a U-shape with the highest incidence at the youngest and oldest ages.1 Our objective was to compare the pregnancy rate per donor oocyte cycle by year of donor age to determine whether younger oocytes have decreased reproductive potential.

MATERIALS AND METHODS: Retrospective cohort study of oocyte-donor recipient cycles at Donor Egg Bank USA between 2013-2021. Only the first oocyte thaw with intended embryo transfer from each donor cycle was included. Primary outcome: ongoing pregnancy (viable intrauterine pregnancy at ≥ 8 weeks gestation). Secondary outcomes: embryo development and pregnancy loss. Patients were stratified by year of age from 21 to 32 years. Data are reported as mean ± SD or %). Generalized estimating equations were used to estimate the RR and 95% CI for outcomes. Age 29 was used as the referent group given previous PGTA data reporting an aneuploidy nadir at this age.2

RESULTS: In total, 3,678 donor oocyte cycles were included with >200 cycles per year of age except age 31 (n=122) and 32 (n=70). Mean donor age was 25.7 ± 2.8 and mean recipient age was 42.0 ± 4.7 years. The ongoing pregnancy rate per thaw cycle for oocytes age 29 (41.0%) was comparable to all other oocyte ages (range: 36.1% to 47.7%). There were also no significant differences for any other pregnancy outcomes including positive hCG (age 29 (55.0%) vs. all other oocyte ages (range: 52.9% to 63.0%), biochemical pregnancy (age 29 (5.9%) vs. all other oocyte ages (range: 5.5% to 8.8%)), and spontaneous abortion (age 29 (7.7%) vs. all other oocyte ages (range: 1.4% to 13.1%)).

Per year of age, the mean number of oocytes thawed ranged from 6.8-7.0. The fertilization rate was significantly decreased in age 28 (range: 66.9% to 69.9%) compared to oocytes age 29 years (71.4%; p < 0.05). The fertilization rates for oocytes age 28 and 30-32 were comparable to oocytes age 29 years. The incidence of having no usable embryos for transfer for oocytes age 29 (11.0%) was comparable to all other oocyte ages (7.1% to 13.0%).

CONCLUSIONS: The pregnancy outcomes per thaw cycle, including ongoing pregnancy, for each year of donor age 21-32 were comparable to donor oocytes age 29 years. However, a decreased fertilization rate was observed for oocytes age 21 to 27 when compared to oocytes age 29. This suggests that the reproductive potential of oocytes may continue to improve until ~27 years, but the small difference in fertilization rate did not result in decreased ongoing pregnancy rates in this patient cohort.

IMPACT STATEMENT: Despite data suggesting increased chromosome errors in younger eggs, patients using vitrified warmed donor eggs can be reassured that donor oocytes between 21-32 years yield a similar ongoing pregnancy rate. However, these data suggest that egg thaws from donors whose eggs were not vitrified prior to age 28 were associated with lower fertilization rates. Given this finding, donors aged 28-32 may be slightly preferable to younger donors, and patients pursuing elective oocyte vitrification for fertility preservation may benefit from delaying ovarian stimulation until at least age 28.

SUPPORT: None

REFERENCES:
OBJECTIVE: The aim of the current study was to investigate the relationship between telomerase activity (RTA) and telomere length (TL) in the follicular fluids of patients with diminished ovarian reserve (DOR) after platelet rich plasma (PRP) and growth hormone (GH) treatments.

MATERIALS AND METHODS: 128 infertile patients aged between 19 and 48 were recruited and these patients were divided into four groups: Group 1: normoresponder patients (n=28); Group 2: DOR patients with no adjuvant therapy (n=25); Group 3: DOR patients with ovarian PRP therapy (n=40) and Group 4: DOR patients with GH therapy (n=35). 12 IU GH was started on the 2nd day of the menstrual cycle and was administered subcutaneously every day until the day of HCG administration. PRP was initiated and was applied within the first 10 days after the end of the menstrual cycle. In the 2nd cycle after PRP stimulation, stimulation was started. Follicular fluids were collected on the day of egg retrieval, centrifuged and stored at -80°C. After DNA extraction, TL was measured using real-time PCR (qPCR) and RTA was measured with telomeric repeat amplification protocol (TRAP).

RESULTS: Group 1 median RTA value was higher than Group 2 and 3 median values (p<0.05). The median RTA value of Group 2 was lower than Group 1 and Group 4 (p<0.05). No difference was found in difference activity in Group 4 compared to Group 1 and Group 3 (p>0.05). The median value of TL in Group 1 was higher than the median value of Group 2 and 3 (p<0.001). The median TL value of Group 2 was lower than Group 3 and Group 4 (p<0.05). When Group 4 and Group 1 were compared, there was no difference in terms of TL (P=0.185), while TL was higher in Group 4 than in Group 3 (P=0.010). When TL and RTA were compared in terms of positive pregnancy test, no significant differences were found between groups 1, 2 and 3 (P>0.05), but RTA and TL were lower in patients with positive pregnancy test compared to group IV (p=0.002, and p=0.034, respectively). Logistic regression analysis revealed cut-off values for RTA and TL at 0.051 and 1.016 respectively for the differentiation of positive pregnancy tests in Group 4. This model calculated the probability of positive pregnancy test as 89.9%, negative pregnancy test as 83.3% and the overall accuracy rate as 86.7%.

CONCLUSIONS: Our study showed that patients with DOR had a shorter TL and a lower level of RTA compared to patients with a normal response. As a result of PRP and GH adjuvant therapy, DOR patients showed a significant increase in RTA levels and a prolongation of TL levels. Randomized controlled studies with a larger population are needed to determine the relationship between RTA and TL with IVF outcomes and pregnancy outcomes.

IMPACT STATEMENT: Patients with DOR have a shorter TL and a lower level of RTA compared to patients with a normal response. PRP and GH adjuvant therapy might cause an increase in RTA levels and a prolongation of TL levels. PRP and GH treatment can potentially improve oocyte quality in patients with DOR.

SUPPORT: Istanbul University Scientific Research Projects Unit

ASSESSMENT OF PREGNANCY OUTCOMES IN DONOR OOCYTE THAW CYCLES COMPARING FRESH EMBRYO TRANSFER TO CRYOPRESERVED-THAWED EMBRYO TRANSFER: A SIBLING OOCYTE STUDY. Lauren E. Harrison, MD,1 Melissa O. Stratton, BA,2 Wayne Caswell, MS,3 Kathleen Devine, MD,4 Phillip A. Romanski, MD, MSc5 MedStar Washington Hospital Center, Washington, DC;6 Donor Egg Bank USA, Rockville, MD; 7Shady Grove Fertility, Rockville, MD; 8Shady Grove Fertility, New York, NY.

OBJECTIVE: Studies evaluating donor oocyte cycles report that embryo transfers using freshly retrieved oocytes result in a higher live birth rate compared to cryopreserved-thawed oocytes.1 However, due to logistics, this can be a financial burden and thus many oocytes are divided into four to utilize cryopreserved oocytes. Following oocyte thaw and fertilization, resulting embryos can either be transferred at that time (fresh) or the embryo cohort can be cryopreserved followed later by a thaw and embryo transfer (cryopreserved-thawed). The objective of this study was to assess the ongoing pregnancy rates among donor oocyte thaw cycles with a fresh embryo transfer compared to a cryopreserved-thawed embryo transfer.

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RESULTS: In total, 1,210 sibling oocyte recipient cycles were included (fresh transfer: 605; cryopreserved-thawed: 605). Mean donor age was 23.0 ± 2.5 with mean recipient age undergoing fresh transfer 42.2 ± 4.5 and undergoing cryopreserved-thawed transfer 42.0 ± 4.7 years.

The pregnancy outcomes are shown in the Table. The ongoing pregnancy rate was comparable between the fresh transfer (51.2%; n=310) and cryopreserved-thawed transfer (49.6%; n=300) groups (p=0.57). Additional pregnancy outcomes including positive hCG, biochemical pregnancy, and spontaneous abortion rate were also comparable between the two groups.

CONCLUSIONS: The pregnancy outcomes per donor oocyte thaw cycle, including ongoing pregnancy, were comparable between recipients undergoing fresh transfer compared to recipients using sibling oocytes undergoing cryopreserved-thawed transfer.

IMPACT STATEMENT: Cryopreserved donor oocytes that are thawed, fertilized, and cultured to the blastocyst stage can again be cryopreserved without a negative impact on the future pregnancy outcome.

**ORAL ABSTRACT SESSION: MALE REPRODUCTION AND UROLOGY 1**

O-145 10:45 AM Tuesday, October 25, 2022

**TESTOSTERONE THERAPY IS ASSOCIATED WITH DEPRESSION, INTENTIONAL SELF-HARM AND SUICIDALITY: ANALYSIS OF A NATIONAL FEDERATED DATABASE.** Sirpi Nackeana, BA; Mehul S. Patel, MD; Devi Nallakumar, BS; Jesse Ory, MD; Taylor Kohn, M.D.; Christopher M. Deibert, M.D.; M.P.H.; Chase Carto, BS; Ranjith Ramasamy, M.D.; University of Miami Miller School of Medicine, Miami, FL; Northwestern University, Chicago, IL; University of Miami; Dalhousie University, Halifax, Canada; Johns Hopkins University School of Medicine, Baltimore, MD; University of Nebraska Medical Center.

OBJECTIVE: To assess genetic differences between azoospermia and oligospermia, we performed miRNA expression profiling in the peripheral blood of monzygotic discordant twins. Investigating the miRNAs derived from the peripheral blood samples can be used as a marker in the diagnosis and treatment prognosis of men with infertility.

MATERIALS AND METHODS: Participants (38-year-old twin males) provided semen sample after 2 to 7 days of abstinence. Whole blood was collected, RNA was extracted, quality was assessed, library was generated and subjected to RNA sequencing. Data analysis was performed using standardized protocol which involved normalization and enrichment using Ingenuity pathway analysis. Over 50,000 genes were evaluated based on expression levels. Differences in expression were computed using fold change with respect to the control (subject with oligospermia).

RESULTS: Results of semen analysis showed that one brother with history of male factor infertility had azoospermia due to production defect. His twin brother had oligospermia and previously conceived a child naturally. In data analysis, Long-noncoding RNA samples and samples with low differential expression (under a factor of 2-fold) were excluded from consideration, the remaining genes were subjected to enrichment using Ingenuity pathway analysis. Analysis highlighted two genes to be potentially involved in spermatogenesis: Hoxb9 and E2f1. Of these, E2f1 was 18X upregulated and Hoxb9 was 11 folds downregulated in the peripheral blood of males with oligospermia. These findings were validated using immunohistochemistry.

CONCLUSIONS: We have identified that E2f1 and Hoxb9 mRNA expression differs in identical twins with differential reproductive capacities. We discovered evidence that E2f1 and Hoxb9 are associated with spermatogenesis and fertility.

IMPACT STATEMENT: This work presents a unique opportunity to assess differences in RNA expression in genetically identical patients. We found that Hoxb9 and E2f1 expression may impact spermatogenesis. Hoxb9 plays a role in embryonic development, including embryonic axonal positioning. E2f1 has been linked to cases of non-obstructive azoospermia in mice and humans. Notably, E2f1 mRNA down-regulation has been linked to normal spermatogenesis. Understanding the genetic basis of infertility is an important step to developing new treatments and interventions.

**SUPPORT:** This work was supported by NIH Health Grant RO1 DK130991 and Clinician Scientist Development Grant from the American Cancer Society to RR.
PREDICTORS OF A CLINICALLY SIGNIFICANT RESPONSE TO ANASTROZOLE THERAPY IN A MULTI-INSTITUTIONAL COHORT OF MEN WITH IDIOPATHIC INFERTILITY. Bryan Douglas Naclitz, MD, MS, Tommy Jiang, B.A., Carlos J. Munoz, BS, John Tucker Sigalos, M.D., Neilufar Moridi, B.S., Jesse Mills, M.D., Neel Parekh, MD, Sarah C. Vj, MD, Sivaram V. Eleswarapu, M.D., Ph.D., Scott Lundy, MD PhD.1 Cleveland Clinic Foundation, Cleveland, OH;2David Geffen School of Medicine at UCLA, Los Angeles, CA;3Cleveland Clinic, Cleveland, OH;4University of California, Los Angeles, Los Angeles, CA.

OBJECTIVE: Anastrozole is a selective aromatase inhibitor commonly prescribed as empiric medical therapy for men with idiopathic infertility and elevated estradiol levels. The goal of this study is to identify patient factors associated with a clinically significant improvement in semen parameters on anastrozole.

MATERIALS AND METHODS: We performed a multi-center, retrospective cohort study of men with idiopathic infertility who were prescribed anastrozole at two tertiary referral institutions. Demographic, history and physical examination, and laboratory data were captured from the medical record. Exclusion criteria included pre-treatment normozoospermia, recent or current exogenous testosterone use, previous orchectomy, and scrotal surgery during the treatment period. The primary outcome was an upgrade in World Health Organization sperm concentration category (WHO-SCC). Multivariable logistic regression modeling and partitioning analysis were performed to identify statistically significant predictor variables.

RESULTS: 90 men were included in the analysis cohort. Median age was 36 (IQR: 32-41) and median BMI was 32 kg/m² (IQR: 27-43). Compared to baseline, treatment increased levels of LH (8.5 vs. 6.4 IU/L, p < 0.001), FSH (8.5 vs. 5.6 IU/mL, p < 0.001), and testosterone (469 vs. 299ng/dL, p < 0.0001), with 79% (61/77) of patients achieving estradiol levels below the detection cutoff of 25 pg/mL. Median semen concentration increased from 2.4 M/mL to 4.4 M/mL (p < 0.0001) following treatment, with an increase in sperm concentration of 3.6 M/mL and 23.0 M/mL among the 46% (41/90) of men experiencing a WHO-SCC upgrade (p < 0.0001). Multiple clinical and laboratory values were significantly associated with a positive response to treatment, including combined testicular volume (OR: 1.08, 95% CI: 1.02-1.13, p = 0.004), sperm production at baseline (OR: 6.1, 95% CI: 1.6-23.0, p = 0.002), baseline LH (OR: 0.87, 95% CI: 0.78-0.95, p = 0.0003), baseline testosterone (OR: 1.003, 95% CI: 1.000-1.005, p = 0.03), and the baseline testosterone-to-LH (T/LH) ratio (OR: 1.020, 95% CI: 1.008-1.033, p < 0.0001). Multivariable logistic regression analysis revealed that the T/LH ratio (OR: 1.015, 95% CI: 1.003-1.027, p < 0.0001) and baseline sperm production (OR: 9.4, 95% CI: 1.1-78.9, p = 0.009) were statistically significant predictors of WHO-SCC upgrade (AUC: 0.773). The partitioning model inclusive of patients with either T/LH ≥ 100 or baseline sperm production (cryptozoospermia status or better) was 98% sensitive and 33% specific for WHO-SCC upgrades, and was comparably selective to the best performing multivariable model (AUC: 0.771).

CONCLUSIONS: Anastrozole decreased serum estradiol, increased serum gonadotropins, and clinically improved semen parameters in 46% of patients with idiopathic male infertility. Baseline sperm production and higher T/LH ratios were predictive of a WHO-SCC upgrade with treatment.

IMPACT STATEMENT: Anastrozole is most likely to produce a clinically significant change in semen concentration in patients with lower gonadotropin levels and evidence of baseline sperm production.

O-147 11:15 AM Tuesday, October 25, 2022

O-148 11:30 AM Tuesday, October 25, 2022

IDENTIFICATION AND TREATMENT OF COUPLES SUFFERING TOTAL FERTILISATION FAILURE (TFF): A CLINICAL SERVICE EVALUATION AND PROPOSED PHENOTYPIC SCREENING SOLUTION. Cara L. Nicholson, MSc, BSc (Hons), Sarah Martins da Silva, M.B.B.CH, M.D.1 University of Dundee, Dundee, Angus, United Kingdom; 2University of Dundee, NHS Tayside.

OBJECTIVE: Total fertilisation failure (TFF) is estimated to affect 4-7% IVF and 3-5% ICSI cycles1. Treatment for TFF and low-fertilisation (<30%) is challenging due to poorly understood underlying molecular mechanisms. There are no present regulations on Assisted Oocyte Activation (AOA) treatment for TFF from any ART regulatory body. The sperm protein Phospholipase C zeta (PLCζ) plays an essential role in oocyte activation, a major contributor to TFF2. However, not all TFF patients benefit from AOA. We hypothesised that retrospective analysis of the AOA treatment cohort, and development of a pre-treatment phenotypic diagnostic PLCζ assay could positively impact ART outcomes TFF patients.

MATERIALS AND METHODS: We evaluated treatment results from couples (n=43) attending for AOA following ≥1 cycle of ART (IVF/ICSI) and unexplained low-TFF. Where possible, idiopathic infertility patients were offered investigation via the Sperm Studies Clinic, including PLCζ assessment3. Patients identified with deficient PLCζ were offered AOA cycles.

ICSI-AOA was performed using commercial ready-made media containing Ca²⁺ ionophore A23187 (GM508 Cult Activ, Gynemed). Post-injection, oocytes were incubated in media in 5-7% CO₂/37°C conditions for 15 minutes, before washing and incubation as in conventional ICSI.

Sperm samples surplus to treatment were subjected to computer-assisted semen analysis (CASA) and PLCζ assessment via immunocytochemistry and flow cytometry.

Statistical analysis was performed with Graphpad Prism 9. Data subject to Kolmogorov Smirnov, Wilcoxon matched pairs, and student’s t-test. Statistical significance determined as p < 0.05.

RESULTS: 43 couples underwent 41 index cycles of ART (IVF/ICSI), followed by 53 ICSI-AOA cycles. AOA treatment resulted in a significant increase in mean fertilisation rate (%2PN) compared to couples’ conventional IVF cycles (11.5% vs 5.0%, p < 0.0001). A decrease in cycle cancellation rate due to TFF was observed following ICSI-AOA (53.7% to 3.8%), as well as an increase in live birth rate (0.07 to 0.28 per embryo transfer) and ongoing clinical pregnancy (0.0 to 0.13 per embryo transfer).

In patients with an identified reduced proportion and/or total relative fluorescence of PLCζ (n=11), the effectiveness of AOA was even more profound, with mean fertilisation rate significantly increasing from 11.5% in index cycles to 64.7% following AOA (p = 0.01).

CONCLUSIONS: AOA is a powerful tool, capable of transforming treatment outcomes, when offered to patients demonstrated as likely to benefit due to previous TFF or other diagnostic means. PLCζ screening via immunofluorescence can identify individuals with oocyte activation issues, who more likely suffer TFF. AOA treatment of patients with deficient PLCζ recovers fertilisation rates to near normal (<70%).

IMPACT STATEMENT: This PLCζ assay has potential for implementation as a clinical diagnostic test. By identifying couples who will likely benefit from ICSI-AOA, we offer the comfort of a diagnosis with personalised treatment, preventing the distress of unnecessary conventional ART cycles doomed to fail.

O-149 11:45 AM Tuesday, October 25, 2022

MACHINE-LEARNING ENABLED PREDICTION OF SUCCESSFUL SPERM RETRIEVAL FOR MICRODISSECTION TESTICULAR SPERM EXTRACTION. Daniel R. Greenberg, MD, Hriday P. Bhambhvani, MD, Evan J. Panken, MD, Jasmine Lin, BA, Jordan Rich, BA, Justin M. Dubin, MD, Robert E. Brannigan, MD, Joshua A. Halpern, MD, MS1 Northwestern University, Feinberg School of Medicine, Chicago, IL; 2Stanford University, Stanford, CA; 3Northwestern University; 4Department of Urology, Northwestern University Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: Successful sperm retrieval (SSR) for microdissection testicular sperm extraction (mTESE) is reported in only 50% of patients. Therefore, identifying demographic and clinical factors associated with SSR is essential to improve preoperative decision-making. We utilized machine learning (ML) to develop predictive models of SSR for mTESE.

MATERIALS AND METHODS: We retrospectively reviewed patients who underwent mTESE between 2002-2021. Demographic and clinical information including age, BMI, race/ethnicity, urologic history, semen volume, testis size, and preoperative testosterone, follicle stimulating hormone (FSH), and luteinizing hormone (LH) were collected. Univariate logistic regression was used to identify factors associated with SSR. Covariates with p < 0.30 were included as inputs to each of five supervised ML models: elastic net-regularized logistic regression, random forest, support vector machine, neural network, and eXtreme gradient boosting (XGBoost). The dataset was partitioned into training (80%) and testing (20%) sets, and
hyperparameter optimization was conducted in a 5-fold cross-validated fashion with training data. Lastly, models were assessed for accuracy, discrimination via area under the receiver operating characteristic curve (AUROC), calibration, and Brier score on the hold-out test set.

RESULTS: 217 patients undergoing mTESE were included, of whom 123 (56.7%) had SSR. The random forest algorithm achieved the best performance in the hold-out test set (86% accuracy, 0.94 [95% CI 0.81-0.98] AUROC, calibration slope 1.33, calibration intercept 0.02, Brier score 0.10). The most important predictive factors associated with SSR in the ML model were preoperative FSH, preoperative LH, age at time of mTESE, and preoperative semen volume. Per univariate logistic regression, preoperative FSH (OR 0.95, 95% CI 0.93-0.97, p<0.001), LH (OR 0.91, 95% CI 0.86-0.96, p<0.001), and semen volume (OR 0.67, 95% CI 0.55-0.80, p<0.001) were significantly inversely associated with SSR.

CONCLUSIONS: Preoperative demographic and clinical factors, namely FSH, LH, preoperative semen volume, and patient age at time of mTESE, were utilized in ML models to accurately predict SSR for mTESE. This approach may improve prognostication for patients with male factor infertility.

IMPACT STATEMENT: Machine-learning models may be used by both patients and clinicians to improve preoperative clinical decision-making and enable accurate prediction of SSR for mTESE.

SUPPORT: None
OBJECTIVE: Longitudinal trends of ovarian reserve among patients with Turner Syndrome have been described in European cohorts; however, data in racially diverse populations are limited. Given that ovarian reserve differs by race and ethnicity in the adult population, we sought to determine the association between trends in follicle stimulating hormone (FSH) levels and karyotype, onset of spontaneous menarche, and race in a longitudinal study of Turner Syndrome patients in a diverse United States population.

MATERIALS AND METHODS: 150 patients with Turner Syndrome evaluated at an academic tertiary care center from January 2015 to January 2022 with serum FSH levels were included for analysis. Longitudinal measurements of FSH prior to hormone replacement therapy were evaluated according to karyotype (45X0, 45X0/46XX, and other karyotypes [45X0/47XXX, isochromosomes, deletions, or ring chromosomes]), onset of spontaneous menarche (yes vs. no), race, and ethnicity. A linear mixed-effects regression model was used to assess FSH trends among the described covariates.

RESULTS: In all, 407.6 person-years of data were available for analysis. Of 419 FSH values, patients contributed an average of 2.8 values (range 1-12). Of 150 patients, 106 (70.7%) were White, 15 (10.0%) were Black, 10 (6.7%) were Asian, and 19 (12.7%) identified as other race. Additionally, 130 (86.7%) were non-Hispanic and 20 (13.3%) were Hispanic. 53 (35.3%), 36 (24.0%), and 61 (40.7%) patients had 45X0, 45X0/46XX, or other karyotypes, respectively. 55 (36.7%) underwent spontaneous menarche compared to 79 (52.7%) who did not; menarche status was missing in 16 (10.7%). Among karyotype categories, FSH trend was significantly different in each group (45X0 vs. 45X0/46XX, p = 0.0031; 45X0 vs. other, p = 0.031), but not among 45X0/46XX (White vs. Black, p = 0.867). When grouped by spontaneous menarche and race, FSH trends were different among all groups (White with menarche vs. Black with menarche, p < 0.0001). White no menarche vs. Black no menarche, p = 0.033).

CONCLUSIONS: After adjusting for the effects of karyotype and spontaneous menarche status in a group of patients with Turner syndrome, trends in serum FSH remained different by race.

IMPACT STATEMENT: Although karyotype and menarche status show strong associations with trends in FSH in those with Turner Syndrome, incorporation of race is critical in interpreting anticipated values of ovarian reserve.

O-154 11:30 AM Tuesday, October 25, 2022

INFERTILITY AND INVOLUNTARY CHILDLESSNESS ARE ASSOCIATED WITH DEPRESSIVE AND ANXIETY SYMPTOMS IN WOMEN WITH A HISTORY OF OPTIMAL MENOPAUSE: A SWAN COHORT STUDY

AUTHORS: Victoria W. Fitz, MD, MSCR,1 Laura Grau, MPH,2 Savannah Mierau, BA,2 Robin Green, PsyD,4 Carol Derby, PhD,4 Ellen B. Gold, MA, PhD,4 Jan Leslie Shifren, MD,4 Genevieve S. Neal-Perry, M.D., Ph.D.,5 Mary Sammel, D.S.C.,6 Nanette Santoro, MD1 Massachusetts General Hospital, Boston, MA;6 Albert Einstein College of Medicine, Bronx, NY; UC Davis, Davis, CA;5 Fruit St, Yawkey 10A, Boston, MA;6 University of North Carolina, Chapel Hill, NC,8 University of Pennsylvania Health System, Philadelphia, PA;8 University of Colorado School of Medicine, Aurora, CO.

OBJECTIVE: Data on the menopause experience in women with a history of infertility are limited. Our objective was to determine if more women with a history of infertility or involuntary childlessness report menopausal symptoms than women without infertility.

MATERIALS AND METHODS: Longitudinal data from 16 years of follow up were analyzed from Study of Women’s Health Across the Nation (SWAN) cohort participants, excluding participants missing information on pregnancy, fertility history, systemic hormone use, or diabetes. Participants who reported a history of infertility and nulliparity were deemed involuntarily childless (IC). Vasomotor, sleep, and depressive and anxiety symptoms were assessed at follow up visits. Vasomotor symptoms (VMS) were assessed using 2-week recall and defined as any vs none. Elevated depressive symptoms was defined as a score ≥ 16 on the Center for Epidemiological Studies-D scale. Anxiety was defined as a Generalized Anxiety Disorder-7 score ≥ 5. Sleep problems were defined as responding yes to the question “problems sleeping 3+ times per week”. Covariates included study site, body mass index (BMI), race/ethnicity, marital status, education, difficulty paying for basics, insurance status and oral contraceptive use. Symptoms were tracked across menopausal transition stages. Data were analyzed using Kruskal-Wallis and chi-square tests as appropriate, with multivariable logistic models with robust variance to estimate risk ratios (RR) and 95% confidence intervals (CI).

RESULTS: Among the 3061 participants, 600 (19.6%) reported infertility and were parous while 172 (4.1%) were IC. Women with IC were younger, had lower BMI, were more likely to be Caucasian, married, have more education, and not struggle with paying for basics than women without a history of infertility or those who reported infertility but were parous.

<table>
<thead>
<tr>
<th>Age</th>
<th>Europe</th>
<th>Indian Control</th>
<th>Indian Infertile</th>
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<tr>
<td>20</td>
<td>4.28 (3.51-5.22)</td>
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<td>25</td>
<td>3.71 (3.33-4.14)</td>
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<td>35</td>
<td>2.29 (2.02-2.59)</td>
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<td>40</td>
<td>1.29 (1.13-1.47)</td>
<td>0.90 (0.67-1.21)</td>
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<td>45</td>
<td>0.60 (0.48-0.75)</td>
<td>0.36 (0.17-0.75)</td>
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O-153 11:15 AM Tuesday, October 25, 2022

ETHNIC DISCORDANCE IN SERUM ANTI-MÜLLERIAN HORMONE IN EUROPEAN HEALTHY CONTROL, INDIAN HEALTHY CONTROL AND INDIAN INFERTILE WOMEN: A POPULATION STUDY FROM INDIA AND EUROPE

AUTHORS: Piotr S. Gromski, PhD,1 Rajendra Sadashiv Patil Dr., MD, Pathology,1 Shruti Chougule,1 Deepali Bhomkar,1 Padma Rekha Jirge, M.D.,4 Scott M. Nelson, MD, PhD,4 University of Glasgow, Glasgow, United Kingdom;1 MD,Pathology; Karv, Maharashtra, India;1 IVF Specialist, Kolhapur, India.

OBJECTIVE: To determine whether anti-Mullerian hormone (AMH) differs between healthy European and Indian women, and are potential ethnic differences in AMH associated with infertility diagnosis.

MATERIALS AND METHODS: Cross-sectional analysis of three prospectively recruited cohorts. Healthy European women (n = 758) from Netherlands, Belgium, Germany, France and Turkey, were compared to a healthy community cohort from Kolhapur, India (n = 400) and a cohort from Fertility clinic in Kolhapur, India (n = 1600). AMH was measured by the Roche Elecsys Plus assay. AMH, ethnicity, age and cause of infertility were included a priori as candidate predictors of infertility.

RESULTS: Healthy Indian women had lower AMH than their healthy European counterparts (population estimates 20.0% lower (95% confidence intervals (CI), 7.2-36.5), with increasing discordance with increasing age; at 25 years AMH was 11.9% (95% CI, 9.4-14.1) lower, increasing to 40.0% (95% CI, 0-64.6) lower by age 45. Comparison of healthy and infertility Indian women revealed differences that were related to cause of infertility. Women whose male partner had severe oligospermia were studied (n = 95) that similar AMH to controls, women with polycystic ovary syndrome (n = 220) had higher AMH, especially those < 30 years and women with a principal diagnosis of unexplained infertility (n = 757) AMH was lower (median difference 22.6% lower 95% CI 9.1-37.7) than controls.

CONCLUSIONS: AMH is substantially lower in healthy Indian women at all ages. Infertile Indian women have variable differences in AMH from there healthy Indian controls, with the extent and direction of differences primarily reflects the underlying cause of infertility. Recognition of ethnic and cause specific differences are critical to ensure accurate contextualization of results and clinical outcomes for patients.

IMPACT STATEMENT: AMH declines with advancing age in both European and Indian healthy women, but AMH is substantially lower in healthy Indian women at all ages consistent with their known earlier age at natural menopause.

Table. Predicted AMH from quantile regression model and associated 95% confidence intervals for age relative to ethnic background.

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FERTILITY & STERILITY® e63
Compared to no infertility, infertility and IC were not associated with VMS at any menopausal stage (RR 1.01, CI 0.10, 9.0, 1.12 for infertility and RR 1.05, CI 0.87, 1.28 for IC). No association was observed with sleep problems and infertility or IC. Women with infertility (RR 1.25, CI 1.06, 1.49) and IC (RR 1.44, CI 1.02, 1.98) were at greater risk of depressive symptoms in pre-menopause compared to no infertility group, adjusting for oral contraceptive use, marital status, difficulty paying for basics, insurance, education, race/ethnicity, and site. Also, a higher risk of anxiety was observed in women with IC in postmenopause compared to non-infertile participants (RR 1.38, CI 1.06, 1.79).

CONCLUSIONS: Our findings confirm that a history of infertility or involuntary childlessness is associated with depressive symptoms at midlife, with the greatest impact in premenopausal stage, while IC is associated with anxiety in postmenopause.

IMPACT STATEMENT: Information is limited on the impact of infertility during the menopause experience. Results suggest that women with infertility are not at increased risk for VMS or sleep problems during the menopause experience but are at greater risk of depressive symptoms and anxiety, suggesting implications for care at midlife.

SUPPORT: The Study of Women’s Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women’s Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495, and U19AG063720). The content of this abstract is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH.

O-156 12:00 PM Tuesday, October 25, 2022

FOLLICLE STIMULATING HORMONE LEVEL AS A PREDICTOR OF SPONTANEOUS MENARCHE: A RETROSPECTIVE COHORT STUDY OF 133 PATIENTS WITH TURNER SYNDROME. Monica Ailawadi Mainigi, MD,1 Kassie Jean Bollig, MD,1 Suneeta Senapati, MD, MS,2 Nathan C. Koelpel, MPH,1 Aimee Morrison, MD,4 1University of Pennsylvania, Philadelphia, PA; 2Fellow Physician, University of Pennsylvania, Philadelphia, PA; 3University of Pennsylvania, Philadelphia, PA; 4UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, Philadelphia, PA.

OBJECTIVE: Onset of spontaneous menarche in patients with Turner Syndrome has been used as a predictor of future fertility potential and for timing of hormone replacement therapy (HRT), but methods for prediction of spontaneous menarche itself is lacking. We sought to evaluate if follicle stimulating hormone (FSH) at the time of hypothalamic pituitary ovarian (HPO) axis activation can predict onset of spontaneous menarche in a racially and ethnically diverse population of patients with Turner Syndrome.

MATERIALS AND METHODS: 133 patients with Turner Syndrome evaluated at an academic tertiary care center from January 2015 to January 2022 with FSH levels available at the time of HPO axis activation (defined as age six or older) were included for analysis. The threshold of six years was chosen to represent two years prior to the lower limit age range for menarche in the general population. Measurements of FSH prior to HRT were compared among three karyotype categories (45X0, 45X0/46XX, and other karyotypes [45X0/47XXX, isochromosomes, deletions, or ring chromosomes]). Multivariable logistic regression was used to analyze rates of spontaneous menarche in patients with a premenopausal FSH, defined as FSH <30 IU/L, compared to those with a postmenopausal FSH, defined as FSH ≥30 IU/L.

RESULTS: In 133 patients evaluated, 95 (71.4%) were White, 14 (10.5%) were Black, 6 (4.5%) were Asian, and 18 (13.5%) identified as other race. Additionaly, 114 (85.7%) were non-Hispanic and 19 (14.3%) were Hispanic. Overall, 78 (58.7%) did not have spontaneous menarche and 55 (41.4%) underwent spontaneous menarche. 53 (39.9%) had postmenopausal FSH levels and 80 (60.2%) had premenopausal FSH levels.

Of those with a premenopausal FSH, 56.3% underwent spontaneous menarche compared to 43.8% who did not. Among those with a premenopausal FSH and spontaneous menarche, 3 (6.7%), 28 (62.2%), and 14 (31.1%) had 45X0, 45X0/46XX, and other karyotypes, respectively. Of those with a postmenopausal FSH, only 18.9% later underwent spontaneous menarche with all karyotype groups represented (4, 2, and 4 patients had 45X0, 45X0/46XX, or other karyotypes, respectively). Patients with a premenopausal FSH at the time HPO axis activation were more likely to have spontaneous menarche compared to those with a postmenopausal FSH (OR 5.6, 95% CI 2.44-12.52, p<0.0001). Karyotype was an effect modifier in the relationship between menarche status and FSH (p<0.0001). Of patients with a 45X0/46XX karyotype, the model perfectly predicts the odds of spontaneous menarche, however, after adjusting for race and ethnicity, FSH and spontaneous menarche was no longer significant in those with 45X0 and other karyotypes (aOR 1.77 95% CI 0.32-9.66; p=0.51; aOR 2.85 (95% CI 0.73-11.09; p=0.131).

CONCLUSIONS: Adjusting for race and ethnicity, karyotype modified the relationship between FSH at the time of HPO axis activation and onset of spontaneous menarche in patients with Turner Syndrome.

IMPACT STATEMENT: In a racially and ethnically diverse population with Turner Syndrome, prepubertal FSH and karyotype alone could not be used to predict onset of spontaneous menarche.

ORAL ABSTRACT SESSION: PRACTICE MANAGEMENT

O-157 10:45 AM Tuesday, October 25, 2022

INTRAUTERINE INSEMINATION OUTCOMES BETWEEN REPRODUCTIVE ENDOCRINOLOGY & INFERTILITY (REI) FELLOWS AND WOMEN’S HEALTH NURSE PRACTITIONERS (NP). Sonali Iyer, BS,1 Pietro Bortoletto, MD, MSc,2 Phillip A. Roman, MD, MS,3 Steven D. Spandorfer, MD,4 Weill Cornell Center for Reproductive Medicine, New York, NY; 1The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; 2New York, NY; 3NewYork-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY.
OBJECTIVE: To evaluate intrauterine insemination (IUI) outcomes performed by reproductive endocrinology & infertility (REI) fellows versus women’s health nurse practitioners (NP) when accounting for patient and procedure specific variables.

MATERIALS AND METHODS: Retrospective cohort study performed at the Weill Cornell Center for Reproductive Medicine between 2019 and 2020. A total of n=1,911 women undergoing ovulation induction, controlled ovarian hyperstimulation, or natural cycles with intrauterine insemination were included. Patients were stratified on who performed the IUI procedure: REI fellows (1st and 2nd year) versus women’s health NPs. Pregnancy rate by provider type was the primary outcome. A multivariable logistic regression for positive HCG outcome with adjustment for age, parity (nulliparous or parous), treatment type (OL, OH, or natural cycle), provider type (NP or fellow), position of uterus (Anteverted, retroverted, or "down then up"), direction of cervix (straight or curved), and subjective procedure difficulty (easy or tricky) was performed.

RESULTS: Of the n=1,911 women included, 43.1% (n=823) were performed by REI fellows whereas 56.9% (n=1088) by NPs. There were no differences in patient demographics including age, parity, BMI, AMH, or infertility diagnosis between both groups (p>0.05). Similarly, there were no differences in stimulation protocols, number of dominant follicles recruited, and rates of bilateral tubal patency between the two groups (p>0.05). The pregnancy rate was 20.2% for REI fellows and 18.3% for NPs (p=0.290). In a multivariable logistic regression, compared to REI fellows, NP performed IUI’s had similar odds at achieving pregnancy (aOR: 0.83, 95% CI: 0.65-1.05). Increasing age was associated with decreased odds of achieving pregnancy (aOR: 0.95, 95% CI: 0.92-0.98) whereas increasing parity was associated with increased odds (aOR: 1.60, 95% CI: 1.21-2.13). There were no significant differences in odds of achieving pregnancy by treatment type, position of uterus, or perceived difficulty. Only a ‘curved’ cervical path, as perceived by the operator, was associated with decreased odds of achieving pregnancy (aOR:0.64, 95% CI:0.41-0.99).

CONCLUSIONS: When adjusting for patient and procedure specific variables, nurse practitioner performed IUI’s had similar odds of achieving a pregnancy as those performed by REI fellows. Utilizing nurse practitioners to perform IUI’s appears to be an effective way to improve access to fertility care.

IMPACT STATEMENT: REI fellows and nurse practitioners have similar pregnancy rates following intrauterine insemination.

O-158 11:00 AM Tuesday, October 25, 2022

DON’T DIVIDE THE DOSE: ONCE DAILY (QD) AND TWICE DAILY (BID) EARLY CYCLE GONADOTROPIN (GND) DOSING HAVE EQUIVALENT ASSISTED REPRODUCTIVE TECHNOLOGY (ART) OUTCOMES—A QUALITY IMPROVEMENT (QI) PROJECT. Sarah D. Cascante, MD,1 Jacquelyn Shaw, MD,2 Frederick Licciardi, M.D.,3 Mary Elizabeth Fino, M.D.,4 James A. Grifo, MD, PhD,5 Jennifer K. Blakemore, MD, MSc6 NYU Langone Prelude Fertility Center, New York, NY; 7NYU Langone Fertility Center, New York, NY; 8New York University Langone Fertility Center, New York, NY.

OBJECTIVE: For more than 25 years, our academic fertility center has prescribed GNDs BID between cycle start and the next monitoring visit 2-5 days later, when QD dosing is initiated. However, BID dosing is more complicated, leads to more medication errors and is less preferred by patients.1 Studies evaluating the impact of GND timing on ART outcomes are limited and outdated.1 Thus, we performed a QI project to assess whether changing early GND dosing to QD impacted ART outcomes.

MATERIALS AND METHODS: We reviewed all in vitro fertilization (IVF), embryo banking (EB) and oocyte cryopreservation (OC) cycles before and after changing all GND dosing to QD at our center. Cases from 28 days before (1/10-2/6/22) and 28 days after (2/7-3/6/22) the intervention were compared. We excluded cycles deviating from the protocol. Outcomes included cycle cancellations, number of oocytes and metaphase II oocytes (MII), 2-pronuclear fertilization (2PN) rate, blastocyst formation rate (BFR) and euploidy rate. Statistics included Mann Whitney U tests, t-tests and Fisher’s exacts tests (p<0.05 significant).

RESULTS: 540 cycles were included (266 BID and 274 QD). Among BID and QD cycles, dose types were similar (67% IVF/EB + 33% OC vs. 67% IVF/EB + 33% OC, p=0.93). Median age (37 vs. 36 years, p=0.09) and mean day 2/3 follicle stimulating hormone (7.5 vs. 7.7 IU/mL, p=0.45) did not differ among BID and QD doses. Cycle cancellation for low response (3% vs. 4%, p=0.82) and ovulation (2% vs. 1%, p=0.44) was similar among BID and QD doses. See table for parameters and outcomes of cycles resulting in oocyte retrieval. Median number of oocytes and M2s did not differ among doses. In IVF/EB cycles, 2PN rate and BFR were equivalent, and rate of cycles with no embryos for transfer, biopsy or cryopreservation did not differ among BID and QD doses (10% vs. 7%, p=0.44). In PGT cycles, euploidy rate was similar.

CONCLUSIONS: Early cycle QD GND dosing does not negatively impact oocyte yield or ART outcomes compared to early cycle BID GND dosing. Notably, this is the first study to show that ploidy rates are not impacted. Given that QD dosing is preferred by patients and may decrease medication errors, other centers may benefit from establishing QD injection protocols.

IMPACT STATEMENT: Early cycle QD GND dosing has equivalent ART outcomes to early cycle BID GND dosing and may improve patient satisfaction.

O-159 11:15 AM Tuesday, October 25, 2022

THE ROLE OF ADVANCED PRACTICE PROVIDERS IN THE MODERN IVF PRACTICE, CAN THEY HELP FILL THE DEARTH OF NEW REPRODUCTIVE ENDOCRINOLOGISTS? Tyl H. Taylor, PhD,1 Taylor Holt, PA-C,2 Ann Merline, PA-C,3 Stephanie Harrell, BA,3 Grace Perez, PA-C,1 Seth E. Katz, M.D.4 1REACH, Charlotte, NC; 2REACH, Charlotte, NC, NC; 3Reproductive Endocrinology Associates of Charlotte (REACH), Charlotte, NC; 4Reach, Charlotte, NC.

OBJECTIVE: IVF procedures nationwide have increased over the last decade while the graduation of fellowship trained reproductive endocrinologists (RE) has decreased; thus, creating an imbalance in doctor to patient ratios. This imbalance results in larger wait times and general patient dissatisfaction. One way to meet the growing need of infertile patients is the introduction of advanced practice providers (APP’s) to the modern IVF practice. It is the goal of study to determine and compare the conversion rates of APPs to those of RE’s.

MATERIALS AND METHODS: All new patients for the year 2021 were followed throughout treatment. The conversion rate to IVF was compared between APP’s and RE’s. Additionally, since APP’s perform ET’s, chemical and clinical pregnancy rates were compared between APP’s and RE’s. Only single embryo transfers were included in the ET data analysis. Due to the sensitive nature of the data, only percentages will be utilized for new patient volume.


RESULTS: Of the new patients seen in 2021, APPs converted 15.8% of those to IVF treatment while RE’s converted 28.3% (P<0.01). In terms of single ET’s, 55 and 400 ETs were performed by the APP’s and RE’s, respectively. There was no significant difference in average oocyte age at ET between APP’s and RE’s. There was no ET and the RE’s had over 30 years of combined experience. Regardless, APPs are still able to effectively guide patients into IVF treatment. Additionally, APP’s can also perform ET’s just as successfully as RE’s. Thus, the only role that APPs cannot successfully fulfill is surgical in nature. The role of the APP varies from practice to practice and so may the results; however, APP’s can be an effective addition to a modern IVF practice.

IMPACT STATEMENT: APP’s are able to fill the needs of a modern IVF by cycling patients through IVF and by effectively performing ET’s.

SUPPORT: none

O-160 11:30 AM Tuesday, October 25, 2022

EMBRYOLOGIST BURNOUT: PHYSICAL AND PSYCHOSOCIAL SYMPTOMS AND OCCUPATIONAL CHALLENGES CURRENTLY REPORTED BY U S EMBRYOLOGISTS. Anar Murphy, Ph.D., 1 Haley Baltimore, BS, 2 Mark S. Lapczynski, MBA, BS, 2 Glenn Proctor JR, B.S., M.H.A., 2 Elaine C. Meyer, PhD, RN, MBE, 2 Timothy Glynn, BA, 2 Alice D. Domar, Ph.D., 2 Michael G. Collins, II, PH.D. 2 New York, NY; 1TMRW Life Sciences, New York, CA; 1TMRW Life Sciences, New York, NY; 2Conceptions Reproductive Associates of Colorado, Littleton, CO; 2Psychology, Cranston, RI; 2Dudley Associates, Maplewood, NJ; 2Boston IVF, Waltham, MA; 1TMRW Life Sciences, Inc., New Orleans, LA.

OBJECTIVE: To examine (1) the prevalence of physical and psychological symptoms reported by U.S. embryologists related to their occupation, and how workplace fatigue and burnout may affect their quality of life, professional outlook, efficiency, safety, and attention to detail. (2) to determine how the current workflow and organizational characteristics of the embryology laboratory affect embryologists’ physical and psychological health; and (3) the potential measures that can be taken to improve both working conditions and embryologists’ health and well-being, and patient care.

MATERIALS AND METHODS: A cross-sectional design using a web-based survey was sent to 487 embryologists working in U.S. licensed ART/IVF clinics and private practices in 2022. The response rate was 38%. Respondents self-reported their burnout and stress levels, physical health status, and work conditions they perceived as related to their occupation using the nationally validated Maslach Burnout Inventory-General Survey (MBI-GS), a single-item work unit grade (A–F), and an occupational questionnaire. Weighted percentages for the reported physical and mental health components were calculated using univariate statistics. Student’s t-test and ANOVA to compare the means between the groups categorized based on the levels of fatigue and burnout. Pearson’s correlation coefficients to correlate the mental and physical components of their responses, and multivariate analysis to cross-correlate statistically significant and biologically important parameters will be utilized once the survey is closed.

RESULTS: A total of 71% of the embryologists reported symptoms of burnout on the exhaustion dimension and 63% on cynicism, and 54% of the respondents reported that they could not cope with their workload. The PSS showed moderate perceived stress and the PHQ-15 showed low somatic symptom severity, with 45% reporting fatigue and 47% insomnia. In addition, 3% experienced constant, 17% high, 33% moderate, and 31% mild anxiety; 43% reported anxiety was caused by the current cryopreservation processes and 43% reported technology would lessen their work-related stress. Regarding organizational characteristics, 79% reported working overtime, 75% found themselves doing double work due to lack of technology integrations and analog record, and 88% felt their employers did not understand their occupational challenges. Overall, 37% of embryologists gave their laboratories work unit grade of A (excellent), 44% – B (very good), 16% – C (acceptable), 2% – D (poor), and 2% – F (failing).

CONCLUSIONS: The surveyed embryologists reported low somatic symptom severity and moderate perceived stress, but high levels of burnout and stressful working conditions that negatively affect their well-being and may adversely affect the quality of their work.

IMPACT STATEMENT: U.S. embryologists report symptoms of stress and burnout and occupational challenges that may adversely affect the quality of their work and could be addressed by organizational enhancements and technology improvements.

O-161 11:45 AM Tuesday, October 25, 2022

ASSESSING THE EFFECTIVENESS OF A PREGNANCY-SPECIFIC OBSTRUCTIVE SLEEP APNEA SCREENING TOOL IN NON-PREGNANT, REPRODUCTIVE-AGED WOMEN. Leeann Bu, MD, 1 Laura G. Cooney, MD, 2 Mihaela Bazalakova, MD, PhD, 3 Kathleen M. Antony, MD 4 University of Wisconsin, Madison, WI; 1University of Wisconsin; 3University of Wisconsin Madison; 4University of Wisconsin-Madison, Madison, WI.

OBJECTIVE: To study whether a pregnancy-specific screening tool for obstructive sleep apnea (OSA) can be used in non-pregnant, reproductive-aged women of childbearing age.

MATERIALS AND METHODS: Cross-sectional study analysis of 3,906 non-pregnant, female participants between ages 18–45 across four datasets, Hispanic Community Health Study (HCHS), Cleveland Family Study (CFS), Wisconsin Sleep Cohort (WSC), and Stanford Technology Association and Genomics in Sleep (STAGES), provided by the National Sleep Research Resource (NSRR). For all studies, the participants completed baseline health and sleep questionnaires, anthropomorphic measures, and an overnight polysomnographic study. Facco’s four-variable sleep screening tool is a validated model to screen for obstructive sleep apnea (OSA) in pregnant women where a risk score is calculated by age + body mass index (BMI) + 15 (if history of hypertension) + 15 (if history of snoring). A positive four-variable score (≥ 50) was compared to polysomnography—the gold standard for diagnosing OSA. The severity of OSA was defined using apnea/hypopnea index (Mild OSA ≥ 5 but <15; Moderate OSA ≥ 15 but <30, and Severe ≥ 30). Sensitivity, specificity, and area under the receiver-operating curve (AUROC) were calculated.

RESULTS: 3,906 non-pregnant, female participants were included in our study (HCHS n=3,473; CFS n=72; WSC n=17; STAGES n=398). A total of 826 patients (21.1%) scored positive for OSA (HCHS: 17.0%; CFS: 34.7%; WSC: 85.7%; STAGES: 51.8%). We found that Facco’s four-variable screening tool that accurately predicts sleep apnea in pregnancy had sensitivity (36.8%) and specificity (82.3%) in predicting OSA in non-pregnant, reproductive aged women. The AUROC was 0.6 across all studies.

CONCLUSIONS: Our findings indicate that Facco’s four-variable screening tool had moderate specificity but poor sensitivity in predicting sleep apnea in non-pregnant, reproductive-aged women. Further research is needed to understand the impact of sleep apnea in women seeking fertility treatment.

IMPACT STATEMENT: Popular OSA screening questionnaires like the STOP-BANG give higher weight to male sex and age >50, which do not apply to young reproductive aged women. Given the association between OSA and adverse pregnancy outcomes including fetal growth restriction, hypertensive disorders of pregnancy, and gestational diabetes mellitus, development of screening questionnaires tailored to identify at risk women seeking fertility care is imperative.

SUPPORT: N/A


O-162 12:00 PM Tuesday, October 25, 2022

OBJECTIVE: In the online world of today, savvy patients seek reproductive health information primarily from the websites of fertility clinics. On its websites, the presence of a digital identity of the team has the power to influence patients in choosing a practice. Typically, the team of fertility clinics is made up of physicians, nurses, embryologists, and administrative staff. In particular, embryologists might seem in a unique position because, unlike the bedside and the counter staff, they spend less time developing a relationship with the patient. In this framework, the objective of this study was to conduct profiles textual analysis on fertility clinic websites, measuring the degree to which embryologists are e-visible.

MATERIALS AND METHODS: The Society for Assisted Reproductive Technology (SART) and the Human Fertilisation and Embryology Authority (HFEA) registries publicly available websites were used to identify fertility clinics in the United States and the United Kingdom. The “Our team” page within each website was accessed during the month of March 2022. Information on all clinic providers was collected and analyzed including specialty, professional headshot, and biography.

RESULTS: The search scanned 447 fertility clinic websites. Embryologists have the least commonly professional identification by their names (29.79%) compared to physicians (95.97%, p < 0.0001), nurses (55.70%, p < 0.0001), embryology laboratory directors (46.63%, p < 0.0001), and administrative staff (39.64%, p = 0.000058). This finding also consistently applies across other professional identifiers such as professional headshots and biographies. Professional headshots of embryologists (26.94%) were less prominent than those of physicians (92.75%, p < 0.00001), nurses (50.00%, p < 0.0001), and embryology laboratory directors (43.52%, p < 0.00001). Similarly, biographies of embryologists were underrepresented (19.43%) as opposed to physicians (94.30%, p < 0.0001), nurses (42.23%, p < 0.00001) and embryology laboratory directors (42.23%, p < 0.00001). Further, embryology laboratory directors also lack name recognition on websites (46.63%) compared to physicians (95.97%, p < 0.00001) and nurses (55.70%, p < 0.01).

CONCLUSIONS: The present study showed that embryologists and embryology laboratory directors have low professional visibility on fertility clinic websites. Fertility clinics may consider bolstering embryology laboratory team professional internet presence. This will seemingly help to increase the transparency of care and to fuel the competitive advantage of the clinic.

IMPACT STATEMENT: Working behind closed doors, embryologists may be well positioned as leaders in creating and evaluating institutional policies and ensuring early counseling surrounding reproductive desires and legacy.

MATERIALS AND METHODS: The Society for Assisted Reproductive Technology (SART) and the Human Fertilisation and Embryology Authority (HFEA) registries publicly available websites were used to identify fertility clinics in the United States and the United Kingdom. The “Our team” page within each website was accessed during the month of March 2022. Information on all clinic providers was collected and analyzed including specialty, professional headshot, and biography.

RESULTS: The search scanned 447 fertility clinic websites. Embryologists have the least commonly professional identification by their names (29.79%) compared to physicians (95.97%, p < 0.0001), nurses (55.70%, p < 0.0001), embryology laboratory directors (46.63%, p < 0.0001), and administrative staff (39.64%, p = 0.000058). This finding also consistently applies across other professional identifiers such as professional headshots and biographies. Professional headshots of embryologists (26.94%) were less prominent than those of physicians (92.75%, p < 0.00001), nurses (50.00%, p < 0.0001), and embryology laboratory directors (43.52%, p < 0.00001). Similarly, biographies of embryologists were underrepresented (19.43%) as opposed to physicians (94.30%, p < 0.0001), nurses (42.23%, p < 0.00001) and embryology laboratory directors (42.23%, p < 0.00001). Further, embryology laboratory directors also lack name recognition on websites (46.63%) compared to physicians (95.97%, p < 0.00001) and nurses (55.70%, p < 0.01).

CONCLUSIONS: The present study showed that embryologists and embryology laboratory directors have low professional visibility on fertility clinic websites. Fertility clinics may consider bolstering embryology laboratory team professional internet presence. This will seemingly help to increase the transparency of care and to fuel the competitive advantage of the clinic through its human capital.

IMPACT STATEMENT: Working behind closed doors, embryologists remain overlooked on fertility clinic websites.

ORAL ABSTRACT SESSION: PEDIATRIC OR ADOLESCENT

O-163 10:45 AM Tuesday, October 25, 2022

LEAVING A LEGACY: ALLIED HEALTH PROFESSIONALS’ PERCEPTIONS OF FERTILITY PRESERVATION AND POSTHUMOUS REPRODUCTION FOR ADOLESCENT AND YOUNG ADULTS WITH A POOR CANCER PROGNOSIS. Francesco Barrett, MD MBA, Amani Sampson, B.A, M.S, L Lisa Campo-Engelstein, Ph.D., Arthur L. Caplan, Ph.D., Susan T. Vadaparampil, Ph.D., Gwenølynn P. Quinn, Ph.D.; NYU Langone School of Medicine, New York, NY; ‘550 First Ave, New York, NY; University of Texas Medical Branch; New York University School of Medicine, Department of Population Health, Division of Medical Ethics, New York, NY; Moffitt Cancer Center, Tampa, FL, New York University School of Medicine, Department of Obstetrics and Gynecology, New York, NY.

OBJECTIVE: To explore allied health professions (AHPs) experiences and with perceptions of posthumous assisted reproduction (PAR) among patients, families, and partners in cancer care and fertility.

MATERIALS AND METHODS: We conducted a qualitative analysis of video-based 90 minute focus groups (FGs) of AHPs who participated in the Enriching Communication Skills for Health Professionals in Oncofertility (ECHO) training program from May to August 2021. Moderator-facilitated discussions were guided by topics related to experiences around discussions and utilization of PAR amongst AYA with a poor cancer prognosis. Thematic analysis was conducted using the constant comparison method.

RESULTS: 43 AHPs participated in one of seven FGs (mean = six/group). Three themes emerged: 1) PAR as palliative care: preserving patient’s legacy for their partner, siblings, and parents; 2) ethical and legal considerations for balancing patient’s time-sensitive needs; and 3) barriers AHPs encounter navigating complex dynamics of care in this population.

CONCLUSIONS: AHPs desired conversations around legacy building are what the deceased wanted. Subthemes included an emphasis on patient autonomy, a multidisciplinary approach to counseling, early initiation of fertility discussions continuing over time, documenting reproductive desires, and concerns for family and offspring after patient death.

Many participants described insufficient policies and guidance within their institutions, with few noting that ethics committees were involved with complicated PAR cases. Several discussed desire for early implementation of advanced directives to clarify AYA’s explicit reproductive wishes. However, several acknowledged these conversations rarely happened in this population.

IMPACT STATEMENT: The development of transparent institutional policies, implementation of multidisciplinary care teams, and oversight with ethics committees may improve the provision of reproductive health care and/or end-of-life care for AYAs with a poor cancer prognosis and their families.

MATERIALS AND METHODS: The Growing Up Healthy Study (G-UHS) is a prospective cohort study, investigating the long-term health of offspring conceived after ART (aged 14, 17 and 20 years), in the two operational fertility clinics in Western Australia 1991-2001. Their long-term health outcomes were compared to those of offspring conceived without ART from the Raine Study Generation 2 (Gen2). Both cohorts are representative of the local adolescent population.

Mental health parameters and behavior were assessed at ages 14 and 17, through the parent completed ‘Child Behavior Checklist’ (CBCL) (ART vs. non-ART: age 14: N=150 vs. N=1,781, age 17: N=160 vs. N=1,351), and the adolescent completed equivalent ‘Youth Self-report’ (YSR) (age 14: by N=151 vs. N=1,557, age 17: N=161 and N=1,232). Both tools generate a T-score (standardized for age and sex) for internalizing (withdrawn, somatic complaints, anxious/depressed), externalizing (delinquent/aggressive behavior), and total behaviour. Adolescents also completed the
‘Beck Depression Inventory for Youth’ (BDI-Y) (age 14: N=151 vs. N=1563, age 17: N=161 vs. N=1219). Higher scores indicate more problems on all of the above tools.

Generalized estimating equations adjusted for the following covariates: non-singleton, primiparity, primary caregiver smoking, family financial problems, socio-economic status, maternal and paternal age at conception, and gestational age.

RESULTS: At both 14 and 17 years, ART vs. non-ART adolescents reported lower mean T-scores for externalizing problems (age 14: 50 vs. 52, p=0.044, age 17: 49 vs. 52, p<0.0001). A similar effect was reported by parents, although not significant (age 14: p=0.336, age 17: p=0.168). Less ART adolescents reported a T-score above the clinical cut-off for externalizing behavior (≥ 60) (age 14: 7.3% vs. 16.3%, p=0.003, age 17: 8.1% vs. 19.7%, p<0.0001). At both ages, no differences in internalizing behavior were reported by adolescents (age 14: p=0.269, age 17: p=0.870), however higher mean scores were reported by ART vs. non-ART parents (age 14: 51 vs. 48, p=0.040, age 17: 50 vs. 45, p<0.0001). No differences in internalizing behavior above the clinical cut-off (≥ 60) were observed. At age 17, ART parents reported higher total behavior scores than non-ART parents (47 vs. 44, p=0.003).

At age 14, ART vs. non-ART adolescents reported significantly higher mean scores on the BDI-Y (8 vs. 5, p=0.007), a higher percentage of adolescents with a score indicating clinical depression (≥ 17) (12.6% vs. 8.5%, aOR 2.16 (1.06-4.40), p<0.007), as well as more moderate/severe depression (≥ 21) (9.3% vs. 4.0%, p=0.009). At age 17, no differences were reported on the BDI-Y.

CONCLUSIONS: Our study observed less externalizing behavior (delinquent/aggressive), and more parent reported internalizing behavior, as well as more (clinical) depression at age 14, in ART vs. non-ART adolescents.

IMPACT STATEMENT: The use of ART is common, and mental health disorders are increasing, therefore knowledge about a potential association is important for parents and health care providers.

SUPPORT: This project was funded by an Australian NHMRC Grant (Hart et al., ID. 1042269).

O-165 11:15 AM Tuesday, October 25, 2022

TOTAL TESTICULAR VOLUME AND TESTICULAR VOLUME DISCREPANCY IN THE ASSESSMENT OF MALE FERTILITY POTENTIAL IN ADOLESCENT VARIOCELE. Adele Raymo, BS,1 Maria Camila Suarez Arbelaez, MD,2 Samantha Isern, MD, Vinayak Madhusoodan, M.D., M.B.A.,1 Daniel E. Nassau, MD,1 Alireza Alam, MD,2 Ranjith Ramasamy, M.D.1 Nicklaus Children’s Hospital, Miami, FL;2 University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Adolescent varicocelectomy is recommended when either an abnormal semen analysis (SA) or testicular volume discrepancy (TVD) ≥20% is present. However, TVD may occur in the healthy pediatric population. We hypothesized that lower than expected ultrasonographic TVD and total testicular volume (TTV) are indicative of poor semen parameters in adolescents with varicocele.

MATERIALS AND METHODS: We retrospectively identified by diagnosis-codes boys <21 years with left varicocele from 2013-2022. Inclusion criteria were Tanner stage of ≥3, and having a SA and ultrasound prior to surgery. Semen parameters and clinical variables were compared among patients with TVD<20% to those with ≥20%TVD. For Tanner 5 patients, the total motile sperm count (TMSC) was compared between patients with TTV≥30cc (normal cutoff for post-pubertal patients) and TTV<30cc. Comparison among groups was assessed by unpaired t-test and Chi-square test (p<.05).

RESULTS: A total of 127 patients were included in the study. The mean age at the time of the SA was 17.3 years (range of 14-21). TVD<20% was observed in 86 patients and TVD≥20% in 41 patients. TVD was not associated to any of the analyzed variables (table). Of 81 Tanner 5 patients, 23 had TTV≥30cc and 58 had TTV<30cc. The mean TMC and TVD for Tanner 5 boys with TTV≥30cc was 132.6±176.6 million and 13.3±9.3%, compared to 57.5±73.9 million and 18.3±12.7% for boys with TTV<30cc (p=0.03 and p=0.03, respectively).

CONCLUSIONS: In this cohort of Tanner 5 patients with varicocele, TTV<30cc was associated with low TMSC and high TVD. We therefore recommend considering TVD as an indicator of testicular growth arrest in Tanner 5 adolescents.

IMPACT STATEMENT: In patients with varicocele and Tanner stage 5, TTV<30cc should be considered an indicator for male fertility potential.

O-166 11:30 AM Tuesday, October 25, 2022

THE RELATIONSHIP BETWEEN ESTROGEN AND SUBSEQUENT GROWTH RESTRICTION AMONG ADOLESCENTS WITH HEAVY MENSTRUAL BLEEDING. Jessie M. Hoxie, B.S.,1 Sarah D. Compton, Ph.D., M.P.H.;1 Mina M. Farahzad, M.D., Ph.D.,2 Olivia K. Winfrey, M.D., M.P.H.,3 Monica W. Rosen, M.D.4 1University of Michigan Medical School, Ann Arbor, MI; 2University of Michigan, Ann Arbor, MI.

OBJECTIVE: To evaluate the relationship between estrogen-containing treatments for heavy menstrual bleeding (HMB) and subsequent growth restriction compared to progesterone-only or non-hormonal treatments among adolescent girls at menarche.

MATERIALS AND METHODS: A retrospective chart review was performed of adolescent females aged 10-15 years who presented to an institution-affiliated outpatient, inpatient, or emergency department setting for management of HMB within 3 months of menarche. Heights (cm) at menarche, 6 months, 12 months, and 24 months were compared among patients treated with 1) estrogen-containing methods, 2) progesterone-only methods, and 3) non-hormonal methods (controls). The primary outcome measure was the difference in height between menarche and 24 months. Groups were compared using bivariate analysis with chi-square or Fisher’s exact test where appropriate and linear regressions. All statistics were performed in Stata v16 using a significance level of 0.05.

RESULTS: At 24 months, the mean increase in height from menarche was 6.4 cm among the control group (n=54), 7.2 cm among the progesterone-only group (n=10), and 3.8 cm among the estrogen group (n=16). The increase in height for the estrogen group was significantly decreased compared to the control group (p=0.041). A significant difference was not observed when comparing the progesterone-only group to the control group (p=0.87). Adolescents receiving estrogen had an average of 1.8 fewer cm of growth (absolute change in height) compared to those receiving either progesterone-only or non-hormonal treatment. No significant differences existed between groups at the 6-month or 12-month timepoints. Additionally, for each year younger an adolescent was at menarche, she had 1 fewer cm of growth (change in height) at 24 months after menarche (p<0.002).

CONCLUSIONS: Estrogen-containing treatments for HMB initiated within 3 months of menarche was associated with reduced height at 24 months compared to treatment with progesterone-only or non-hormonal methods. The clinical applicability of the 1.8 cm absolute reduction in height in the estrogen group may be of considerable significance for those who are shorter at baseline.

IMPACT STATEMENT: The risks and benefits of implementing estrogen-containing methods for management of HMB must be considered when discussing treatment options for adolescents near menarche given estrogen’s potential to limit height up to 24 months after menarche.

<table>
<thead>
<tr>
<th>Variables</th>
<th>TVD &lt; 20% n=86</th>
<th>TVD ≥ 20% n=41</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at SA (years)</td>
<td>17.5±0.13</td>
<td>16.9±1.3</td>
<td>0.03</td>
</tr>
<tr>
<td>Varicocele grade</td>
<td>0</td>
<td>2</td>
<td>0.09</td>
</tr>
<tr>
<td>1</td>
<td>13</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>73</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>51.2±56.8</td>
<td>60.1±83.0</td>
<td>0.27</td>
</tr>
<tr>
<td>Sperm-concentration (millions)</td>
<td>74.5±113.8</td>
<td>74.6±114.3</td>
<td>0.50</td>
</tr>
<tr>
<td>TMSC (millions)</td>
<td>21</td>
<td>12</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Vol. 118, No. 4, Supplement, October 2022
OBJECTIVE: Sickle Cell Disease (SCD) and associated gonadotoxic treatments may impair fertility. The hereditary nature of SCD can have implications for reproductive decision-making and outcomes, though little is known about how these topics are discussed between patients and providers. Our objective was to examine fertility-related care and genetic counseling among adolescents and young adults (AYAs) with SCD.

MATERIALS AND METHODS: This is a retrospective chart review of all patients ages 14-21 with SCD (all genotypes) from two large medical centers (Site A: Ohio and Site B: New York) from 1/1/2015 – 12/31/2019. Demographics, medical characteristics, if gonadotoxic treatment was received (hydroxyurea and bone marrow transplant (BMT), and discussion of fertility related to SCD/treatment were abstracted from medical charts. ANOVA and chi-square were conducted (p<0.05 considered significant).

RESULTS: The final sample (N=167) included 139 (83.2%) patients from Site A and 28 (16.8%) from Site B. Mean age was 18.15 (SD 3.11) and 90 (53.9%) patients were female. 7 (4.2%) patients had documented discussions related to SCD/treatment were abstracted from medical charts. ANOVA and chi-square were conducted (p<0.05 considered significant).

CONCLUSIONS: Despite the potential impact of SCD and gonadotoxic treatments on reproductive health, fertility was rarely addressed in our study population. Rates of counseling about the hereditability of SCD varied by site, with genetic counseling being documented more frequently at Site A (where a genetic counselor is present within the comprehensive care team) compared to Site B (where genetic counseling is not available).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Yes, N (%)</th>
<th>No, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyurea Treatment</td>
<td>104 (62.3%)</td>
<td>63 (37.7%)</td>
</tr>
<tr>
<td>Fertility Implications (FI) Documented</td>
<td>8 (7.7%)</td>
<td>96 (92.3%)</td>
</tr>
<tr>
<td>Before Use</td>
<td>1 (1.0%)</td>
<td>103 (99.0%)</td>
</tr>
<tr>
<td>Fertility Preservation (FP) Options</td>
<td>0 (0.0%)</td>
<td>104 (100%)</td>
</tr>
<tr>
<td>Fertility Specialist (FSR) Referral Provided</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMT Treatment</td>
<td>2 (1.2%)</td>
<td>165 (98.8%)</td>
</tr>
<tr>
<td>FI</td>
<td>1 (50)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>FP</td>
<td>1 (50)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>FSR</td>
<td>0 (0)</td>
<td>2 (100%)</td>
</tr>
</tbody>
</table>

O-167 11:45 AM Tuesday, October 25, 2022

FERTILITY & STERILITY

O-169 10:45 AM Tuesday, October 25, 2022

EXPOSURE TO REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY (REI) AMONG OBSTETRICS & GYNECOLOGY RESIDENCY PROGRAMS. Rebecca Zaidaun, BA,1 Eve C. Feinberg, MD,2 Mary Ellen Pavone, MD1 1Midwestern University Chicago College of Osteopathic Medicine, Chicago, IL;2Northwestern University, Chicago, IL.

OBJECTIVE: As prior studies have found that Ob-Gyn trainees believe they have inadequate experience in the REI subspecialty, we sought to evaluate the amount of time devoted to REI within the four-year rotation schedule of ACGME accredited Ob-Gyn residency programs, comparing exposure in programs with and without an REI fellowship.

MATERIALS AND METHODS: This study was approved by the Institutional Review Board of Northwestern University. A list of current Ob-Gyn residency programs with and without an REI fellowship was compiled from ACGME and ACOG databases. The programs’ websites were reviewed to determine the number of REI rotations and the type of rotations pursued by alumni. If the information was not found on the website, program coordinators were contacted either by email or phone.
Wilcoxon rank sum test was utilized to assess differences in total REI rotation time between REI-affiliated and non-affiliated programs, while Spearman’s correlation was utilized to assess association between total REI exposure and percentage of alumni pursing REI fellowships.

RESULTS: Data was accrued from 46 of 49 REI-affiliated programs and 145 of 170 non-REI affiliated programs. The cumulative length of REI rotations throughout residency ranged from 0 weeks to 20 weeks. Cumulative rotation length was greater in non-REI than REI-affiliated programs (median=8 weeks vs. 5 weeks, p=0.005). Among all programs, 24% had a required REI rotation in PGY-1, 61% in PGY-2, 50% in PGY-3, and 16% in PGY-4. Compared to REI-affiliated programs, a larger proportion of non-REI affiliated programs had required REI rotations in the last two years of training (63% vs. 46%, p=0.040). The proportion of alumni pursuing REI fellowship was significantly greater in REI affiliated programs than non-REI affiliated programs (9.5% vs. 3.1%, p<0.001).

CONCLUSIONS: Compared to non-REI affiliated programs, Ob-Gyn residencies affiliated with REI fellowships spent less time throughout residency training in REI rotations but had a greater proportion of residents matriculate to REI fellowships.

IMPACT STATEMENT: The length of REI exposure throughout Ob-Gyn residencies varies greatly across ACGME accredited programs. Further research is needed to assess the appropriate amount of REI exposure necessary to adequately prepare Ob-Gyn trainees, and whether the length of REI rotations should be standardized across programs. While REI-affiliated programs had less cumulative exposure to REI, it is possible that these programs allow residents to foster relationships with REI faculty, develop research skills, and increase engagement in the field which prepares them to matriculate to REI fellowships.

O-170 11:00 AM Tuesday, October 25, 2022

REPRODUCTIVE EXPERIENCES OF PHYSICIANS: WHAT ARE WE MISSING? Jensen Reckhow, MD, MPH,1 Alessandra J. Ainsworth, MD,1 Elizabeth B. Habermann, PhD,2 Kimberly Holst, MD,3 Ruth Bates, MD,4 Susan Kók, MD,5 Chandra C. Shenoy, MD,1 Mayo Clinic, Rochester, MN; 2Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery Surgical Outcomes Program, Mayo Clinic, Rochester, MD, Rochester, MN.

OBJECTIVE: More women are entering medicine today than ever before. Previous research has shown that female physicians have later pregnancies, higher rates of infertility, and higher rates of adverse obstetrical outcomes. How a career in medicine impacts reproductive experiences and decision making remains important.

MATERIALS AND METHODS: A 54-item survey was sent to all non-trainee physicians at a single institution. This subset analysis was limited to those who identified their gender as female. Data were summarized using frequency tables and comparisons were made using chi-square and one-way ANOVA tests.

RESULTS: A total of 422 completed surveys were included. The response rate was 24.3%. Of the 223 respondents who identified as women, 170 were from medical specialties and 53 were from surgical specialties. Female respondents reported higher rates of infertility as compared to the general US population (23.9% vs 19%), and 62.6% reported perceived increased risk of subfertility, infertility, and pregnancy complications because of their profession. Compared with women in medical specialties, those in surgical specialties were significantly more likely to report physically demanding work conditions (78.4% vs 33.0%, p<0.001) and radiation exposure (32.4% vs 10.3%, p=0.002) as increased work-related risks, while most women in all specialties (85.1%) reported long work hours as a significant occupational risk. There was no difference in infertility or adverse obstetrical outcome rates between female respondents in medical and surgical specialties. Among women diagnosed with infertility, those in surgical specialties were more likely to utilize in vitro fertilization (IVF) (66.7% vs 19%). Nearly all respondents in surgical specialties (96.2%) reported a stigma regarding having children in the medical field. Many (72.7%) of the female respondents reported delaying childbearing. The most cited reason for this in both groups was the need to focus on education, training, and professional development.

CONCLUSIONS: These results support previous trends showing delayed childbearing and increased rates of infertility among physicians, while shedding new light on stigma associated with childbearing and perceived occupational hazards of a career in medicine. Although perceived occupational hazards are increased among surgical colleagues, rates of infertility and adverse pregnancy outcomes are similar compared to those in medical specialties. Further research as to why those in surgical specialties required more aggressive infertility treatments is needed. Removing the stigma surrounding childbearing remains of utmost importance.

IMPACT STATEMENT: Better understanding of the reproductive experiences of physicians is critical to recruiting and retaining a skilled workforce and fostering career and life satisfaction in this profession. Continued research on the impact of specific occupational hazards and increased need for IVF is important, but women should not be discouraged from choosing a surgical specialty based on a similar overall risk of infertility and pregnancy outcomes across specialties.

O-171 11:15 AM Tuesday, October 25, 2022

ONE RESULT, MANY EYES: CREATING A RESULTS SAFETY NET IN A UNIVERSITY HOSPITAL-BASED REPRODUCTIVE ENDOCRINOLOGY & INFERTILITY CLINIC. Blake Vessa, M.D.; Radhika Malhotra, B.S.; Anat Chemerinski, M.D., David L. Howard, M.D., Ph.D.; Sara Morelli, M.D., Ph.D.; Rutgers New Jersey Medical School, Newark, NJ; Dumont, NJ.

OBJECTIVE: To assess the effectiveness of a quality improvement project aimed at reducing the time interval from when the results of laboratory tests ordered in a university-based outpatient Reproductive Endocrinology and Infertility (REI) clinic (Newark, NJ) are published to the electronic medical record, to when those laboratory test results are reviewed by a physician.

MATERIALS AND METHODS: A quality improvement project was implemented in February 2021. Previously, laboratory test results only went to the inbox of the attending physician who supervised care of the patient on the day of order entry. The intervention consisted of changing the settings in the electronic medical record so that results of tests ordered by any fellow or attending physician in the REI division would simultaneously be published to the inbox of all fellows. Charts were reviewed from 3 months prior to the intervention (October, November, December of 2020) and from 3 months after the intervention (April, May, June 2021). Demographic data including age, race, ethnicity, and insurance type were recorded. The primary endpoint was time interval (in days) from when laboratory test results were published to when the results were reviewed by a provider. The median time interval pre- versus post-intervention was compared using the Wilcoxon rank sum test.

RESULTS: A total of 142 patients were included in the study (87 in the pre-intervention group, and 55 patient charts in the post-intervention group). Demographics were similar between the two groups: median age was 35 years old, 79.3% of patients in pre-intervention group were seen for infertility vs. 69.8% in the post-intervention group, and 32.2% patients were uninsured in the pre-intervention group vs. 32.1% in the post-intervention group. The median time interval from laboratory results being published to the electronic medical record to being reviewed by a physician was 6.0 days [IQR 3.1-29.3] in the pre-intervention group vs. 2.4 days [IQR 0.9-6.4] in the post-intervention group (p<0.001).

CONCLUSIONS: A simple quality improvement effort consisting of publishing laboratory test results to the inboxes of a pool of physicians rather than a single physician resulted in a 59% decrease in the median interval from when test results were published to when test results were reviewed by a physician. The results of this study, if replicated, have broad implications for improving quality of care in the outpatient setting.

IMPACT STATEMENT: This intervention optimized the ability of providers to deliver the highest quality healthcare within a university-based REI clinic, with an added educational benefit for trainees.

OBJECTIVE: To assess obstetrics and gynecology (OB/GYN) residents’ and program directors’ perceptions of current transgender care training as well as to identify barriers that prevent clinical competency and application to care for transgender and gender diverse patients.

MATERIALS AND METHODS: An electronic survey was sent to 183 OB/GYN residency programs identified through the American College of Obstetricians and Gynecologists (ACOG) list of OB/GYN residencies in the U.S. Two surveys were created, one for residents and one for program directors (PDs). Both surveys consisted of questions regarding personal experiences with transgender care, perceptions about current transgender care training approaches, as well as self-perceived level of preparedness, comfort, and knowledge in providing care for transgender patients. Data were collected via Qualtrics and analyzed using IBM SPSS Statistics. Composite measures were calculated where appropriate.

RESULTS: Data were collected from 23 PDs and 63 residents across five regions defined by the Council on Resident Education in Obstetrics and Gynecology (CREOG). Over 70% of PDs reported not having an established transgender training curriculum in their residency program. The most cited barrier was lack of topic-specific competency among faculty (40.9%), while limited curricular time was also a commonly cited barrier (36.4%). However, among PDs who reported not having an established transgender care training curriculum, a majority (71.4%) reported that there were plans to implement one within the next year. On a scale of 1 to 5, the mean knowledge of transgender care among PDs was 2.98 (SD = 0.98). Approximately half of PDs reported low knowledge of transgender care (score of less than 3.00) and approximately three-quarters of residents reported low knowledge of transgender care (score of less than 3.00, M = 2.46 (SD = 0.75)). On a scale of 1 to 5, the mean satisfaction of PDs for the transgender care curriculum was 2.42 (SD = 0.84). Most PDs (63.2%) were dissatisfied (score of 2.5 or below) with the current curriculum, and most residents (94.7%) reported that they would like their program to include more education on how to provide healthcare for transgender patients. Most PDs were supportive of using standardized training materials as part of their transgender care curriculum if they were available (94.4%).

CONCLUSIONS: Results from this study indicate that while >70% of residency programs do not have an established transgender training curriculum, the majority would be supportive of using standardized training materials if they were available; this is especially important given that the current knowledge of transgender care amongst both program directors and residents is low.

IMPACT STATEMENT: In light of ongoing proposed and passed legislation across the country that threaten access to gender-affirming, and arguably lifesaving, healthcare by transgender individuals, this study contributes to the limited pool of data that aims to improve care for transgender and gender diverse patients provided by OB/GYN physicians.

SIMULATION IN REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY (REI): CLOSING THE COUNSELING GAP. Jacquelyn Shaw, MD,1 Brielle Blatt, BS,2 Virginia Drda, BA, Sondra R. Zabar, MD,1 Frederick Licciard, MD,1 NYU Langone Fertility Center, New York, NY;2 Huntington, NY;1 New York Simulation Center For Health Sciences, New York, NY;1 NYU Grossman School of Medicine, New York, NY;2 NYU Langone Health, New York, NY.

OBJECTIVE: Simulation is a well-established, effective method of education.1 In REI, existing simulations focus on procedure based surgical2 and transfer skills.3 However, there is a gap in how to educate fellows and mid-level providers to best manage challenging patient encounters experienced during morning monitoring. Due to time limitations, these interactions are brief, but with complex medical and emotional issues that require acknowledgement and resolution.

MATERIALS AND METHODS: A simulation with three standardize patients (SP) presenting common challenging patient encounters was developed and implemented at a single academic REI program. The encounters included patients with: 1) poor stimulation response; 2) miscarriage diagnosed; and 3) complex cycle preparation logistics. All fellows and midlevel providers were invited to participate. Encounters were observed by REI attending physicians and feedback was provided by both the SPs and attending observers. Participants completed a debrief and quality improvement survey at the completion of the simulation to evaluate the utility and areas of improvement.

RESULTS: Six REI providers participated in the simulation program: four fellows (PGY5 to PGY7) and two nurse practitioners, all with experience monitoring cycling patients. All participants completed all three encounters and encounter specific evaluations (6/6); 83% (5/6) completed a survey on the overall simulation experience. A Likert scale of 1 (strongly disagree) to 5 (strongly agree) was used to evaluate participant perception of the experience. Overall, participants felt moderately prepared for (3, range 1-5) and somewhat anxious (4, range 3-5) during the encounters. Participants felt strongly that the encounters: 1) modeled real-life scenarios (5, range 2-5); 2) will change their approach to future patients (5, range 3-5); 3) should be offered to others (5, range 3-5); 4) enhanced their teaching skills (4.5, range 3-5); and 5) should be repeated in future simulations (5, range 3-5). The majority of participants strongly felt this should have been offered earlier in their training or when they first started working in their current role (5, range 4-5). Participants felt simulation in general: 1) could be offered more frequently (4, range 2-5); 2) is effective at demonstrating existing skills (4, range 2-5); and 3) reflect real life scenarios (4, range 4-5). Based on surveys of the SPs, learners scored highest in providing clear explanations, being non-judgmental, and non-verbal behavior. Areas most in need of improvement included clarification through repetition, providing understanding of the next steps and providing alternative treatment options.

CONCLUSIONS: This new simulation program was highly received by our learners. Simulation should be expanded in REI programs to include experiences commonly encountered during morning monitoring sessions. While this is most crucial early in training, participants with higher level of experience continue to benefit from simulation.

IMPACT STATEMENT: REI trainees welcome and benefit from simulation experiences focused on patient counseling.

SUPPORT: None

REFERENCES:
DETECTION OF EUPOD PREGNANCY LOSS FINGERPRINT FROM SERUM VIA QUANTUM DEFECT-MODIFIED CARBON NANOTUBE ARRAYS. Pietro Bortolato, MD, MSc.1 Mijin Kim, PhD.2 Declan Gwynne, BS.2 Ewelina A. Randall, BS.2 Dylon James, PhD.3 Daniel A. Heller, PhD4 The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; 1Memorial Sloan Kettering Cancer Center; 2Weill Cornell Medicine, New York, NY; 3Memorial Sloan Kettering Cancer Center, New York, NY; 4The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: We sought to utilize quantum defect-modified carbon nanotube biosensors to build an array platform to detect a euploid pregnancy loss fingerprint from patient’s sera at their first pregnancy test following euploid embryo transfer.

MATERIALS AND METHODS: Patients undergoing IVF with preimplantation genetic testing for aneuploidy (PGT-A) at the Weill Cornell Center for Reproductive Medicine between 2019 and 2021 were reviewed. We included the serum of patients undergoing single euploid embryo transfer and excluded those with vanishing twins or more than one gestational sac on ultrasound. We synthesized a library of DNA-stabilized organic color centers (OCCs) and interrogated a small cohort of patients (n=15) with euploid miscarriage or biochemical pregnancy (i.e. pregnancy loss) versus live birth to identify the best performing combinations in their ability to discriminate between the two pregnancy outcomes. Variance in the intensity and/or wavelength of the E11 or E13 fluorescence bands were assessed via t-test. After screening and selecting the OCC/DNA combinations that provided highest degree of variance (p<0.10) we then performed large-scale screening on the sera of patients who had a live birth (n=595), miscarriage (n=111), biochemical pregnancy (n=213), or did not achieve pregnancy (n=250). Variance was assessed via one-way ANOVA with Tukey correction for multiple comparisons.

RESULTS: Of the 13 unique DNA-stabilized OCC’s screened on the sera of patients with resulting pregnancy loss (n=5, biochemical, n=5 miscarriage) or live birth (n=5) we identified 5 combinations that provided the highest degree of discrimination between these two pregnancy outcomes (p<0.10): 3F-4-CO2H*CT2C3T2C, 3,4,5 -F3*(AT)15, 4-NET2*(TAT)4, 4-NET2*(GT)15, 4-NET2*(AT)4. We then expanded our screening of these 5 OCC/DNA combinations to the larger study cohort (n=1,169). Each of the 5 OCC/DNA combinations tested provided statistically significant (p<0.05) differentiation between pregnant (live birth, biochemical, or miscarriage) and non-pregnant states utilizing either E11 or E13 wavelength or intensity data. Differentiation between miscarriage vs. live birth and biochemical vs. live birth was more variable among the 5 OCC/DNAS tested with certain fluorescence spectra features providing statistically significant differentiation. Four of the five OCC/DNA combinations tested provided at least 2 statistically significant findings between the pregnancy outcomes of interest.

CONCLUSIONS: Quantum defect-modified carbon nanotube biosensors can differentiate between biochemical, miscarriage, and live birth outcomes from the sera of patients at their first pregnancy test following euploid embryo transfer. Given variability in spectra features with statistical significance for the 5 OCC/DNA combinations tested, we plan to apply a machine learning approach to integrate data with clinical variables to improve the accuracy of differentiation.

IMPACT STATEMENT: Quantum defect-modified carbon nanotube biosensors can detect a euploid pregnancy loss signature.
channel regulation, metabolism, and a variety of secreted proteins. Filtered markers allowed us to re-classify single cells from a publicly available dataset with high resolution. In addition to distinguishing ICM from TE, we identified clusters of primitive endoderm, epiblast, and polar trophectoderm in a single analysis.

CONCLUSIONS: Using a mechanical dissociation approach, we have identified a cohort of high-quality marker genes that distinguish human TE from ICM across multiple stages of blastocyst development. This molecular insight into early lineage differentiation will dramatically simplify and improve reliability in lineage calls for subsequent single cell analyses. These findings permit for more detailed studies on cellular differentiation, including distinguishing high from low quality TE or ICM, identifying core transcriptional networks and regulators of each respective cell fate, and assessing how TE and ICM differ across the sexes.

IMPACT STATEMENT: Our identification of novel ICM and TE markers allows for reliable determination of cellular lineage in the human blastocyst, facilitating future single cell analyses and advancing understanding on the transcriptional profiles of these core blastocyst cell types.

REFERENCES:


O-177 11:15 AM Tuesday, October 25, 2022

LIVE-IMAGING OF HUMAN EMBRYOS REVEALS NUCLEAR DNA RELEASE. Robin Skory, MD, PhD,1
Ana Domingo-Muelas, PhD,1
Adam A. Moverley, MSc,2
Goli Ardestani, PhD,1
Oz Pomp, PhD,1
Carmen Rubio Lluesa, PhD,1
Piotr Tetlak, PhD,2
Blake Hernandez, BS,1
Luis Navarro Sanchez, PhD,1
Carmen M. Garcia Pascual, PhD,1
Stephanie Bissiere, PhD,2
Denny Sakkas, PhD,1
Carlos Simon, MD, PhD,1
Nicolas D. Plachta, PhD,1
1University of Pennsylvania, Philadelphia, PA; 2University of Valencia, Valencia, Spain.

OBJECTIVE: The main events driving human preimplantation development have thus far been inferred from live-imaging mouse embryos. Challenges in human embryo research include access, technical limitations of live-imaging, and restrictions on genetic modification. Here we present a non-invasive method to perform 4D live-imaging of human embryos. This enabled us to characterize key morphogenetic events from cleavage stage to hatched blastocyst.

MATERIALS AND METHODS: Human embryos were obtained under Protocol WO 1-6450-1 from the New England Institutional Review Board. Standard clinical protocols were used for embryo collection, cryopreservation, thawing and culture. Thawed cleavage-stage embryos (n = 6) and blastocysts (n = 10) were incubated in SPY650-DNA and SPY555-actin to label nuclei and cell contours, respectively. Embryos were cultured at 37°C and 5% CO2 in an incubator adapted for the microscope. Imaging was performed using a laser scanning confocal microscope (Nikon A1RHD25) with scan frequencies of 7-15 minutes. Image analyses were performed using Imaris 8.2. Interphase duration was compared using an unpaired, two-tailed Student’s t-test.

RESULTS: Human embryos stained with SPY650-DNA and SPY555-actin survived up to 40 hours of imaging and completed compaction, cavitation and hatching. Key differences in cell cycle dynamics and morphogenesis between human and mouse were identified: 1) longer blastomere interphase duration in human (16.1 h vs. 13.0 h, p < 0.0001); 2) diffuse cortical actin organization in human compared to actin ring structures in mouse during polarization; and 3) concomitant polarization and compaction in human versus sequential events in mouse. Analysis of DNA morphology revealed cytoplasmic DNA structures (cytDNA) distinct from mitochondrial DNA and micronuclei. Over 15 hours we identified the appearance of zero to five cytDNA structures within trophectoderm cells per blastocyst. Importantly, cytDNA were not produced by mitotic chromosome segregation errors, but instead originated from the interphase nucleus after translocation into the cytoplasm. Furthermore, cells containing cytDNA did not undergo programmed cell death (cleaved caspase 3 negative) and completed subsequent cellular divisions. Similar appearing cytDNA structures were also identified in fixed human blastocysts stained with DAPI, Hoechst-33342 and an antibody recognizing dsDNA.

CONCLUSIONS: Non-invasive 4D live-imaging of human embryos can be performed using fluorescent dyes, enabling real-time tracking of DNA and cytoskeletal components. This approach revealed nuclear DNA release in the blastocyst independent of mitotic errors and programmed cell death.

IMPACT STATEMENT: This study provides a new tool for non-invasive live-imaging of human embryos, which enabled here the identification of nuclear DNA release in the trophectoderm. This provides a possible mechanism for mosaic aneuploidy distinct from mitotic segregation errors. Furthermore, this imaging approach will allow us to gain a deeper understanding of the cellular processes underlying human preimplantation development.

O-178 11:30 AM Tuesday, October 25, 2022

HUMAN BLASTOCYSTS UPTAKE EXTRACELLULAR VESICLES SECRETED BY PRIMARY ENDOMETRIAL EPITHELIAL CELLS CONTAINING MIRNAS RELATED TO IMPLANTATION AND EARLY EMBRYO DEVELOPMENT. Marina Segura-Benitez, MSc,1 Alba Bas-Rivas, MSc,2 Elena Juarez-Barker, MS,2 Maria Cristina Carbajo-Garcia, MSc,3 Amparo Faus, B.Sc.,2 Antonio Pellicer, M.D.,3 Hortensia Ferrero, PhD
1Universidad de Valencia - IVI Foundation, Valencia, Spain; 2IIS La Fe - IVI Foundation, Spain; 3IVIRMA Rome - IVI Foundation, Italy.

OBJECTIVE: To describe the miRNA cargo of extracellular vesicles (EVs) secreted by primary human endometrial epithelial cells (pHEECs) and to demonstrate their uptake by human embryos, in order to study the role of this communication system in implantation and embryo development.

MATERIALS AND METHODS: pHEECs obtained from fertile women (n=8 replicate) were hormonally treated and cultured in vitro. Ultraentrifugation was used for EV isolation from the culture medium, and EVs were characterized by Nanoparticle Tracking Analysis (NTA), Western Blot and Transmission Electron Microscopy (TEM). EVs were labelled with BODIPY TR ceramide and labelling was confirmed with NTA. Day 5 human embryos were co-cultured with labelled EVs for 5h, and images were obtained every hour with a fluorescent microscope. miRNAs from EVs (n=3 replicates) were extracted and miRNAseq was performed on Illumina’s NextSeq 550 system. Counts per million were used to select the 25% of miRNAs with the highest median expression in all replicates, and target genes were annotated using miRTarBase. Functional enrichment analysis was performed by ShinyGO.

RESULTS: EV characterization revealed a size within 100-300 nm, obtaining a mean size of 213 nm, and expression of EV protein markers HSP70, TSG101, CD9 and CD81. EV size range and morphology was corroborated by TEM. Fluorescent microscopy showed an efficient EV internalization by human blastocysts within 2-3h, being the fluorescent signal stronger in the inner cell mass. miRNAseq generated reads for 149 annotated miRNAs in common between the replicates. Top 37 most expressed miRNAs targeted 6592 genes, and functional enrichment analysis indicated that these participate in several processes related to embryo development, oxygen metabolism, cell cycle, cell differentiation, apoptosis, metabolism, or cellular organization. Among these miRNAs there were hsa-miR-200c-3p, hsa-miR-92a-3p and hsa-miR-23a-3p, which have been suggested to be involved in embryo attachment, embryo interaction with maternal endometrium during implantation and early embryo development. In addition, hsa-miR-30d-5p also presented high expression in these EVs, which positively regulates embryo adhesion and development, as well as endometrial receptivity. More miRNAs found in these EVs were some members of the hsa-let-7 family (let-7a-5p, let-7b-5p and let-7f-5p), as well as hsa-miR-21-5p, hsa-miR-20a-5p and hsa-miR-10a-5p, which are important for enhancing endometrial receptivity during implantation.
CONCLUSIONS: Our data suggest that EVs secreted by human endometrial epithelial cells are internalized by human blastocysts, and transport miRNAs to modulate biological processes related to implantation events and early embryo development.

IMPACT STATEMENT: Knowledge of the communication system between human endometrium and embryo via miRNA cargo of EVs secreted by endometrial cells could describe biomarkers of endometrial receptivity and embryo competence, which could be used to improve embryo competency and implantation rates.

SUPPORT: F19/000110, ACIF/2019/139, CP20/00120.

ANTIFACTOR PROTEIN REGULATES CRISPR CAS9 ACTIVITY IN HUMAN EMBRYOS

OBJECTIVE: Genome editing of human embryos using CRISPR-Cas9 frequently leads to mosaicism, chromosome loss, and unintended off-target editing. To avoid mosaicism and allow inference of the inner cell mass (ICM) genotype from a trophectoderm biopsy, Cas9 editing has to be limited to the 1-cell stage. Reducing the time that Cas9 is active in a cell may also decrease off-target effects which tend to be delayed relative to on-target edits. This study aims to determine if the anti-CRISPR protein, AcrIIA4, can effectively regulate Cas9 activity by minimizing off-target editing and mosaicism in human embryos while still allowing for on-target editing of the germline.

MATERIALS AND METHODS: Human oocytes and semen samples were anonymously donated for research. A bacterial culture harboring the plasmid #101043 with GST-AcrIIA4 fusion protein was obtained commercially. The AcrIIA4 protein was purified and injected into human oocytes either at the time of intracytoplasmic sperm injection (ICSI) together with Cas9 Ribonucleoprotein (RNP), or 12-16 hours post-ICSI into zygotes exposed to Cas9. Single blastomeres were collected on Day 3 and were amplified and analyzed for insertions/deletions (indels) using PCR and Sanger sequencing. A high-throughput SNP array platform validated for Preimplantation Genetic Testing was used to assess chromosomal aneuploidies.

RESULTS: Cas9 mediated cleavage is significantly inhibited by AcrIIA4 in human embryos when co-injected with Cas9 RNP at the time of (ICSI). The frequency of indels was reduced by 92% when AcrIIA4 was co-injected with Cas9-RNP compared to Cas9 alone (73.9% vs 6%, p = 0.00001, OR = 31). Similarly, Cas9 mediated segmental chromosome losses were also reduced with AcrIIA4 co-injection (0% vs 27.9%, p = 0.00001). The delayed introduction of AcrIIA4 (12-16 hours) into Cas9 exposed zygotes allowed for varying amounts of on-target Cas9-mediated cleavage while significantly reducing off-target editing as evidenced by significant fewer indels at the off-target sites compared to the on-target sites (32.1% vs 54.7%, p = 0.0046). Mosaicism rates were similar in the edited embryos in both groups, indicating that Cas9 cleavage occurs primarily after S-Phase and DNA replication. Moreover, Cas9 cleavage was observed to occur beyond the first cell cycle, as evidenced by at least three different genotypes within the same embryo.

CONCLUSIONS: AcrIIA4 has the potential to reduce Cas9-mediated indels and segmental chromosomal loss at off-target loci in human embryos when introduced 12-16 hours after fertilization. However, delayed injection of AcrIIA4 does not appear to improve mosaicism rates, as Cas9-mediated cleavage in human embryos primarily occurs after DNA replication.

IMPACT STATEMENT: AcrIIA4 is a possible tool for reducing off-target editing in human embryos. However, the timing of Cas9-cleavage relative to the first S-phase remains a limiting factor in reducing the rate of mosaicism in developing blastomeres.

SUPPORT: None

DETERIORATION IN OOCYTE QUALITY WITH CHRONOLOGICAL AGING IS ASSOCIATED WITH TETRAHYDROBIOPTERIN AND ZINC DEFICIENCY IN THE OOCYTES

OBJECTIVE: To examine the implications of decreased zinc (Zn) and tetrahydrobiopterin (H4B) associated with chronological aging on oocyte quality using a mouse model. Chronological aging is associated with an increase in oxidative stress generation in tandem with a decrease in zinc and H4B. Age-related increase in nitric oxide synthase activity (NOS) secondary to the activation of inflammatory pathways leads to the generation of higher nitric oxide (NO) combined with high NO consumption with resultant protein nitration. We have previously shown NO to be important in maintenance of oocyte quality.

MATERIALS AND METHODS: Sibling oocytes were retrieved from superovulated B6D2F1 mice from three age groups, namely, 8-14 weeks (young breeders, YB, n=112), 48-52w (retired breeders, RB, n=115) and 80-84w (old animals OA, n=75). They were: 1) scored for ooplasmic/spindle morphology, chromosomal alignment, and cortical granule (CG) intactness using immunofluorescence and confocal microscopy with 3-D image reconstruction (n= 62, 65 and 35 in YB, RB and OA respectively); Scores 1 and 2 (good) represent organized microtubules and normal morphology of the spindles and chromosome metaphase plate. Scores of 3 and 4 (poor) are characterized by spindle length reduction, disorganization and/or complete spindle absence/disruption and chromosome misalignment; 2) subjected to an HPLC assay to measure concentrations of H4B and its metabolites, as well as Zn measurement using mass spectrophotometry (n= 50, 50 and 40 in YB, RB and OA respectively).

RESULTS: 1) Oocyte scoring showed a significant reduction in “good” quality oocyte percentage as age increased, with YB having the highest percent of quality oocytes followed by RB and OA (Normal spindles: 81.3, 75 and 50 in YB, RB and OA respectively). 2) HPLC analysis showed a significant progressive decrease in H4B and its metabolites in RB and OA (77 and 48% respectively, compared to 96% in YB). Mass spectrophotometry revealed a significant progressive decrease in Zn concentration in RB and OA compared to YB (71 and 49% respectively).

CONCLUSIONS: Age related diminution in oocyte quality is paralleled by a decline in the levels of H4B and Zn. Resultant deficiency in the oocytes can lead to the inability of NOS to maintain dimerization. Consequently uncoupling of NOS generates superoxide (O2−) and peroxynitrite (ONOO−) instead of NO, which participates in a multitude of reactions contributing to oxidative stress.
BISPHENOL F INDUCED REPRODUCTIVE TOXICITY BY DISRUPTING STEROIDOGENIC ENZYMES ACTIVITIES AND UPREGULATING XANTHINE OXIDASE/URIC ACID SIGNALING. 

OBJECTIVE: Bisphenol F (BPF) is an endocrine disruptor being considered as a major replacement for bisphenol A. It is commonly found in plastics, cans, thermal paper receipts, feeding bottles, and medical devices, and has been implicated as a gonadotoxic substance. Bisphenol F has been reported to induce hormonal imbalance and oxidative damage in testicular tissue and sperm cells. However, the mechanism associated with testicular toxicity is yet to be fully explored. Whether or not steroidogenic enzymes are affected is not known. Also, the role of xanthine oxidase (OX)/ uric acid (UA) signaling in BPF testicular toxicity has not been studied. This study investigated the effect of bisphenol F (BPF) on testicular integrity and function. The roles of xanthine oxidase/uric acid signaling and steroidogenic enzymes were also probed.

MATERIALS AND METHODS: Male Wistar rats were randomized into vehicle-treated control, BPF-treated (10, 30, and 50mg/kg for low dose (BPF-L), medium dose (BPF-M), and high dose (BPF-H) respectively), and BPF-treated recovery (animals treated with varying BPF doses and allowed a 28-day exposure free period for recovery) (n = 6 rats per group). The administration was via gavage and lasted for 28 days. Animals in the recovery groups were allowed a 28-day exposure-free period after the initial 28 days of BPF exposure.

RESULTS: BPF resulted in the distortion of the testicular hist architecture (using Cosentino’s score), spermatogenesis (using Johnson Biopsy score and sperm parameters), seminiferous tubular diameter, and epithelial height which were accompanied by a significant rise in testicular GGT and LDH activities and a decline in SDH activity. Also, BPF caused a significant reduction in plasma LH, FSH, and testosterone, which is associated with the downregulation of testicular 3beta-hydroxysteroid dehydrogenase and 17beta-hydroxysteroid dehydrogenase activities. Furthermore, BPF induced testicular inflammation (evidenced by an increase in myeloperoxidase activity, TNF-alpha, IL-6, redox imbalance (evidenced by a decrease in testicular antioxidants glutathione, superoxide dismutase, catalase, glutathione peroxidase, and glutathione-S-transferase), and apoptosis (increased in DNA Fragmentation Index) which were accompanied by elevated xanthine oxidase activities and uric acid concentration. Again, the observed toxic effects of BPF were dose-dependent and not reversed by BPF exposure withdrawal.

CONCLUSIONS: BPF induced gonadotoxicity by down-regulating the activities of steroidogenic enzymes and upregulation of xanthine oxidase/uric acid signaling.

IMPACT STATEMENT: BPF is not a safe alternative to bisphenol A and it should be handled with caution to prevent regrettable substitution.

SUPPORT: Self Funded.

O-182 11:00 AM Wednesday, October 26, 2022

THE UBQUITOUS MITOCHONDRIAL PROTEIN UNFOLDASE CLPX IS REQUIRED FOR OOCYTE COMPETENCE AND EMBRYO DEVELOPMENT. Renwu Hua, Ph.D., Zhuo Hai, M.S., Jingkai Gu, M.S., Chenxi Guo, Ph.D., Yuan Xiao, M.S., Jiaping Su, B.S., William S. B. Yeung, Ph.D., Tianwen Wang, M.D., Ph.D. The University of Hong Kong-Shenzhen Hospital, Shenzhen, China.

OBJECTIVE: To explore the role of caseinolytic mitochondrial matrix peptidase chaperone subunit (CLPX) during oocyte and embryo development and to investigate fertility in mice with oocytes lacking CLPX.

MATERIALS AND METHODS: The oocyte-specific Clpx knockout (Clpxo/–, Zp3-Cre) mice were generated via the Cre-LoxP conditional knockout system. Female mice from each group (Clpxo/–, Zp3-Cre or Clpx+/-, 8-week-old) were mated with adult Clpxo/– males of proven fertility to evaluate the fecundity. Metaphase II (MI) oocytes and two-cell embryos were collected after superovulation. Immunostaining of oocyte spindles and confocal microscopic imaging were applied to assess the spindle and chromosome morphology. JC-1 staining was used to measure the mitochondrial membrane potential.

RESULTS: The Clpxo/–, Zp3-Cre mice consistently exhibited reduced fertility with a significant reduction in litter size (2.5 vs. 7.0, p<0.001) and number of pups per female at 5 months (5.5 vs. 17.8, p<0.001) when compared with the Clpx+/- mice. Although the number of MI oocytes between two groups was comparable (16.7 ± 17.3 vs. 16.7 ± 15.8, p > 0.05), the ratios of aberrant spindle (44.2% vs. 11.6%, p<0.001) and misaligned chromosomes (49.3% vs. 11.6%, p<0.01) in MII oocytes from Clpxo/–, Zp3-Cre mice were significantly elevated. The JC-1 staining analysis revealed that the MI oocytes from the Clpxo/–, Zp3-Cre mice had significantly lower mitochondrial membrane potential (0.4 vs. 3.1, p<0.05). In addition, the two-cell embryo development rate per MI oocyte (50.4% vs. 82.8%, p<0.05) was also significantly lower in the Clpxo/–, Zp3-Cre mice.

CONCLUSIONS: Loss of mitochondrial quality control protein CLPX in the oocytes results in a significant decline in fertility with decreased oocyte and embryo development competence, increased rate of aberrant spindle and misaligned chromosomes in MII oocytes and impaired mitochondrial function. Further investigation is needed to explore the mechanism of CLPX in energy dynamics and fertility regulation.

IMPACT STATEMENT: In recent years, there has been great interest in the role of mitochondria in female fertility. To date, much remain unknown about mitochondria quality control (MQC) and its effect on oocyte competence and embryo development. Previous studies have indicated mitochondrial unfolded protein response genes (including Clpx) play a crucial role in MQC. Herein, we investigated Clpx and found it had critical effects on oocyte and embryo development. This study provides important insights into the relationship between MQC and female fertility.

SUPPORT: This work was supported by the National Natural Science Foundation of China (No: 81971453); Shenzhen Fundamental Research Program, China (No: JCYJ20200109150429414); Shenzhen Science and Technology Program, China (No. RCXYX202007141470573, No. KQTD20190929172749226); Sanning Project of Medicine in Shenzhen, China (No: SZSM201612083).

O-183 11:15 AM Wednesday, October 26, 2022

TRACKING IMMATURE TESTICULAR TISSUE AFTET VITRIFICATION IN VITRO AND IN VIVO FOR PRE-PUBERTAL FERTILITY PRESERVATION: A TRANSLATIONAL, TRANSGENIC MOUSE MODEL. Buojia Lu, B.B.A., M.D., Chi-Huang Chen, MD, PhD Taipei Medical University Hospital, Taipei, Taiwan.

OBJECTIVE: Pediatric cancer survivors experiencing gonadotoxic chemotherapy may encounter subfertility or permanent infertility. However, previous studies of cryopreservation of immature testicular tissue (ITT) have mainly been limited to in vitro studies. In this study, we aimed to evaluate in vitro and in vivo bioluminescence imaging (BLI) for solid surface-vitrified (SSV) ITT grafts until adulthood.

MATERIALS AND METHODS: A total of twelve pairs of donor and recipient mice were included in our experiments. The donors were immature transgenic mice, and the recipients were wild-type male mice. In the vitrification group, ITT were vitrified and rewarmed before transplantation. Otherwise, ITT was transplanted to the recipients immediately in the control group. After warming, we measured the survival by in vitro BLI and immunohistochemistry (IHC) and scanning electron microscope (SEM). More importantly, we monitored the transplanted graft in vivo by using non-invasive BLI technology until adulthood.

RESULTS: After SSV/rewarming, the ITT presented BLI intensity and cells and ultrastructures for spermatogenesis similar to fresh control in vitro. Grafts survival were analyzed by BLI on days 1, 2, 5, 7, and 31 after transplantation. The signals decreased by quantum yield between days 2 and 5 in both groups, but gradually increased afterwards until day 31, which were significantly stronger than day 1 after transplantation. The differences between the two groups were constantly insignificant, suggesting that both fresh and SSV ITT can survive, accompanied by spermatogenesis, until adulthood.

CONCLUSIONS: Based on our surrogate mouse model, this translational transgenic study provides unique in vitro and in vivo evidence that lends weight to SSV for ITT cryopreservation. Also, this model may serve as a platform for future versatile study designs and applications from bench to bedside for pre-pubertal male fertility preservation.

IMPACT STATEMENT: This translational model demonstrates the great potential of SSV for ITT in pre-pubertal male fertility preservation.
OBJECTIVE: The high incidence of chromosome aneuploidy in early human development is the primary cause of pregnancy loss, miscarriage, and still birth following normal conception as well as in vitro fertilization (IVF). Preimplantation genetic testing for aneuploidy (PGT-A) of IVF embryos at the blastocyst stage has confirmed the prevalence of aneuploidies of putative meiotic and postzygotic mitotic origins. However, only about half of normally fertilized embryos develop to the blastocyst stage in vitro, while the others arrest at cleavage to late morula or early blastocyst stages. To investigate the role of aneuploidy in developmental arrest, we compared the incidence of various forms of aneuploidy in a large series (n = 909) of trophectoderm biopsies and arrested embryos and correlated them with abnormalities of the first two cleavage divisions using time lapse imaging (n = 843).

MATERIALS AND METHODS: 125 patients (mean 38.9 years) underwent a total of 165 IVF cycles with extended embryo culture and biopsy of 4601 trophectoderm cells on days 5-7 post-insemination for PGT-A. We defined the range for putative mitotic (i.e., mosaic) aneuploidy at 50-70% of the expected copy number change for uniform aneuploidy. We used time-lapse imaging to record the first two cell divisions of 843 embryos derived from 2PN zygotes following fertilization. Assessment included: (1) formation of pronuclei, (2) first cleavage division, (3) second cleavage division, (5) cell compaction, (6) cavitation, (7) expanded blastocyst, or (8) embryo arrest. The predicted risks between probability of embryo arrest and various predictor variables were modeled using binomial generalized linear mixed effects models with patient as a random effect.

RESULTS: The combined incidence of meiotic and mitotic aneuploidies was strongly associated with blastocyst morphological grading ($X^2$ [9, N = 612] = 62.0, p = 1.23 x 10^7), with the proportion ranging from 20% to 90% for the highest to lowest grades, respectively. In contrast, the incidence of aneuploidy among arrested embryos was exceptionally low (94%), dominated by mitotic aneuploidies affecting multiple chromosomes. In turn, these mitotic aneuploidies were strongly associated with abnormal cleavage divisions, such that 51% of abnormally dividing embryos possessed mitotic aneuploidies compared to only 23% of normally dividing embryos ($OR = 3.41, 95\% CI [2.30, 4.67], p = 6.93 x 10^{-15}$).

CONCLUSIONS: Our results suggest that the transition from the cleavage to blastocyst stage acts as a strong bottleneck wherein numerous aneuploid embryos are eliminated prior to implantation, while persisting aneuploidies may compromise organization and function of the differentiating cell lineages. The timing of this bottleneck is consistent with the increasing reliance of development on embryonic gene expression after the 4-cell stage.

IMPACT STATEMENT: Our work provides a more complete view of the causes of the high rates of embryo loss during preimplantation human development. Understanding the factors that modulate risk of early mitotic errors could help improve IVF outcomes over the longer term.

SUPPORT: RCM is supported by the National Institute of General Medical Sciences of the National Institutes of Health under Award R35GM133747. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

O-185 11:45 AM Wednesday, October 26, 2022

THE SUCCESSFUL DEVELOPMENT AND CLINICAL VALIDATION OF STORK, A RAPID ANEUPLOIDY DETECTION METHOD USING NANOPORE SEQUENCING. Shan Wei, Ph.D., 1 Mary D’Alton, M.D., 1 Brynn Levy, M.Sc.(Med.), Ph.D., FACMG, 2 Zev Williams, MD, PhD 1 Columbia University Medical Center, New York, NY; 2 Columbia University, New York, NY.

OBJECTIVE: Aneuploid pregnancies are a significant cause of pregnancy loss, fetal structural anomalies, and developmental delays. Consequently, the identification of genetic abnormalities is an important component of prenatal and fertility care. However, existing tests for aneuploidy have shortcomings that reduce access to reproductive care, delay diagnosis and treatment, and increase costs. We developed a nanopore-based DNA sequencing technology that enables low-cost, same-day, point-of-care, aneuploidy testing of reproductive tissues that we termed STORK (Short-read Transpose Rapid Karyotyping). Here we report on the first clinical validation of STORK in a CLIA-approved laboratory.

MATERIALS AND METHODS: At the developmental stage, we systematically evaluated the performance of each step, from genomic DNA extraction to data analysis, to develop a robust and low-cost STORK method. At the clinical validation stage, STORK was performed on 218 blinded, sequential, remnant, reproductive specimens comprised of products of conception (POC, n = 64) following spontaneous losses, chorionic villi following chorionic villus sampling (CVS, n = 52), amniotic fluid from amniocentesis (Amnio, n = 50), and trophectoderm biopsies of embryos undergoing preimplantation genetic testing for aneuploidy (PGT-A, n = 52) and the results were compared with those obtained using standard clinical testing. To validate the reproducibility of the STORK method, STORK was performed independently in a CLIA-certified laboratory on 60 clinical samples and the results were compared to standard clinical testing.

RESULTS: STORK detected full aneuploid, large CNVs, and high-level mosaicism on up to 10 clinical samples within 2 hours of sequencing time. Compared with the standard clinical testing results of the 218 blinded clinical samples (CVS, n = 64; CVS, n = 52; Amnio, n = 50; PGT-A, n = 52), STORK was 98.100% accurate. In the independent validation in a CLIA-certified laboratory, STORK results were 100% concordant with standard clinical testing.

CONCLUSIONS: Collectively, this study demonstrates the utility and accuracy of short-read nanopore-based sequencing for aneuploidy testing of reproductive tissues. The low-cost, same-day, point-of-care aneuploidy testing using STORK could potentially reduce healthcare barriers and costs leading to improved access to reproductive care.

IMPACT STATEMENT: STORK, a nanopore-sequencing-based rapid low-cost aneuploidy detection method, can significantly shorten the waiting and enhance access to critical clinical testing results for patients in reproductive medicine.

SUPPORT: This research was supported by the National Institutes of Health Grants HD085846, U19CA179564, HD100013, and Columbia University’s BiomedX.

O-186 12:00 PM Wednesday, October 26, 2022

ENHANCED PHOSPHATASE REGENERATING LIVER-1 ACCELERATES VASCULAR REMODELING IN INJURED RAT Ovary VIA PLATELET-DERIVED GROWTH FACTOR SIGNALING PATHWAY. Hyeri Park, Ph.D., 1 Dae Hyun Lee, M.S., 2 Jin Seok, Ph.D, 3 Su Kyec Kim, M.S., 1 Kyu Hwan Na, Ph.D, 1 Won Tae Jeong, M.S, L. I. M. Ja-Yun, Ph.D., 1 Gi Jin Kim, Ph.D. 1 CHA University, Seongnam-si, Korea, Republic of (South); 2Seongnam, South Korea; 3The University of Chicago, Chicago, IL; 4Gyeonggi-Do, South Korea; 5Hyjeon College, Chungnam-do, Korea, Republic of (South); 6CHA University, Seongnam-Si, South Korea.

OBJECTIVE: Vascular abnormalities in the ovary cause ovarian dysfunction due to a microenvironment of barren ovarian tissues. Platelet-derived growth factor signaling pathway in vascular structure and their function are critical factor in follicular development and ovarian function. In previous reports, we demonstrated placenta-derived mesenchymal stem cells (PD-MSCs) restore ovarian function via antioxidants effect. However, there is still unclear the therapeutic mechanism between ovarian function and vascular remodeling. Therefore, we examined whether phosphatase regenerating liver-1 overexpressed PD-MSCs (PD-MSCs ePK1), which is correlated
with angiogenesis in reproductive systems, could maximize the angiogenic effects in an ovarian tissue model and their therapeutic mechanism by enhanced vascular function via PDGF signaling.

MATERIALS AND METHODS: PD-MSC-PRL-1 was generated by nonviral AMAXA gene delivery system and analyzed the vascular remodeling and follicular development in ovary. One week after Sprague-Dawley (SD) rats ovariectomy, PD-MSCs and PD-MSCs-PRL-1 were transplanted into the injured rat model by tail vein. After transplantation, the expressions of factors for angiogenic and follicular development were analyzed. In addition, we analyzed the effect of PD-MSCs-PRL-1 on vascular permeability of human umbilical vein endothelial cells (HUVECs) with 5-FU treatment by dextrans assay regardless of co-cultivation.

RESULTS: Vascular structures in ovarian tissues (e.g., number of vessels, thickness and lumen area) showed changes in the PD-MSCs and PD-MSCs-PRL-1 transplantation (Tx) groups compared to the non-transplantation (NTx) group. Especially, PD-MSCs-PRL-1 induced to increase the expression of PDGF compared to the NTx (*p<0.05). The pericyte recruitment was significantly enhanced in PD-MSCs-PRL-1 compared to the NTx via activated PDGF (*p<0.05). The expression of genes related to vascular permeability (e.g., erg-3) and follicular development (e.g., Nobox, BMP15 and EGFR) in ovarian tissues was significantly improved in the PD-MSCs-PRL-1 compared to the NTx (*p<0.05). Also, PD-MSCs-PRL-1 enhanced the vascular formation and decreased permeability of human umbilical vein endothelial cells (HUVECs) via activated the PDGF signaling pathway. Otherwise, the expressions of PDGF-BB and PDGFRA were significantly decreased in si-PRL-1 or PDGF inhibitor treatment compared to control. However, their expression was significantly increased in PD-MSCs and PD-MSCs-PRL-1 cocultivation group compared to si-PRL-1 or PDGF inhibitor treatment (*p<0.05).

CONCLUSIONS: Our results show that increased PRL-1 restored ovarian function by enhanced vascular function via activated PDGF signaling pathway.

IMPACT STATEMENT: These findings offer new insight into the effects of functionally enhanced stem cell therapy for reproductive systems and should provide new avenues to develop more efficient therapies in degenerative medicine.

SUPPORT: This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2020M3A9B302618221).

REFERENCES:

ORAL ABSTRACT SESSION: ART LAB 2

O-187 10:45 AM Wednesday, October 26, 2022

THE IMPACT OF FRESH VERSUS FROZEN-THAWED EMBRYOS ON MATERNAL SERUM ANALYTES IN IVF TWIN PREGNANCIES, Alexandra Peyster, M.D., Moti Gulersten, MD, MSc,2 Xueying Li, M.S.,3 David Kranz, M.D.,1 Burt Rochelson, M.D.,2 Eran Bornstein, M.D.,4 Christine Mullin, M.D.,1 Randi H. Goldman, M.D.1 1Northwell Health Fertility, Zucker School of Medicine at Hofstra Northwell, Manhasset, NY; 2Zucker School of Medicine at Hofstra Northwell, North Shore University Hospital, Manhasset, NY; 3Eurofins NTD, Melville, NY; 4Lenox Hill Hospital, Zucker School of Medicine at HofstraNorthwell, New York, NY; 5Northwell Health Fertility, Northwell Health, Manhasset, NY.

OBJECTIVE: The impact of embryo cryopreservation on first and second-trimester serum maternal analytes within twin pregnancies is not well known. Our ongoing research suggests that singleton pregnancies from fresh (FR) transfers is associated with lower analyte levels compared to frozen-thawed (FT) transfers. The objective of this study was therefore to determine whether FR versus FT embryo transfer is associated with a change in maternal serum analytes independent of the patient’s reproductive history or the use of assisted reproductive technologies (ICSI or IVF).

MATERIALS AND METHODS: This was a retrospective cohort study of twin pregnancies conceived via IVF from a university health system from 01/2014 to 09/2019. Patients with available first and second trimester serum analyte data were included and analyzed separately. Multiple of the median (MoM) values, adjusted for weight, ethnicity, smoking, diabetic status, and fetal number, for free β-human chorionic gonadotropin (β-hCG), pregnancy-associated plasma protein A (PAPP-A), alpha-fetoprotein (AFP), Inhibin A, and unconjugated estriol (UE3), were compared between two groups: twin pregnancies conceived after the transfer of FR embryos versus twin pregnancies conceived after the transfer of FT embryos. Serum analyte data was also quantitized “extreme” based on acceptable percentile cut-off levels defined by Eurofins, NTD (i.e. ≤5th percentile or ≥95th percentile). All fertilization was performed via ICSI. Multiple linear regression of log MoM values with F test was performed to adjust for a priori for the following potential confounders: age, weight, ethnicity and preimplantation genetic testing (PGT).

RESULTS: There was a total of a 142 twin pregnancies, 44 (31%) resulting from FR embryo transfers and 98 (69%) from FT embryo transfers. Twenty eight percent of the FT underwent PGT. There were no significant differences between first trimester (β-hCG: FR: 1.0 MoM vs. FT:1.0 MoM, PAPP-A; FR: 1.2 MoM vs. FT:1.0 MoM, AFP; 1.4 MoM vs 1.3 MoM) and second trimester (UE3; FR:1.0 MOM vs. FT: 1.1 MoM, β-hCG: FR: 1.2 MoM vs 1.1 MoM, Inhibin A; FR: 1.1 MoM vs. 1.3 MoM, AFP: FR 1.0 MoM vs. 1.2 MoM) analyte levels amongst twin gestations by transfer type. No difference in extreme analyte levels were noted between the two groups.

CONCLUSIONS: Twin pregnancies resulting from FR vs. FT embryo transfers do not demonstrate differences in maternal serum analyte levels. Future research with a larger sample size is needed to confirm these findings.

IMPACT STATEMENT: There is no difference in serum maternal analyte levels in twin pregnancies conceived from fresh versus frozen embryos.

O-188 11:00 AM Wednesday, October 26, 2022

CHANGE IN PROTOCOL AFTER IVF CYCLE CANCELLATION INCREASES ODDS OF LIVE BIRTH IN FRESH CYCLES: A SART CORS ANALYSIS OF 13,135 AUTOLOGOUS CYCLES, Jenna Kahn, M.D., Haotian Wu, Ph.D., Harry Lieman, MD, Manvinder Singh, MD, Staci E. Pollack, M.D., M.S., Sangita K. Jindal, Ph.D., Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY; 2Columbia University; 3Albert Einstein College of Medicine / Montefiore Medical Center, Hartsdale, NY.

OBJECTIVE: To determine if changing the controlled ovarian hyperstimulation (COH) protocol in the cycle following an IVF cycle cancellation affects the odds of live birth or recurrent cycle cancellation.

MATERIALS AND METHODS: Retrospective cohort study of 13,135 autologous cycles from SART member clinics between 2014-2017 that resulted in a cancellation, and were followed by a second cycle within the study period. Canceled cycles were those in which the cycle was stopped during COH, before the intended egg retrieval. We excluded donor and fertility preservation cycles. Patients who received the same protocol for both cycles were compared to those who changed their protocol for the second cycle. Protocols tracked by SART include Antagonist (A), agonist suppression (AS), and agonist flare (AF). Primary outcomes were live birth and recurrent cycle cancellation. All cycles were included for outcome of cycle cancellation and a sub-analysis of 12,472 fresh cycles was performed for outcome of live birth.

RESULTS: On second stimulation, 49% (n=6643) used the same protocol and 51% (n=6701) underwent a different protocol. Demographic characteristics, infertility diagnoses, and reason for initial cycle cancellation were similar between groups. 78% of all patients had their first cycle cancelled for low response. Compared to the initial cycle, increased total gonadotropin doses were given in both groups, however, a higher average gonadotropin dose was given in the changed protocol group (p<0.001). After adjusting for age, race, BMI, smoking status, AMH, and infertility diagnosis, those who changed protocol were 14% less likely to have a recurrent cycle cancellation (AOR 0.86; 95%CI, 0.76-0.97; P=0.01) and 7% more likely to have a live birth (AOR 1.17; 95% CI, 1.1-1.37; P=0.04). When looking at the drivers for these change in specific protocol sequence, we found that compared to those who stayed on “AS” for both cycles, a change to “A” resulted in a 36% increase in odds of live birth in the second cycle (AOR 1.36; 95% CI, 1.02-1.79; P=0.03) independent of oocyte yield. Infertility diagnoses were comparable between the same and changed protocol groups. Compared to those who stayed on “AF”, a change to “AS” resulted in a 68% decrease in odds of cycle cancellation (AOR 0.33; 95% CI, 0.09-0.89; P=0.047). There was no change in live birth when switching to or from AF in the second cycle.
Conclusions: In patients with a previous a or AS-4 cycle cancellation, changing their protocol to the alternate protocol in the subsequent cycle results in a higher odds of live birth, regardless of their infertility diagnosis. There is no utility of an AF cycle in patients with prior cycle cancellation.

Impact statement: Patients with prior cycle cancellations represent a unique group within the infertility population. While specific changes in stimulation protocols may not benefit all patients, it seems to provide a clinically meaningful benefit in this population.

Objective: More than 10 million infants have been born worldwide using assisted reproduction technology in last three decades. The sex ratio at birth is also known as secondary sex ratio (SSR). According to WHO SSR ranges between 103-107 with an average of 105 male birth per 100 females, an increase in SSR has been reported in assisted reproduction (ART). Few studies suggested that different IVF (laboratory procedures (transfer stage, cryopreservation, culture media, incubation conditions, standard IVF or ICSI etc.) can lead to biased SSR. The SSR has not been studied in different types of incubators yet.

Materials and Methods: This study included 5963 single embryo transfer (SET) cycles from 4123 patients with an average oocyte age of 29.58 yrs. in different time-lapse (TL) incubators, Embryoscope+ (ESD), Geri® and Embryoscope++(ESD+) and 1045 SET cycles from benchtop incubators (SD) from 6132 patients with an average oocyte age of 28.90 yrs. This study includes the cycles from 2016 to 2020. The result of 2264 live birth in TL incubators and 3424 live births in SI incubator recorded. The oocytes were retrieved from patient/donors using standard ovarian stimulation protocol during 2016 to 2020. ICSI were performed on all the MI aspirated in the retrieval cycle. All the fertilized oocytes were cultured in TL incubator and subsequently with single-step culture medium. The transfer was done after blastocyst stage and for the frozen/thawed transfer(FET), the blastocysts were vitrified using standard protocol followed by devitrification before transfer.

Results: Significant difference (p<0.001) was found in overall SSR (113 male births per 100 females) of TL incubator compared to SI incubator (106 male births per 100 females). There was significantly high difference in the SSR of FET in TL incubator (101 male birth per 100 female), SI incubator (104 male births per 100 female) compared to fresh transfer (FT) in TL incubator (138 male birth per 100 female) and SI incubator (110 male birth per 100 female). The FET had better result for SSR compared to FT in both incubators but high difference was observed in TL incubator. Overall live-birth rate was less in SI incubator (32.75%) from TL incubator (38%). In different TL incubators, overall SSR in ESD+ (0.98) was significantly better than ESD(1.15) and Geri® (1.32) respectively. In ESD, SSR of FT vs FET was 1.43 and 1.02 while in ESD+ 1.19 and 0.89 and Geri 1.61 and 1.16 respectively, shows that FET are significantly better than FT in all TL incubators in terms of SSR. There was no significant difference in SSR of autologous transfer (1.12) compared to donor transfer(1.13) in TL.

Conclusions: The SSR is better in ESD+, SI Incubators and FET compared to FT and other TL in general. One of the reasons could be the culture conditions, selection methods and the criteria for cryopreservation that different incubators support female embryos. The reason FET has higher SSR in FET need to be understood, so that the SSR can be improved in ART.

Impact statement: SSR is an important social indicator. The relation of increased in SSR with IVF procedure/technology and other fertility factor need to be studied in more detailed, to improve it.

Support: The authors’ research is supported by the European Union’s Horizon 2020-MSCA-ITN-2018 programme under grant agreement No. 812660
MATERIALS AND METHODS: A retrospective dataset of 5,620 patients (16,261 oocytes) from TRIO Fertility (Toronto, ON). The known outcomes were examined to label each oocyte according to their Gardner blastocyst development stage by Day 5 or 6 of culture. In this study, blastocyst quality was classified based on the following criteria: Non Blastocyst (failed fertilization/embryo arrest), Low Quality (expansion grade of 1-6, ICM or TE grade of C or D), Medium Quality (expansion grade of 1-3, ICM and TE grade of A or B), or High Quality (expansion grade of 4-6, ICM and TE grade of A or B). The mean Magenta Score for the oocytes within each blastocyst quality group was calculated and the difference between Magenta Scores of sequential groups was compared by a Welch’s Two Sample t-test.

RESULTS: Each oocyte image was analyzed by Magenta and given a score on a scale of 0-10. The Magenta Score positively correlated with the quality of the blastocyst that developed in a stepwise manner (Table 1). The mean Magenta Score of the oocytes that did not develop into a blastocyst was the lowest (4.6), followed by High Quality (5.8), Low Quality (6.2), and Medium Quality (6.3). The Magenta scores were significantly different between the Non Blastocyst and Low Quality group, as well as the Low Quality and the Medium/High Quality Groups (p.value < 0.001) by a Welch’s Two Sample t-test.

CONCLUSIONS: There is no standardized oocyte scoring system, therefore, even trained embryologists cannot predict the outcomes of oocytes based on visual assessment. This analysis shows that Magenta Scores display a stepwise correlation with the quality of blastocyst development; the higher the Magenta Score, the more likely the oocyte would develop into a high-quality blastocyst.

IMPACT STATEMENT: Using an image analysis AI tool on mature denuded oocytes can provide more insight into oocyte quality and reproductive potential. A prospective study is currently underway to validate these findings. Future direction will focus on extending the outcomes to PGT-A screened blastocysts with implantation results.

ORAL ABSTRACT SESSION: ART TECHNIQUES

O-193 10:45 AM Wednesday, October 26, 2022

SIGNIFICANT DIFFERENCES IN PERCEIVED UTILITY OF DIRECT-TO-CONSUMER FERTILITY TESTS AMONG PATIENTS AND REPRODUCTIVE ENDOCRINOLOGISTS. Benjamin J. Peipert, MD, Benjamin S. Harris, MD, MPH, Jessica Selter, MD, Khaila Ramey-Collier, BS, Randa Blenden, BSN, RN, Shakthi Unnithan, MS, Alaattin Erkanli, PhD, Thomas M. Price, M.D. 1 Duke University Medical Center, Durham, NC; 2 Durham, NC; 3 Chapel Hill, NC; 4 Duke Fertility Center, Morrisville, NC; 5 Department of Biostatistics & Bioinformatics, Duke University Medical Center, Durham, NC.

OBJECTIVE: To characterize the perceived utility of direct-to-consumer home fertility tests (HFTs) among patients and reproductive endocrinologists (REIs).

MATERIALS AND METHODS: New patients visiting the Duke Fertility Center for evaluation and management of infertility between December 2020 – December 2021 were identified via ICD 10 code and sent an invitation to participate via electronic patient portal. HFTs were defined as tests not ordered by a physician or performed at a physician’s office, including home ovulation prediction, send-out hormone analysis, and home or send-out semen analysis. Patients reporting use of specific HFTs and REIs were asked to rate how likely they were to recommend a given HFT on a 0 to 10 Likert scale. For each HFT, scores were compared between patients and REIs using Wilcoxon Rank Sum Tests at a significance level of p < .05. The study was approved by the Duke University Institutional Review Board.

RESULTS: In total, 425 patients and 178 REIs completed the survey (Response Rate = 50.5% and 21.4%, respectively). HFT utilization rates among patients and utility scores among patients and REIs are reported in Table 1. Ovulation prediction was the most commonly used home fertility test among patients. REIs rated the utility of all HFTs significantly lower than patients, except for urinary ovulation prediction, which REIs gave a significantly higher score.
CONCLUSIONS: Significant discordance exists in the perceived utility of HFTs between patients and REIs. Other than urinary ovulation prediction kits, REIs gave significantly lower utility scores for all HFTs compared to patients.

IMPACT STATEMENT: Direct-to-consumer HFTs, including methods of ovulation prediction, hormone analysis, and semen analysis, represent an accessible first step for many couples and individuals struggling with infertility. Despite rapid growth in the HFT industry, academic societies currently offer limited guidelines to patients and providers with respect to the utility of HFTs. Future efforts are needed to provide greater education and guidance to patients considering HFTs to manage their fertility.

SUPPORT: This project is generously supported by a grant from the Charles B. Hammond Research Fund.

Table 1.

<table>
<thead>
<tr>
<th>Ovulation prediction</th>
<th>HFT Patient Utilization (N, %)</th>
<th>Utility Scores1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary ovulation prediction kits</td>
<td>335 (78.8%)</td>
<td>7.8</td>
</tr>
<tr>
<td>Calendar methods of ovulation prediction</td>
<td>360 (84.7%)</td>
<td>7.3</td>
</tr>
<tr>
<td>Basal body temperature monitoring</td>
<td>131 (30.8%)</td>
<td>5.5</td>
</tr>
<tr>
<td>Hormone analysis</td>
<td>39 (9.2%)</td>
<td>6.8</td>
</tr>
<tr>
<td>Ovarian reserve testing (e.g., AMH)</td>
<td>39 (13.9%)</td>
<td>7.2</td>
</tr>
<tr>
<td>Semen analysis</td>
<td>43 (10.1%)</td>
<td>6.3</td>
</tr>
<tr>
<td>Genetic testing (e.g., 23andMe)</td>
<td>33 (7.8%)</td>
<td>6.2</td>
</tr>
</tbody>
</table>

0-10 Likert scale, 0 = “Not likely to recommend” and 10 = “Extremely likely to recommend”

*p < 0.05

OBJECTIVE: The increasing reliance on blastocyst vitrification in Assisted Reproductive Technologies (ART) during the past decades has led to a significant surge in frozen embryo transfer (FET) cycles. Therefore, greater focus has aimed to optimize the protocols for FET as well as the timing between thaw and embryo transfer. In this study, our objectives were to examine the impact of duration of post thaw culture until embryo transfer on (i) pregnancy outcome and (ii) on metabolic stability of blastocysts post thaw.

MATERIALS AND METHODS: A retrospective analysis of all blastocyst vitrification FET cycles from January 2015 to December 2020 was performed. Basal body temperature monitoring of 131 (30.8%) patients considering HFTs to manage their fertility.

IMPACT STATEMENT: Timing of warming blastocysts to transfer can be flexible. This is particularly important in laboratories with heavy workloads as well as labs with reduced staff.

RESULTS: Our results indicates that the mean (±SD) age of women throughout these time categories was 35.6 (4.0) and did not differ between time categories. The number of embryos transferred (+ SD) was 1.0 ± 0.2, (not significantly different between groups). We observed no significant differences across time categories for pregnancies and live birth rate for both PGT and Non-PGT cases (Table 1). The number of PGT transfers in the later times was however small. Using FLIM, we confirmed that the metabolic status of blastocysts remained stable (P > 0.05) during the first 7 hours.

CONCLUSIONS: These data show that the time between warming to transfer of blastocysts has a minimal impact on pregnancy and live birth rate.

O-194 11:15 AM Wednesday, October 26, 2022

EFFECT OF POST THAW TO EMBRYO TRANSFER CULTURE PERIOD ON EMBRYO METABOLISM AND PREGNANCY OUTCOME. Goli Ardestani, PhD, 1 Marion Martins, MSc, 2 Olcay Ocali, B.SC., 1 Tim H. Sanchez, PhD, 1 Colwyn Gulliford, PhD, 4 C. Brent Barrett, Ph.D., 1 Denny Sakkas, PhD, 3 Boston IVF, Waltham, MA; 4Wien, Wien, Austria; 2None; 3Optiva Fertility Inc, Malden, MA; 3Boston IVF - The Eugin Group, Waltham, MA.

Table 1.

<table>
<thead>
<tr>
<th>Time</th>
<th>Non-PGT</th>
<th>PGT</th>
</tr>
</thead>
<tbody>
<tr>
<td>% LBR</td>
<td>% LBR</td>
<td>% LBR</td>
</tr>
<tr>
<td>0 (&lt;1h)</td>
<td>44.16</td>
<td>107</td>
</tr>
<tr>
<td>1 (1-2h)</td>
<td>43.49</td>
<td>1088</td>
</tr>
<tr>
<td>2 (2-3h)</td>
<td>40.79</td>
<td>1543</td>
</tr>
<tr>
<td>3 (3-4h)</td>
<td>44.47</td>
<td>619</td>
</tr>
<tr>
<td>4 (4-5h)</td>
<td>42.70</td>
<td>102</td>
</tr>
<tr>
<td>5 (5-6h)</td>
<td>42.41</td>
<td>25</td>
</tr>
<tr>
<td>6 (6-7h)</td>
<td>37.56</td>
<td>5</td>
</tr>
<tr>
<td>7 (7-8h)</td>
<td>38.95</td>
<td>2</td>
</tr>
</tbody>
</table>

OBJECTIVE: We previously developed a machine learning model for selecting an individualized gonadotropin dose for ovarian stimulation based on patient similarity matching [1]. The purpose of this study was to evaluate this methodology on a large and diverse dataset to retrospectively determine associations between machine learning predictions, patient outcomes, and total gonadotropin used.

MATERIALS AND METHODS: We analyzed 365,473 autologous retrieval cycles from 2014-2019 in the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System (SART CORS). Cycle information included patient age, BMI, AMH, total FSH dose, cycle length, and outcomes. The cumulative live birth rate (CLBR) for each retrieval cycle was calculated as at least one live birth from all linked embryo transfers. For cycles with blastocyst transfers (n = 161,035), the total blastocysts was defined as the number of embryos transferred plus embryos frozen. A K-nearest neighbors model was trained on all cycles to identify the 500 most similar cycles to a patient-of-interest using age, BMI, and AMH. For each cycle in the dataset, a patient specific dose-response curve was created by fitting a constrained second order polynomial to 2PNs retrieved relative to the average daily dose of FSH (the total FSH divided by the number of cycle days) across that patient’s 500 neighbors. Each patient’s individual dose-response curve was used to determine if there was an optimal daily dose of
that maximized the predicted 2PNs (called dose-responsive) or if the dose-response curve showed that the predicted 2PNs were approximately constant across the dose range (called flat-responsive).

RESULTS: 27% of the cycles were identified as dose-responsive, while 73% were flat-responsive. Dose-responsive patients who received an optimal daily dose had, on average, 1.2 more 2PNs, 0.5 more blastocysts, and 4% higher CLBR using 840 IU’s less of total FSH compared to propensity-matched patients with non-optimal doses. Flat-responsive patients who received a low daily dose (below the median of their neighbors) had, on average, 0.3 more 2PNs, 0.3 more blastocysts, and 3% higher CLBR using 2,020 IU’s less of total FSH compared to propensity-matched patients with a high daily dose.

CONCLUSIONS: Using the SART CORS dataset, this study shows that patient similarity modeling for selecting gonadotropin doses may be associated with improved ovarian stimulation outcomes and a reduction in total gonadotropin used. While propensity matching ensured covariates (age, BMI, and AMH) were similarly distributed when comparing outcomes between groups, future prospective studies are needed to determine potential clinical benefit of this machine learning approach.

IMPACT STATEMENT: Machine learning tools to aid in decision making during ovarian stimulation show potential for improving outcomes including live birth while reducing the total amount of FSH.

REFERENCES:

O-196 11:30 AM Wednesday, October 26, 2022

UTILIZATION OF INTRACYTOPLASMIC SPERM INJECTION VERSUS CONVENTIONAL IVF IN NON-MALE INFERTILITY PATIENT POPULATION: AGE BASED ANALYSIS. Papri Sarkar, MD,1 Rachel Sprague, M.D.,2 Zoran J. Pavlovic, M.D.,3 Samad Jahandideh, PhD,4 Mariana Barreto, BSc,1 Renata Erberelli, BSc,1 Jose Roberto Alegretti, MSc,1 Eduardo L.A. Motta, MD, PhD,4 Marcelo Fábio Gouveia Nogueira, Associate Professor, José Celso Rocha, PhD,5 Aline R. Lorenzo, PhD1
1Huntington Medicina Reproductiva - Eugin Group, Sao Paulo, Brazil; 2Universidade Estadual Paulista (UNESP), Faculdade de Ciências e Letras (Câmpus de Assis), Assis - SP, Brazil; 3Huntington Medicina Reproductiva, Sao Paulo, Brazil; 4Huntington Medicina Reproductiva - Eugin Group, Sao Paulo, Brazil; 5São Paulo State University (UNESP), Faculdade de Ciências e Letras (Câmpus de Assis), Assis - SP, Brazil; 6State University of São Paulo Júlio de Mesquita Filho, Assis, Brazil.

OBJECTIVE: The primary indication for intracytoplasmic sperm injection (ICSI) is for treatment of couples with male factor infertility. However, ICSI has been proposed as a tool to overcome difficulties in sperm-oocyte interaction secondary to oocyte age and not necessarily sperm abnormalities. Our hypothesis is that ICSI might be helpful in assisting sperm penetration in oocytes from older women. Therefore, the objective of this study was to investigate if there is any advantage of performing ICSI over conventional fertilization in different age groups.

MATERIALS AND METHODS: We conducted a retrospective analysis of all autologous IVF/ fresh embryo transfer (ET) between January 2010 – December 2019 at Shady Grove Fertility Centers. Patients with male factor infertility explained by abnormal sperm analysis (SA), or sperm function defect in the setting of normal SA and functional male defects, were excluded. Pregnancy outcomes [clinical pregnancy rate (CPR), miscarriage rate (MR), and live birth rate (LBR)] after single embryo transfer were compared between ICSI, and conventional fertilization cycles. Secondary outcome was rate of embryo cryopreservation per embryo transfer. Cycles with preimplantation genetic testing or split ICSI and conventional insemination were excluded.

RESULTS: A total of 150,648 oocytes underwent ICSI resulting in successful fertilization in 113,902 (75.6%) while 71,059 oocytes underwent conventional insemination leading to successful fertilization in 43,215 (60.8%), this difference was statistically significant (p<0.001). Failed fertilization (non 2 pronuclei formation) was significantly lower with ICSI compared to conventional insemination (24.4% vs 39.2%, p<0.001). A total of 9,703 ET were performed in the ICSI group compared to 4,759 in the conventional insemination group. There was no difference in baseline characteristics between the two groups. Transfer of embryo(s) from ICSI was associated with lower CPR and LBR (49.0% vs 53.5, p<0.0001) and (40.4% vs 44.4%, p<0.01) compared to transfer of embryo(s) from conventional insemination respectively. There was no difference in MR between the two groups. In women < 35 years old, CPR and LBR were significantly lower with ICSI (55.2 vs 59.7%, p=0.008) and (47.1% vs 50.6%, p=0.025) compared to conventional insemination respectively, but there was no difference in the number of embryos cryopreserved and MR between the two groups. In the older patients (35-37, 38-40 and >40 years old), there were no difference in CPR, MR and LBR between the two groups. In women between 35-37 years old, the rate of embryo cryopreservation per ET was lower (64.6% vs 73.7 %, p=0.002) after ICSI compared to conventional insemination.

CONCLUSIONS: Although ICSI resulted in higher fertilization rate in patients without male factor infertility, no improvement in pregnancy outcomes were noted among different age-group women for cycles with ICSI.

IMPACT STATEMENT: In patients with advanced maternal age undergoing IVF, there is no evidence to support performing ICSI over conventional insemination if the etiology of infertility is not male factor.

SUPPORT: None

O-197 11:45 AM Wednesday, October 26, 2022

EMBRYOLOGISTS VERSUS ARTIFICIAL INTELLIGENCE: PREDICTING CLINICAL PREGNANCY OUTCOME OF A TRANSFERRED EMBRYO WHO PERFORMS IT BETTER? Catherine K. Jacobs, MSc,1 André Satoshi Satoshi Ferreira, Undergraduate,2 Doris Chéles, MSc,3 Mariana Barreto, BSc,1 Renata Erberelli, BSc,1 José Roberto Alegretti, MSc,1 Eduardo L.A. Motta, MD, PhD,4 Marcelo Fábio Gouveia Nogueira, Associate Professor, José Celso Rocha, PhD,5 Aline R. Lorenzo, PhD1
1Huntington Medicina Reproductiva - Eugin Group, Sao Paulo, Brazil; 2Universidade Estadual Paulista (UNESP), Faculdade de Ciências e Letras (Câmpus de Assis), Assis - SP, Brazil; 3Huntington Medicina Reproductiva, Sao Paulo, Brazil; 4Huntington Medicina Reproductiva - Eugin Group, Sao Paulo, Brazil; 5São Paulo State University (UNESP), Faculdade de Ciências e Letras (Câmpus de Assis), Assis - SP, Brazil; 6State University of São Paulo Júlio de Mesquita Filho, Assis, Brazil.

OBJECTIVE: Morphology, morphokinetics, preimplantation genetic screening and lately artificial intelligence (AI) algorithms are used to rank and select embryos with higher potential to achieve a live birth. Training and validating an AI for embryo selection evolves the analysis of their pregnancy prediction potential out of a transferred embryo. In order to truly understand the efficiency of an in development algorithm, we compared senior (>8 years of experience) embryologists (EMBs) and an AI algorithm abilities for pregnancy prediction in a cohort of single-embryos transferred.

MATERIALS AND METHODS: This is a retrospective cohort study using data of 136 fresh and frozen single-blastocyst transfers with a known outcome performed between January-July 2021. All embryos were cultured in a time-lapse system incubator (Embryoscope Plus). In our laboratory routine, morphology and morphokinetic parameters/score are taken into consideration prior to embryo selection for uterine transfer. An AI collected a single 2-D image from each blastocyst of this cohort with the inner cell mass and trophoectoderm well visualized. Other three independent EMBs (EMB A, EMB B and EMB C) received the entirely anonymous set of blastocysts images and answered the question “Does this embryo result in a clinical pregnancy (presence of gestacional sac and heartbeat)” with “Yes” or “No”. No extra data was provided. The set of images was also evaluated by an in-house AI algorithm previously trained with a distinct dataset, which performed in the validation test an area under curve of 0.62 for positive clinical pregnancy and 0.52 for negative clinical pregnancy. Answers were compared to the reproductive outcome and the agreement between the embryologists was also assessed. Fleiss kappa and Chi-square tests were used for statistical analysis, p<0.05 was considered significant.

RESULTS: EMB A prediction for a correct in 54% of the cases (CP positive: 89.7% and CP negative: 19.1%); EMB B prediction was 49% correct (CP positive: 64.7% and CP negative: 32.4%) and EMB C prediction was also 49% correct (CP positive: 55.9% and CP negative: 41.2%). Overall, EMBs mode was 70.6% positive and 27.9% negative clinical pregnancy prediction, 49% of the cases. Fleiss kappa value for agreement reliability between the EMB was 0.43 (moderate agreement). AI algorithm prediction was correct in 62.5% of the cases (CP positive: 63.9% and CP negative: 61.3%). Comparing the AI showing a higher prediction performance than the EMBs mode (p=0.00057).

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CONCLUSIONS: AI did overcome experienced embryologists on overall pregnancy prediction of previously selected embryos. Embryologists were less likely to predict a negative outcome than the AI algorithm.

IMPACT STATEMENT: The new emerging technologies of artificial intelligence, mainly machine learning, are helpful tools to assist embryologists on embryo selection task and should be integrated to laboratory routine properly after in house validation.

O-198 12:00 PM Wednesday, October 26, 2022

COVID-19 VACCINATION AND ASSISTED REPRODUCTION OUTCOMES: A LITERATURE REVIEW AND META-ANALYSIS. Isaac J. Chamani, M.D., Laurie McKenzie, M.D.,* Frederick Licciardi, M.D., David H. McCulloh, Ph.D. 1Baylor College of Medicine, Houston, TX; 2NYU Langone Health, New York, NY.

OBJECTIVE: The COVID-19 pandemic remains a significant global health risk and poses an increased danger to pregnant mothers. There remains significant vaccination hesitancy amongst many in the population, in part due to unfounded claims regarding its effect on fertility (1). We conducted a literature review and meta-analysis comparing the available data on effects of COVID-19 vaccination on both ovarian stimulation and embryo transfer outcomes.

MATERIALS AND METHODS: A literature search of PubMed was conducted using the search terms COVID-19, SarCo2v, vaccines, bnt162 vaccines, 2019-ncov vaccine mRNA-1273, in vitro fertilization, egg retrieval, oocyte retrieval and embryo transfer. Reported ovarian stimulation outcomes included number of oocytes retrieved, number of mature oocytes, number of fertilized oocytes, and number of blastocysts formed, and were compared using Student’s t-test. Embryo transfer outcomes included implantation rate, clinical pregnancy rate, and ongoing pregnancy rate, and were compared using chi square. Meta-analysis was performed by Standard Mean Difference method for oocyte outcomes and the Cochran-Mantel-Haenszel method for embryo transfer outcomes.

RESULTS: Our search retrieved 12 studies conducted between August 2021 and March 2022. Of them, only 6 compared outcomes between COVID-19 vaccinated and unvaccinated patients. Two included only ovarian stimulation outcomes, two included only embryo transfer outcomes, and two studies included outcomes for both. Of the ovarian stimulation outcomes reported, data adequate for meta-analyses were only included for the number of oocytes retrieved and number of mature oocytes. There were no statistically significant differences reported between vaccinated and unvaccinated patients amongst the pooled data from the four studies for the ovarian stimulation parameter — number of oocytes retrieved (mean 10.6 vs 10.6, 95% CI -0.144 – 0.157), or the number of MII oocytes (mean 7.43 vs 7.95, 95% CI -0.055 – 0.247). There were similarly no statistically significant differences amongst the pooled data from the four studies for any of the embryo transfer parameters — implantation rate (OR 0.97, 95% CI 0.76 - 1.24), clinical pregnancy rate (OR 0.88, 95% CI 0.70 - 1.11), or ongoing pregnancy rate (OR 1.22, 95% CI 0.78 - 1.91).

CONCLUSIONS: The current literature demonstrates no differences in either ovarian stimulation or embryo transfer outcomes following COVID-19 vaccination. There remain several key parameters, however, that would benefit from additional investigation.

IMPACT STATEMENT: Patients can be reassured the current evidence reaffirms the safety profile of the mRNA COVID-19 vaccine and does not affect fertility.


ORAL ABSTRACT SESSION: CRYOPRESERVATION

O-199 10:45 AM Wednesday, October 26, 2022

DOES TYPE OF TRIGGER INFLUENCE OOCYTE MATURITY IN PATIENTS UNDERGOING OOCYTE CRYOPRESERVATION, EMBRYO BANKING AND IN VITRO FERTILIZATION CYCLES USING LETROZOLE? Lauren Ursillo, M.D. 1 2Alexandra Peyser, M.D., Christine Mullin, M.D. 3 Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, New York, NY; 3Northwell Health Fertility, Zucker School of Medicine at Hofstra Northwell, Manhasset, NY.

OBJECTIVE: Letrozole is an aromatase inhibitor that is used during oocyte cryopreservation cycles to lower estradiol levels in patients with conditions such as breast cancer, lymphoma, seizures, BRCA mutation carriers and history of venous thromboembolic events (VTE). Many studies have determined that using letrozole has no effect on the number of oocytes retrieved or maturity. The purpose of this study is to determine if the type of trigger affected the percent of mature oocytes retrieved in patients undergoing controlled ovarian stimulation with letrozole.

MATERIALS AND METHODS: A retrospective chart review examined all oocyte cryopreservation, embryo banking, and IVF cycles that utilized letrozole at a single academic medical center between October 2019 and February 2022. Those who used recombinant hCG trigger were compared to those who received a dual trigger shot with GnRHa and hCG. Patients using GnRHa only were excluded. Trigger type was based on the discretion of the patient’s provider using factors such as age, AMH, and risk for OHSS. The primary outcome of this study was oocyte maturity which was stratified based on trigger type. Oocyte maturity was calculated by dividing the number of Metaphase II oocytes (MIIs) by the total number of oocytes retrieved.

RESULTS: Of the 45 cycles, 20 cycles (44.4%) used a recombinant hCG trigger, 22 (48.9%) used a dual trigger with hCG and GnRHa. The dual trigger group had a statistically significantly higher AMH (3.43 vs 1.71 ng/mL, p<0.05), estradiol level on day of trigger (1050 vs 571 pg/mL, p<.05), total number of oocytes retrieved (19.9 vs. 11.5, p<.05) and number of MIIs (14.6 vs. 7.3, p<.05). The mean oocyte maturity was not statistically different between groups (73.2% and 70.9%, p=38).

CONCLUSIONS: Although there was a significant difference in estradiol levels on day of trigger, total number of oocytes retrieved, and total number of mature oocytes, there was no statistically significant difference in maturity rate. These results suggest that type of oocyte maturity trigger used during an oocyte cryopreservation cycle with letrozole should be based on a patient’s individual risk factors for OHSS.

IMPACT STATEMENT: There is no difference in oocyte maturity rates in patient undergoing oocyte cryopreservation cycles using letrozole between dual trigger and hCG trigger alone.

O-200 11:00 AM Wednesday, October 26, 2022

VITRIFICATION WITH SLUSH NITROGEN DOES NOT IMPROVE REPRODUCTIVE POTENTIAL OF FROZEN EMBRYOS: A RANDOMIZED CONTROLLED TRIAL. Amber M Klimczak, MD, Nola Herlihy, MD, Christine V. Whitehead, BSN, RN, Cheri K. Margolis, MD, Leah M. Roberts, MD, Pavan Gill, MD, Andres Reig, MD, Emre Seli, MD, Richard T. Scott, Jr., M.D. IVIRMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: It is known that embryos incur some damage during vitrification leading to reduced reproductive potential. Vitrification with slush nitrogen (SN) provides a faster cooling rate compared to liquid nitrogen (LN), leading to decreased vitrification-induced toxicity as evidenced by improved survival after sequential freeze thaw cycles. It is unknown whether the benefits of SN remain clinically relevant with just one freeze thaw cycle. In this study we aimed to determine whether the use of SN for embryo vitrification can improve embryo transfer outcomes compared to the conventionally used LN.

MATERIALS AND METHODS: A double-blinded, randomized controlled trial was conducted at a university-affiliated infertility clinic between September 2020 and January 2022. Patients undergoing infertility treatment with IVF and PGT-A with a plan for subsequent frozen single embryo transfer (FET) were included in the study. Patients were block-randomized to vitrification with either SN or LN on the first day of blastulation. The study was stopped early due to decreased vitrification-induced toxicity as evidenced by improved survival after sequential freeze thaw cycles. It is unknown whether the benefits of SN remain clinically relevant with just one freeze thaw cycle. In this study we aimed to determine whether the use of SN for embryo vitrification can improve embryo transfer outcomes compared to the conventionally used LN.

RESULTS: Of the 45 cycles, 20 cycles (44.4%) used a recombinant hCG trigger, 22 (48.9%) used a dual trigger with hCG and GnRHa. The dual trigger group had a statistically significantly higher AMH (3.43 vs 1.71 ng/mL, p<0.05), total number of oocytes retrieved (19.9 vs. 11.5, p<.05) and number of MIIs (14.6 vs. 7.3, p<.05). The mean oocyte maturity was not statistically different between groups (73.2% and 70.9%, p=38).

CONCLUSIONS: Although there was a significant difference in estradiol levels on day of trigger, total number of oocytes retrieved, and total number of mature oocytes, there was no statistically significant difference in maturity rate. These results suggest that type of oocyte maturity trigger used during an oocyte cryopreservation cycle with letrozole should be based on a patient’s individual risk factors for OHSS.

IMPACT STATEMENT: There is no difference in oocyte maturity rates in patient undergoing oocyte cryopreservation cycles using letrozole between dual trigger and hCG trigger alone.
significant difference between the two groups in pregnancy rate, clinical pregnancy rate, SIR or clinical miscarriage rate \( (p=0.385, p=0.714, p=0.664, p=0.127) \), respectively. A futility analysis indicated no value in continuing recruitment and therefore the study was closed.

CONCLUSIONS: After a single freeze thaw cycle, pregnancy outcomes are equivalent when embryos are vitrified with either SN or LN.

IMPACT STATEMENT: This study demonstrates that slush nitrogen is a safe alternative to traditional liquid nitrogen for vitrification, however it does not improve the reproductive potential of vitrified embryos.

SUPPORT: This study was funded by a grant from the Foundation for Embryonic Competence.

O-201 11:15 AM Wednesday, October 26, 2022

REPRODUCTIVE OUTCOMES IN SINGLE EUPOLOID EMBRYO TRANSFER CYCLES IS INDEPENDENT OF WHETHER THE EMBRYO ORIGINATED FROM A FRESH OR CRYOPRESERVED OOCYTE. Chelsea M. Canon, MD;1 Carlos Hernandez-Nieto, MD;1 Devora Aharon, MD;1 Dmitry Gounko, B.S.; M.A.;2 Taraneh Gharib Nazem, MD;1 Joseph A. Lee, BA;2 Daniel E. Stein, MD;2 Alan B. Copperman, MD,1 Icahn School of Medicine at Mount Sinai, New York, New York, NY; 2Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: It is common practice in ART treatment to transfer fresh embryos from fresh oocytes. Yet, there is a growing subset of patients who are now returning to treatment and using cryopreserved oocytes to create embryos for transfer. Whether pregnancy rates are affected by the use of embryos developed from cryopreserved oocytes has not been fully assessed in ART literature. The goal of this study is to compare pregnancy outcomes from patients undergoing frozen, single euploid embryo transfers (SEETs) who used embryos developed from fresh oocytes compared to embryos created with cryopreserved oocytes.

MATERIALS AND METHODS: This study included patients who underwent autologous SEET cycles at a single academic center from September 2016 to February 2022. All PGT-A testing was performed on blastocysts using next generation sequencing. Only patients who underwent a SEET under a synthetic endometrial preparation cycle were included. Transfer cycles were grouped based on whether the embryo was derived from fresh oocytes versus cryopreserved oocytes. Vitrification was used for all cryopreservation. Demographic and embryologic characteristics were collected. The primary outcome was ongoing pregnancy and live birth rate. Secondary outcomes included chemical pregnancy rate, implantation rate, biochemical pregnancy rate, and early pregnancy loss rate. Data was analyzed by student’s t-test and chi-square. Data was also analyzed using a multivariate regression analysis fitted with a general estimate equation (GEE) model. A sample size of 93 patients per group was calculated in order to have 80% power to detect a 10% difference in pregnancy outcomes.

RESULTS: Of the total 7,810 SEET cycles identified, 6,870 cycles used euploid embryos developed from fresh oocytes and 1,585 cycles used euploid embryos developed from cryopreserved oocytes. A similar number of oocytes and mature oocytes were collected in each group; however, there were significantly fewer blastocysts \((P=0.001)\) and fewer blastocysts biopsy \((P=0.0005)\) in the group using embryos developed from cryopreserved oocytes. Pregnancy rates did not differ between the two groups. A GEE model was then used and adjusted for oocyte age, age at transfer, BMI, AMH, endometrial thickness at transfer, previous number of PGT-A tested transfers, and embryo morphologic quality. There was no difference in ongoing pregnancy/live birth (aOR 1.0, 95% CI 0.6-1.9), biochemical loss (aOR 1.2, 95% CI 0.5-2.7), or clinical loss (aOR 0.59, 95% CI 0.3-1.3).

CONCLUSIONS: As patients who previously cryopreserved oocytes return and attempt pregnancy, we are challenged with providing personalized predictive tools to support accurate counseling on the reproductive potential of developing these oocytes into embryos. Our study showed that ongoing pregnancy and live birth rates do not differ in SEET cycles in patients whether their embryo originated from a fresh or cryopreserved oocyte.

IMPACT STATEMENT: This study shows that patients who use euploid embryos developed from cryopreserved oocytes have similar pregnancy outcomes compared to using fresh oocytes.

SUPPORT: None

O-202 11:30 AM Wednesday, October 26, 2022

EXPANSION GRADE OF POST THAW EMBRYOS AND IMPLANTATION POTENTIAL. Chelsea M. Canon, MD;1 Carlos Hernandez-Nieto, MD;1 Richard E. Slifkin, B.A.;2 TS(ABB), CLT(NYS));2 Rose Marie Roth, MSc, TS(ABB), CLT (NYS);1 Christine Briton-Jones, PhD,1 Joseph A. Lee, BA;2 Alan B. Copperman, MD;2 Rachel Gerber, MD;1 Icahn School of Medicine at Mount Sinai, New York, NY; 2Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) includes laser-assisted hitching which affects the rate of embryo expansion. The study evaluated the relationship between expansion grades of post thaw, euploid embryos and implantation potential.

MATERIALS AND METHODS: This study included patients who underwent autologous single euploid embryo transfer (SEET) cycles at a single academic center from September 2016 to February 2022. All PGT-A testing was performed using next generation sequencing (NGS). All patients underwent a synthetic endometrial preparation cycle. Transfer cycles were grouped based on blastocyst expansion at cryopreservation and at subsequent thaw. Demographic and embryonic characteristics were collected. The primary outcome was implantation rate. Secondary outcomes included ongoing pregnancy and live birth, biochemical pregnancy rate, and early pregnancy loss rate. Comparative statistics were performed with ANOVA, Kruskal-Wallis, and chi-square. Data was also analyzed using a multivariate regression analysis fitted with a general estimate equation (GEE) model. A sample size of 356 patients per group was calculated in order to have 80% power to detect a 10% difference in implantation rate (alpha=0.05).

RESULTS: A total of 9,628 cycles were identified, in which 6,870 cycles included embryos frozen and thawed with an expansion of 4 or 5 (Group 1), 1,585 cycles included embryos frozen with an expansion of 4 or 5, and thawed with an expansion of 6 (Group 2), and 1,173 cycles included embryos frozen and thawed with an expansion of 6 (Group 3). After adjusting for oocyte age, BMI, endometrial thickness at transfer, number of prior transfers with PGT-A tested embryos, and embryo morphologic quality, embryos from group 1 had a higher odds of implantation when compared to group 3 (aOR 0.90, 95% CI 0.76, 1.06). Similarly, embryos from group 1 had a higher odds of ongoing pregnancy and live birth (OPLB) when compared to group 3 (aOR 1.29, 95% CI 1.12, 1.49), while embryos from group 2 had no difference in implantation when compared to group 3 (aOR 0.90, 95% CI 0.76, 1.06). Similarly, embryos from group 1 had a higher odds of ongoing pregnancy and live birth (OPLB) compared to group 3 (aOR 1.29, 95% CI 1.12, 1.49).

CONCLUSIONS: As patients who previously cryopreserved oocytes return and attempt pregnancy, we are challenged with providing personalized predictive tools to support accurate counseling on the reproductive potential of developing these oocytes into embryos. Our study showed that ongoing pregnancy and live birth rates do not differ in SEET cycles in patients whether their embryo originated from a fresh or cryopreserved oocyte.

IMPACT STATEMENT: This study shows that patients who use euploid embryos developed from cryopreserved oocytes have similar pregnancy outcomes compared to using fresh oocytes.

SUPPORT: None
CONCLUSIONS: This study showed that post thaw, euploid embryo expansion grade affects implantation and OPLB rates. Euploid embryos with post thaw expansion of 4 or 5 have increased odds of implantation and OPLB compared to euploid embryos with a post thaw expansion of 6. Our study findings suggest that euploid embryos transferred with a zona pellucida had higher implantation and OPLB rates, which may suggest protective properties to cellular integrity that may support reproductive potential throughout the vitrification and re-warming process.

IMPACT STATEMENT: Fully hatched embryos with a post thaw expansion grade of 6 are less likely to implant when compared to embryos with expansion 4 or 5.

SUPPORT: None

O-203 11:45 AM Wednesday, October 26, 2022

DOES RACIAL DISparity EXISTS IN PLANNED OOCYTE CRYOPRESERVATION CYCLES? A SART DATABASE ANALYSIS OF 15,806 CYCLES. Bahar D. Yilmaz, MD, 1 Yilmaz, MD, 2 Lutfiya N. Muhammad, PhD, MPH, 3 Chen Yeh, MS, 3 Amanda Adeleye, MD, 3 Eve C. Feinberg, MD 1 Northwestern University, Chicago, IL; 2Northwestern University Feinberg School of Medicine, Chicago, IL; 3The University of Chicago, Chicago, IL.

OBJECTIVE: To determine if FSH treatment dosage, number of mature oocytes, and treatment duration differ by race/ethnicity in planned oocyte cryopreservation (OC) cycles.

MATERIALS AND METHODS: Society for Assisted Reproductive Technology Clinic Outcome Reporting System Database (SART-CORS) was used to analyze 15,806 first OC cycles from 2013-18 in patients aged 18-44 years with a BMI 15-60 kg/m2. Analysis of variance models for continuous variables (age, BMI, smoking status, D3 maximum FSH, AMH, rate of diminished ovarian reserve and ovariolar disorders) were found when comparing Asian, black, Hispanic and other to white. The prevalence of obesity (BMI≥30) was highest in black (23.6%) and Hispanic (17.6%) patients and lowest in Asian (4.2%) patients. Black and Hispanic patients used higher doses of gonadotropins by a total of 240 international units over an average of 12-day stimulation cycle. Differences in treatment duration and number of mature oocytes were statistically significant, but not clinically significant between races. While racial disparity has been reported in population or egg yield among people seeking planned OC. Patients can be counseled that current ART methods of cryopreservation, oocyte transcriptome and mitochondrial function remain susceptible to cryopreservation-related perturbations which may affect treatment outcomes in ART couples and those who require fertility preservation following cancer diagnosis. With established evidence from the Developmental Origins of Health and Disease (DOHaD) hypothesis, and increasing application of cryopreservation procedures, the wider impact of environmental exposures on oocyte mitochondria function and molecular integrity in ART procedures is yet to be fully evaluated.

This study aims to investigate the impact of cryopreservation on oocyte mitochondrial function, as determined by oxygen consumption rate (OCR), and on the transcriptome.

MATERIALS AND METHODS: A real-time Extracellular Flux Assay (EFA) was used to evaluate Oxygen Consumption Rate (OCR) in vitrified/warmed oocytes following exposures to known inhibitors of mitochondria function. cDNA was obtained using the Smart-Seq2 protocol and single-cell RNA-Seq was performed (illumina NextSeq2000). Differentially expressed genes (DEG) were identified using the R package edgeR and functional gene ontology was performed using an over-representation analysis via WebGestalt. Correction for multiple testing was calculated using the Benjamini-Hochberg method.

RESULTS: In the EFA study, vitrified/warmed oocytes (n= 7, survival rates 85.7%) showed a large non-mitochondria component of OCR, reduced spare respiratory capacity, with less than 10% of overall consumed oxygen rate= 85.7%) showed a large non-mitochondria component of OCR, reduced spare respiratory capacity, with less than 10% of overall consumed oxygen associated directly with ATP synthesis. In the transcriptome analysis, genes associated with tricarboxylic cycle (TCA) and RNA polymerase I, were significantly dysregulated with slow freezing relative to control oocytes. 2,465 genes were significantly differentially expressed in slow frozen oocytes relative to vitrified oocytes (FDR<0.05). Similarly, 789 and 1,782 genes were significantly differentially expressed between vitrified and slow freezing group, relative to control oocytes (FDR<0.05). DEGs were associated with metabolic processes, protein binding, nuclear export, including RNA-localization, and chromosome segregation (FDR<0.05).

CONCLUSIONS: Our results show that current ART methods of cryopreservation perturb oocyte OCR and confers a unique transcriptome relative to control oocytes. The observed changes in oocyte mitochondrial respiratory machinery and transcriptome profile maybe consequential to offspring long-term health outcomes. A continuous evaluation of ART method of cryopreservation and the impact of environmental exposures is warranted.

IMPACT STATEMENT: The use of novel tools in evaluating the safety and impact of oocyte cryopreservation, and potential future modifications may improve clinical outcomes, fertility preservation patients counselling experience, and longterm offspring health.

SUPPORT: T.A. is funded by a Clinical Doctoral Research Fellowship (CDFR) grant (reference: ICA-CDFR-2015-01-068) from the National Institute for Health Research (NIHR). The views expressed in this abstract are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health, UK. The authors declare no conflict of interest.

OBJECTIVE: There are significant Black-White racial disparities in in vitro fertilization (IVF) outcomes that are poorly explained by individual-level factors. Therefore, we sought to explore whether neighborhood characteristics may contribute to the racial disparities in IVF outcomes.

MATERIALS AND METHODS: A retrospective cohort study was performed including 1110 patients who underwent 2754 autologous IVF cycles during the years 2014-2019 at an academic fertility center in the Southeastern United States. Patients’ addresses were geocoded and then linked by census tract with the neighborhood deprivation index (NDI), a composite variable measuring community levels of material wealth based off of poverty, occupation, housing, and education domains. Using multivariable log-binomial generalized estimating equations with cluster weighting, we estimated risk ratios (RR) and 95% confidence intervals (CIs) for cycle cancellation, miscarriage, and live birth according to patient NDI. Race was considered as both a potential confounder and effect modifier. Additionally, models were adjusted for age, body mass index (BMI), parity, tubal factor infertility, and uterine factor infertility.

RESULTS: Of the 1110 patients included, 48% identified as White, 27% as Black, 17% as Asian, and 7% as other race. Compared to White patients, Black patients were more likely to have insurance coverage for IVF, live further from the clinic, and live in areas with a higher NDI (indicating higher levels of deprivation). There were positive associations between increasing NDI and BMI, as well as increasing prevalence of tubal and uterine factor infertility diagnoses. The incidence of live birth was lower in Black (24%) versus White patients (32%) and the incidence of miscarriage was elevated in Black (22%) as compared to White patients (12%), without adjusting for age. After adjustment, NDI was not significantly associated with risk of cycle cancellation or live birth, but a trend was seen between increasing levels of neighborhood deprivation and increased risk of miscarriage (RR: 1.24 per interquartile range increase in NDI; 95% CI 0.97, 1.59). Of the NDI components, % of households with incomes <$35k, % of households with >1 person per room, % of females with no high school education, and % living below the poverty line had the strongest association with risk of miscarriage. Results were consistent when analyses were stratified by race.

CONCLUSIONS: Our research demonstrated racial disparities between Black and White women in the incidence of miscarriage and live birth following IVF. While level of neighborhood deprivation was closely related to race, it did not have strong associations with IVF outcomes in our population as a whole or within strata of race. There was some evidence for an association between NDI and risk of miscarriage, which should be further investigated in larger studies.

IMPACT STATEMENT: Given the documented racial disparities in IVF outcomes, future studies are needed to continue to explore other measurable, policy-modifiable neighborhood-level variables and their impact on IVF outcomes.

OBJECTIVE: The coronavirus disease 2019 (COVID-19) pandemic caused radical changes in health care delivery. The American Society for Reproductive Medicine (ASRM) during the COVID-19 pandemic recommended using telehealth to the greatest extent possible to continue evaluating and treating patients. And while generally well-received by patients and providers, there is limited literature on the use of telehealth in low-income, non-English-speaking patients who might have difficulty accessing technology and resources required for telehealth visits. The objective of this survey study was to analyze patient perspectives of telehealth amongst this underserved population seeking infertility care.

MATERIALS AND METHODS: We performed a cross-sectional survey study by distributing an anonymous, web-based survey to patients who had at least one telehealth visit at the Los Angeles County Hospital Reproductive Endocrinology and Infertility clinic between February-April, 2022. The survey included questions from the Telehealth Usability Questionnaire (TUQ), a validated tool that assesses the quality and usability of telehealth on a 5-point Likert scale (strongly disagree to strongly agree), and also gathered demographic data. The primary outcome was overall satisfaction using telehealth. Fisher’s exact tests were used to compare groups, with a P value <0.05 considered statistically significant.

RESULTS: 140 patients were invited to participate in the study, and 98 completed the survey (70%). A majority of respondents were Hispanic (76%), and had an annual income of less than $40,000 (60%). Most respondents believed telehealth improved their access to healthcare (87%), thought telehealth visits were as good as in-person visits (66%), considered telehealth an acceptable way to receive care regarding infertility (76%), and were overall satisfied with their telehealth visit (95%). Only 12% of respondents had difficulty using the telehealth platform or communicating with their doctor, and these patients were more likely to speak Spanish as their primary language (P = 0.04).

CONCLUSIONS: Even among minority and low-income patients, telehealth is an effective and satisfactory method to provide infertility counseling and treatment. Patient satisfaction can be further improved by improving usability by non-English speakers.

IMPACT STATEMENT: Telehealth can improve access to infertility care among minority and low-income patient populations with high rates of patient satisfaction.

REFERENCES:
RESULTS: Of 2,909 patients included, 1,433 (47%) utilized PGT and 1,476 (49%) did not. Hispanic patients utilized PGT significantly less (41%, 66/162) than all other racial/ethnic groups (Multiracial 47% (130/291), NHB 47% (44/93), Asian 52% (125/240), NHW 55% (528/967), p < 0.006). Those whose primary language was not English were significantly less likely to utilize PGT compared to those with English as their first language (Other Language: 34% (21/61) vs. English: 49% (1167/2347), p = 0.02). These associations remained significant after adjusting for maternal age with Hispanic patients less likely to utilize PGT. Overcoming language barriers between providers and patients should be an area of focus to improve patient education of PGT and increase access to care. Future studies with larger cohorts are needed to elucidate reasons underlying these disparities.

IMPACT STATEMENT: PGT utilization varies by race and ethnicity and may represent an area requiring improved patient education and access.

O-208 11:30 AM Wednesday, October 26, 2022
THE ASSOCIATION OF MODIFIABLE RISK FACTORS WITH REPRODUCTIVE HORMONES IN WOMEN UTILIZING AT-HOME SAMPLE COLLECTION FOR LABORATORY TESTING. Kathleen M. Gavin, PhD,1 Natalie M. Daumeyer, PhD,2 Daniel Kreitzberg, PhD,2 Timothy A. Bauer, PhD1 1Denver, CO; 2Everly Health, Inc., Austin, TX.

OBJECTIVE: To identify significant predictors of reproductive hormone levels in women using at-home sample collection for laboratory testing.

MATERIALS AND METHODS: A retrospective analysis was performed using real world data (RWD) from 5,082 females who purchased commercially available at-home sample collection kits for laboratory analysis of reproductive hormones (period: May 2021 - March 2022). Mean age was 38.6 years (sd = 9.1, range 18-94) and the majority identified as White (89.8%) and non-Hispanic (93.3%). Luteinizing Hormone (LH, IU/L) and Follicle Stimulating Hormone (FSH, IU/L) were measured via dried blood spot from day 3 or 4 of the menstrual cycle. Estradiol (E2, pg/ml), free testosterone (FT, pg/ml), and progesterone (pg/ml) were measured in saliva collected on day 19-21. Alcohol use was categorized as: non-drinkers (n = 1,071, 21.1%), moderate (n = 3,214, 63.2%), and heavy (n = 797, 15.7%). Body mass index (BMI) categories: underweight (< 18.5 kg/m², n = 84, 1.7%), normal (18.5–24.9 kg/m², n = 1,919, 37.8%), overweight (25.0–29.9 kg/m², n = 2,584, 51.3%), and obese (≥ 30.0 kg/m², n = 1,548, 30.5%). The majority of women (n = 4,589, 90.3%) reported performing moderate or greater intensity exercise at least once per week. Linear regression models tested the associations between the log-transformed hormone values as dependent variables and alcohol consumption, BMI, physical activity, cycle regularity, ethnicity, race, and age as independent variables. Differences in hormones between groups represent geometric means. P-values were adjusted to account for multiple comparisons using the Bonferroni method with outliers dropped using Cook’s distance.

RESULTS: Women with obesity had 16% lower LH (β = 0.84, 95% CI = 0.81, 0.87, p < 0.001), 11% lower FSH (β = 0.89, 95% CI = 0.86, 0.92, p < 0.001), 29% lower progesterone (β = 0.71, 95% CI = 0.67, 0.74, p < 0.001), and 17% higher E2 (β = 1.17, 95% CI = 1.13, 1.21, p < 0.001) compared with normal weight. Women reporting heavy alcohol consumption had 10% higher E2 levels compared with non-drinkers (β = 1.08, 95% CI = 1.03, 1.12, p = 0.001). Women reporting exercise 3–4 times/week had 10% higher FT (β = 1.10, 95% CI = 1.05, 1.16, p = 0.001), and ≥ 5 times/week 13% higher FT, compared with women reporting none (β = 1.13, 95% CI = 1.08, 1.19, p < 0.001).

CONCLUSIONS: Using RWD from self-reported risk factors and at-home sample collection in a large cohort of women, these data support the relationship of lower gonadotropins and higher E2 in women with obesity, as well as the elevated E2 levels associated with heavy alcohol consumption. The observed higher FT with greater physical activity may be reflective of the higher training status of some women in the cohort and/or the proximity of an exercise exposure to sample collection. The inclusion of wearable devices or detailed physical activity records as additional inputs may augment the assessment of this domain.

IMPACT STATEMENT: Self-reported risk factors can be used to predict altered hormones in reproductive health for personalized interpretations of reproductive health.

O-209 11:45 AM Wednesday, October 26, 2022
ASSOCIATION BETWEEN FERTILITY SERVICE UTILIZATION AND COUNTY-LEVEL MEDIAN HOUSEHOLD INCOME. Urbano L. Franca, PhD,1 Alexis Adler, BS,2 Leslie B. Ramirez, PhD3 Boston Children’s Hospital / Harvard Medical School, Boston, MA; 2Extend Fertility, New York, NY; 3Northwell Health Fertility, Manhasset, Manhasset, NY.

OBJECTIVE: Financial and geographical barriers to access fertility treatments can lead to foregone care, impact outcomes, and adversely affect employment and personal life1. To describe economic and geographic disparities in access to assisted reproduction (AR) treatments, this study evaluates the association between fertility service utilization and county-level median household income in the continental US.

MATERIALS AND METHODS: In this retrospective study, we used the Society for Assisted Reproductive Technology (SART) dataset from 2018 to measure the utilization of AR services. The number of cycles per thousand women was estimated using US Census information on the number of women of reproductive age (20–44 years). Clinics’ addresses were geolocated and assigned to counties. County-level median household income (MHI) was obtained from the US Census Bureau. Trends were evaluated using general linear models, and comparisons were assessed with the Mann-Whitney U test. Statistical significance set at p < 0.05.

RESULTS: Fertility clinics were present in only 195 (6.1%) of the 3,193 counties in the continental US. Counties without fertility clinics had significantly higher MHI compared to counties with fertility clinics (MHI = $52,871 [IQR: $45,987–$61,083] vs. MHI = $69,048 [IQR: $59,471–$82,343], p < 0.001). Considering the 304,085 cycles (5.68/lk women) performed in counties with fertility clinics, the number of cycles per thousand women was significantly associated with county-level median household income. On average, an increase of $5,000 county-level MHI was associated with an additional 110 extra cycles per 100,000 persons (p < 0.003). In the continental US, 25.7 million women (47.7%) lived in counties without a single fertility clinic.

CONCLUSIONS: Almost half of the US reproductive-age women live in counties with no fertility clinics. In counties with fertility clinics, the utilization of fertility services is significantly associated with median household income.

IMPACT STATEMENT: Disparities in access to fertility treatments in the US impact utilization and affect treatment outcomes. Geographic and economic barriers are primary factors leading to disparities1. Almost half of women of reproductive age in the US would have to travel to a different county to receive fertility treatment if needed. Furthermore, among counties with clinics, utilization of fertility treatments is significantly higher in more affluent counties. These results inform the discussion on fertility coverage mandates and need to be taken into account by policymakers and stakeholders when designing policies aimed at addressing economic disparities in fertility care in the US.

SUPPORT: None


O-210 12:00 PM Wednesday, October 26, 2022
RACIAL DISPARITY IN HEALTHCARE EXPERIENCE AMONG PATIENTS SEEKING FERTILITY CARE DURING THE COVID-19 PANDEMIC. Marco Mouanness, MD,1 Serin Seckin, MD,2 Priscilla Morelli, MS,3 Hadi Ramadan, M.D,4 Zahir Merhi, MD, HCLD1 Rejuvenating Fertility Center; 4Columbia University Medical Center, New York, NY; 3FSU College of Medicine, Tallahassee, FL; 4SUNY Downstate Health Sciences University.

OBJECTIVE: Recent data have shown that there are racial disparities in access and outcomes of assisted reproductive technology treatment in the USA (1), however, the effect of the pandemic on this racial disparity has not been studied. Thus, the primary aim of this study was to identify how the pandemic has affected patient decision-making regarding fertility planning and treatment among black versus non-black women.

RESULTS: Patient decision-making regarding fertility planning and treatment during the COVID-19 pandemic has been influenced by various socio-economic factors which may represent an area requiring improved patient education and access.
MATERIALS AND METHODS: Following IRB approval, a link to a survey was sent to the emails of all patients presenting to a university-affiliated fertility clinic between January 2021 and December 2021. The patients were asked to fill out a questionnaire regarding fertility treatment plans prior to and during the pandemic. Data collected included demographics about age, race, ethnicity, employment, vaccination, fertility treatments prior to the pandemic and changes in treatments during the pandemic. Data are presented as percentages and chi-square test was performed for statistical analysis.

RESULTS: A total of 223 patients (mean age 41 ± 1.6) filled out the questionnaire. When all participants were asked about fertility treatment plans before the pandemic, 58% were pursuing IVF, 7% wanted oocyte freezing, 4% wanted IUI, and 31% were doing fertility work-up. The majority (69%) reported that the pandemic did not change their plans and the minority reported either postponing or canceling their treatments with financial instability being the most commonly reported reason (22%). Fewer black women were vaccinated compared to non-black women (35% vs. 52%; p=0.03). When asked whether the pandemic was well-handled by major healthcare systems, black women were less likely to think that it met expectations compared to non-black women (35% vs. 54%; p=0.02). Additionally, black women were less likely to be uncomfortable visiting the office in person during the pandemic compared to non-black women (2% vs. 15%; p=0.02).

Interestingly, there was no difference between black and non-black women when asked whether they think that the vaccine could affect fertility or pregnancy outcomes or whether taking the vaccine stopped them from pursuing fertility treatments (p>0.05).

CONCLUSIONS: Among women undergoing fertility treatments during the pandemic, black race was associated with less likelihood of being vaccinated, less likelihood of being satisfied with major healthcare systems handling the pandemic, and more comfort in visiting physically the fertility clinic.

IMPACT STATEMENT: There is a clear need to understand the underlying reasons why the pandemic contributes to racial disparity in fertility treatments.

SUPPORT: No Financial Support was required for this study.

REFERENCES:


ORAL ABSTRACT SESSION: FERTILITY PRESERVATION

O-211 10:45 AM Wednesday, October 26, 2022

DELAYING CHILDBEARING TO BECOME A DOCTOR: AN EXPLORATION OF MEDICAL STUDENT FAMILY PLANNING GOALS AND KNOWLEDGE OF FERTILITY PRESERVATION OPTIONS. Michelle H. Vu, MD, SAHAVET WONGSUKON, BA, SAVANNA M. MOREHOUSE, BA, Jennifer Talbott, BA, MPH.1, Rachel Yull, BA, MPH.2, Wendy S. Vitek, M.D.3, 1Rochester, NY; 2University of Rochester School of Medicine and Dentistry, Rochester, Rochester, NY; 3Mayo Clinic College of Medicine & Science, Scottsdale, AZ; 4University of Rochester Medical Center, Rochester, NY.

OBJECTIVE: Women pursuing medical education delay child-bearing for many reasons, with career being one of the most salient reasons. Female fecundity declines with age, but the average age of women matriculating to medical school continues to increase. Our study investigated the reproductive goals of medical students and their knowledge and attitudes regarding fertility preservation options.

MATERIALS AND METHODS: From January 1st to March 1st, 2022, an anonymous electronic survey was distributed to medical students in the American Medical Women’s Association (AMWA). The 18-question survey inquired about participants’ career plans, gravidity, family planning goals, level of concern about fertility potential and knowledge of fertility preservation options. Prior to distribution, the survey was tested on a sample group of medical students to ensure comprehensibility. Descriptive statistics were used to summarize results.

RESULTS: The response rate was 25.3% (144/570). The majority of respondents were aged 20-29 years old (93.6%) and assigned female sex at birth (95.7%). 50.7% of participants were single, 37.7% partnered and 11.6% married. Only 3.6% of respondents had been pregnant, but 73.4% of them desired biologically-related children in the future. 80.6% of medical students chose to avoid childbearing in medical school with the most common reasons why including focusing on education/career, not being ready to have a child, financial burden and time commitment. 61.2% of respondents reported being concerned about their fertility potential. 41% of them had considered fertility preservation, but only 1.4% underwent embryo or oocyte cryopreservation. When asked about the most common barriers to fertility preservation, medical students stated cost, not ready to commit to fertility preservation and lack of time. 90.2% of participants had received no information regarding fertility preservation from their medical school and 78.6% of them desired more information on fertility preservation.

CONCLUSIONS: Most female medical student desire biologically related children and expressed concern about their fertility potential. However, they choose to avoid childbearing during their peak fertility years for a number of reasons, including focus on career, financial burden and time commitment. Few medical students have completed fertility preservation, but the majority desire more information on their fertility preservation options. This is the first study investigating U.S. medical students’ interest and participation in fertility preservation, and the findings encourage increased education regarding fertility preservation.

IMPACT STATEMENT: Female medical students desire information on fertility preservation and barriers to fertility preservation, such as cost and lack of time, should be addressed.

O-212 11:00 AM Wednesday, October 26, 2022

ATTITUDES TOWARDS FERTILITY PRESERVATION AND FAMILY PLANNING AMONGST ADULT AND PediatRIC TRANSGENDER PATIENTS PURSUING GENDER AFFIRMING HORMONE THERAPY. Sina Abhari, MD,1, 2 Eric Walton, MD,3, Vin Tangripricha, MD, PhD,2 Michael Goodman, MD, MPH,3 Andrey M. Marsidi, MD,3 Akanksha Mehta, M.D., M.S.1, 2 Johns Hopkins School of Medicine, Ellicott City, MD; 3Emory University School of Medicine; 3Emory University School of Medicine, Atlanta, GA.

OBJECTIVE: The purpose of this study is to examine the rates of fertility counseling and utilization of fertility preservation (FP) among a cohort of individuals with gender dysphoria and their attitudes toward FP and future parenthood.

MATERIALS AND METHODS: We administered a 28-item multiple choice survey to individuals aged >10 who self-identified as transgender, and who presented for outpatient endocrinology consultation to an academic medical center between Jan-July 2021. We included patients considering gender affirming hormone therapy (GAHT) as well as those actively using GAHT at the time of survey distribution. Responses were collected via Redcap. Descriptive statistical analysis was performed using Microsoft Excel.

RESULTS: 58 participants completed the survey. Most (89.5%) did not have genetically related children, however, 20% desired future parenthood with another 31% undecided. 22.8% of participants rated having a genetically related child as somewhat important and 2% rated having a genetically related child as very important. 76% identified adopting as an acceptable or moderately unacceptable. 42% of all participants had considered gamete preservation, but only 25% stated they would temporarily stop GAHT for this reason. Individuals who expressed desire or uncertainty for future parenthood reported higher rates of considering gamete preservation and willingness to discontinue hormone therapy. No assigned female at birth (AFAB) respondents planned to pursue oocyte preservation while 20% of assigned male at birth (AMAB) respondents had either completed or planned to pursue sperm preservation. Cost was reported as a major barrier to gamete preservation for 76% and 44% of AFAB and AMAB individuals, respectively. 56% of participants graded acceptance of society toward LGBTQ parenting as either not acceptable or moderately acceptable. 43% of individuals had planned to discontinue hormones to facilitate gamete preservation. In addition, half of participants reported receiving adequate counseling about fertility preservation. As such, discussion of fertility is essential prior to starting GAHT.

CONCLUSIONS: Approximately 23% of study participants desired future children, biologically related or otherwise. Gamete preservation was considered by some participants, but few intended to pursue this therapy with cost cited as a major barrier. Similarly, only one quarter of participants were willing to discontinue hormones to facilitate gamete preservation. In addition, half of participants reported receiving adequate counseling about fertility preservation. As such, discussion of fertility is essential prior to starting GAHT.

IMPACT STATEMENT: Transgender adolescents and young adults are increasingly seeking hormonal intervention to achieve a body consistent with their gender identity. Given that these interventions affect reproductive capacity, fertility counseling and access to FP are a crucial part of their care. Individual experiences of gender dysphoria, limited access to adequate counseling and cost are primary barriers to FP.
A resilient womb: Maternal age at transfer following autologous oocyte (AO) cryopreservation (Cryo) does not impact ongoing pregnancy + live birth rates (LBRs). Francesca Barrett, MD MBA,1 Sarah D. Cascante, MD,1 David H. McCulloh, Ph.D.,1 James A. Grifo, MD, Ph.D.,2 Jennifer K. Blakemore, MD, MSc.2 1NYU Langone School of Medicine, New York, NY; 2NYU Langone Prelude Fertility Center, New York, NY; 2NYU Langone Health, New York, NY.

Objective: AO cryo is widely used for fertility preservation, but the impact of maternal age on transfer outcomes is unknown. We reviewed our single embryo transfer (SETs) from AO cryo to understand the effect of maternal age at SET on LBR.

Materials and Methods: This retrospective cohort study reviews all patients (pts) who thawed AOs and then underwent SET at a university-based center in 2006-2021. Pts were excluded if AO cryo was performed for a medical reason, as research, due to no sperm or a natural disaster, with embryo cryo or for use with a gestational carrier. Only the 1st SET from each pt was included. SETs < 1 year (y) after cryo and SETs with mosaic/aneuploid embryos were excluded. AO thaw pts were matched 2:1 to IVF pts who underwent SET < 1y later (fresh or frozen as appropriate); matching criteria were at age and retrieval of pre-implantation genetic testing (PGT). Primary outcome was LBR. Secondary outcomes were implantation (IR) and spontaneous abortion (SABR) rates. Statistics included chi squared, fisher exact and Mann-Whitney U tests as well as multinomial logistic regression (p < 0.05 significant).

Results: 278 AO thaw pts were matched to 556 IVF controls. Median age at retrieval was 37y in both groups (p = 0.96); 77% of pts in both groups transferred euploid embryos (p = 0.86). As expected, median age at SET was older in AO thaw than in IVF pts (42 vs. 37y, p < 0.001) and median time from retrieval to SET was longer in AO thaw than in IVF pts (59 vs. 1 month, p < 0.001). In AO thaw pts, IR was 56%, SABR was 7% and LBR was 49%. In IVF pts, IR was 69%, SABR was 9% and LBR was 59%. IR and LBR differed among AO thaw and IVF pts (p = 0.003), but SABR did not (p = 0.24). See table for SET outcomes in AO thaw pts by age at SET; IR, SABR (p = 0.02) and LBR (p = 0.27) did not differ by age group.

In a multiple logistic regression model, age at SET was not predictive of LBR when controlling for age at retrieval, embryo morphology, fresh/frozen cycle and euploid/no result/untested embryo (B = -0.039, adjusted ORs = 0.72, SABR = 0.24). See table for SET outcomes in AO thaw pts by age at SET; IR, SABR (p = 0.02) and LBR (p = 0.27) did not differ by age group.

Conclusions: Maternal age at transfer after AO cryo is not predictive of LBR; this suggests that “an aging womb” does not impair LBR after AO cryo and empowers pts to return for transfer when ready for childbearing. While not significant, there is a trend of improved outcomes at age ≤ 41; this warrants exploration in future studies.

Impact Statement: AO cryo pts can be counseled that age at transfer of resultant embryos is not predictive of LBR.

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<thead>
<tr>
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<th>IR</th>
<th>SABR</th>
<th>LBR</th>
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<td>7%</td>
<td>49%</td>
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O-213 11:45 AM Wednesday, October 26, 2022

FERTILITY PRESERVATION TECHNIQUES WITH OR WITHOUT OVARIAN STIMULATION DO NOT CHANGE DISEASE-FREE SURVIVAL OF YOUNG BREAST CANCER PATIENTS. Michael Gryenberg, M.D., Ph.D.;1 Anne Mayeur, M.D.,2 Christophe Sifer, M.D.,3 Alexandre Benoit, M.D., Ph.D.1 1Hôpital Antoine Béclère, Clamart, France; 2Hôpital Antoine Béclère, Clamart, France; 3Jean Verdier Hospital, France; 4Jean Verdier Hospital, Bondy, France; 5HÔPITAL ANTOINE BECLERE, Clamart, France.

Objective: Fertility is often impaired in young women treated for breast cancer (BC). Therefore, fertility preservation (FP) has become a major issue in this population. Cryopreservation of oocytes or embryos after controlled ovarian hyperstimulation (COH) represents the most established method in this clinical situation. However, the hormonal consequences of COH protocols still pose safety concerns, often leading oncologists to contraindicate the use of this FP technique. Although alternative FP options without exogenous hormone administration may be considered, they remain suboptimal for treating the putative future infertility. The present investigation aimed to evaluate the disease-free survival (DFS) after FP strategies using COH or not, in BC patients.

Materials and Methods: This cohort study included all women, 18-43 years of age, who received primary FP between 2013 and 2019, after a diagnosis of breast cancer (BC). The STIM group were those who underwent at least one COH cycle and the No STIM group those who did not receive FP after hormonal stimulation. DFS was calculated from the date the secondary cancer was diagnosed to the date of death or was last known to be alive.

Results: Currently, 89 girls with TS have had an unilateral ovariotomy. During surgery, 33 girls had macroscopic normal ovaries, while streak ovaries were seen in 56 girls. Five girls reported complications after surgery (e.g. haematomata after blood collection and luxation of psychological symptoms)

Oocytes were found in 33,7% of the girls (n=30; age 19 - 19) of which 13 where prepubertal and 16 had a spontaneous puberty. The estimated ovarian reserve between the girls varied widely between 33 and 80,000 follicles per ovary. In young girls, the chance of finding follicles in ovaries with a 46,XX cell line is 3 times higher than in girls without a 46,XX cell line. One girl with 45,X in extra-ovarian cells had follicles while seven TS patients with structural aberrations had a very low follicle density. In 26/30 patients AMH was measurable (0.1 - 4.7μg/L) and 28/30 patients had a FSH level below 15 E/L.

Ovarian cells of 13 girls with a numerical aberration were karyotyped by FISH and showed that 122 of the 133 oocytes (92%) had a normal X-chromosomal content. Almost all granulosa cells were 45,X, but showed different levels of X chromosome mosaicism between patients and follicles of the same patient. Despite the high level of aneuploidy of up to 80% in ovarian stromal cells in some patients, ovaries were macroscopically normal.

Conclusions: Girls with TS who have favourable predictive parameters (46,XX cell line, a measurable AMH or spontaneous puberty) could benefit from FP by OTC based on the presence and number of oocytes.

Impact statement: Our study provides insights into which girls with TS are most likely to benefit from FP by OTC based on the number of ovarian follicles present. However, further research is required to determine to what extent aneuploidy of granulosa and stromal cells affects follicular development, and consequently the success rate of OTC in girls with TS.

O-215 11:45 AM Wednesday, October 26, 2022

FERTILITY PRESERVATION STUDIES IN YOUNG GIRLS WITH TURNER SYNDROME

BY FREEZING OVARIAN CORTEX

Sapthami Nadesapillai, MD,1 Myra Schleedoom, MD, PhD,1 Janielle van der Velden, MD, PhD,2 Didi Braat, MD, PhD,3 Ron Peek, MD,1 Kathrin Fleischer, MD, PhD1 Radboudumc; 2Bezirkskrankenhaus Lohr; 3Radboudumc, Nijmegen, Netherlands.

Objective: Turner syndrome (TS) is a heterogeneous chromosomal disorder affecting one in 2,500 live-born girls. Most girls with TS are confronted with infertility at an early age. Over the past decades, ovarian tissue cryopreservation (OTC) has been successfully performed and is well documented for young girls facing fertility treatments at an early age. OTC is now a valid fertility preservation (FP) option. OTC might also be a promising technique for FP in girls with TS, as it can be performed regardless of the patient’s age. Although OTC has already been performed in girls with TS, evidence on the effectiveness of OTC and autotransplantation is still lacking.

Materials and Methods: The TurnerFertility study is a national observational intervention study with long-term follow-up and was initiated in the Netherlands in 2017. In total, 106 girls with TS aged 2-18 years were included. Ovarian cortex tissue was obtained after unilateral ovariectomy. One fragment was used to determine follicle density by serial sectioning and staining. Blood samples were obtained before ovariectomy to determine hormonal parameters. Karyotyping of lymphocytes, buccal cells and ovarian cells was performed by Fluorescence in situ hybridization (FISH).

Results: Currently, 89 girls with TS have had an unilateral ovariectomy. During surgery, 33 girls had macroscopic normal ovaries, while streak ovaries were seen in 56 girls. Five girls reported complications after surgery (e.g. haematomata after blood collection and luxation of psychological symptoms)

Oocytes were found in 33,7% of the girls (n=30; age 19 - 19) of which 13 were prepubertal and 16 had a spontaneous puberty. The estimated ovarian reserve between the girls varied widely between 33 and 80,000 follicles per ovary. In young girls, the chance of finding follicles in ovaries with a 46,XX cell line is 3 times higher than in girls without a 46,XX cell line. One girl with 45,X in extra-ovarian cells had follicles while seven TS patients with structural aberrations had a very low follicle density. In 26/30 patients AMH was measurable (0.1 - 4.7μg/L) and 28/30 patients had a FSH level below 15 E/L.

Ovarian cells of 13 girls with a numerical aberration were karyotyped by FISH and showed that 122 of the 133 oocytes (92%) had a normal X-chromosomal content. Almost all granulosa cells were 45,X, but showed different levels of X chromosome mosaicism between patients and follicles of the same patient. Despite the high level of aneuploidy of up to 80% in ovarian stromal cells in some patients, ovaries were macroscopically normal.

Conclusions: Girls with TS who have favourable predictive parameters (46,XX cell line, a measurable AMH or spontaneous puberty) could benefit from FP by OTC based on the presence and number of oocytes.

Impact statement: Our study provides insights into which girls with TS are most likely to benefit from FP by OTC based on the number of ovarian follicles present. However, further research is required to determine to what extent aneuploidy of granulosa and stromal cells affects follicular development, and consequently the success rate of OTC in girls with TS.
RESULTS: Out of the 740 women who underwent FP, follow-up data were available for 269 women in the STIM group (%) and 330 in the No STIM group (%). Median follow-up was 4.2 [2.9-5.8] years vs. 5.6 [4.1-6.7], in both groups respectively. Kaplan Meier estimates of DFS at 4 years was 87.9% [82.8% - 92.2%] and 83.1% [78.4% - 87.3%] in the STIM and No STIM groups respectively. In the multivariable analysis, Disease-free survival was not different between both groups.

CONCLUSIONS: The disease-free survival of young BC patients is not impacted by FP techniques and the use of ovarian stimulation.

IMPACT STATEMENT: Our findings provide reassuring safety data on the use COH for FP in BC patients, whatever the timing of chemotherapy. However, further investigations with a longer follow-up are needed to definitely consider COH safe in particular when performed with a tumor in place until AMH

Table 1. Estimated adjusted oocyte yield in medically indicated FP cycles versus elective OC cycles for categories of AMH. Negative binomial model used and adjusted for age, BMI, smoking status, and gonadotropin usage. Non-significant interaction of AMH and groups, p = 0.95.

<table>
<thead>
<tr>
<th>AMH (ng/mL)</th>
<th>FP</th>
<th>OC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - &lt;0.25</td>
<td>5.40</td>
<td>5.14</td>
</tr>
<tr>
<td>0.25 - &lt;0.5</td>
<td>6.69</td>
<td>6.73</td>
</tr>
<tr>
<td>0.5 - &lt;0.75</td>
<td>7.07</td>
<td>8.08</td>
</tr>
<tr>
<td>0.75 - &lt;1</td>
<td>8.82</td>
<td>9.68</td>
</tr>
<tr>
<td>1 - &lt;2</td>
<td>11.84</td>
<td>12.75</td>
</tr>
<tr>
<td>2 - &lt;3</td>
<td>14.55</td>
<td>16.12</td>
</tr>
<tr>
<td>3 - &lt;4</td>
<td>17.94</td>
<td>18.56</td>
</tr>
<tr>
<td>&gt; 4</td>
<td>21.86</td>
<td>23.43</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The relationship between oocytes retrieved or cryopreserved and AMH is similar in medically indicated FP versus elective OC cycles undergoing COH.

IMPACT STATEMENT: The relationship between ovarian response and AMH in medically indicated FP patients is comparable to healthy peers providing additional reassurance when counseling FP patients prior to gondotropin therapy who undergo COH.

ORAL ABSTRACT SESSION: MALE REPRODUCTION AND UROLOGY 2

O-216 12:00 PM Wednesday, October 26, 2022

OVARIAN RESPONSE AND ANTI-MULLERIAN HORMONE IN FERTILITY PRESERVATION VERSUS ELECTIVE OOCYTE CRYOPRESERVATION CYCLES: A SOCIETY FOR ASSISTED REPRODUCTIVE TECHNOLOGY REGISTRY STUDY OF 10,040 CYCLES. Ivy L. Lersten, M.D., 1 Angela Fought, M.S., 2 Cassandra Roeca, M.D., 3 University of Colorado Anschutz Medical Campus, Aurora, CO; 4University of Colorado School of Public Health; 5University of Colorado School of Medicine, Aurora, CO.

OBJECTIVE: The relationship between anti-Mullerian hormone (AMH) and response to controlled ovarian hyperstimulation (COH) is well established, however, it is unknown whether this relationship is preserved in cancer patients. Thus, we investigated the association between ovarian response and AMH for medically indicated fertility preservation (FP) and elective oocyte cryopreservation (OC) cycles.

MATERIALS AND METHODS: Retrospective cohort study of Society for Assisted Reproductive Technology (SART) registry data including autologous OC and embryo cryopreservation banking cycles for patients undergoing medically indicated FP prior to gonadotoxic therapy (FP group) and elective OC cycles (elective OC group) from Jan 2016 - Dec 2018. Cycles for elective embryo banking, missing AMH, age > 45 years old, and missing covariates were excluded. Primary and secondary outcomes were oocyte yield at retrieval and number of oocytes cryopreserved. A negative binomial model accounted for cycle repeats and estimated associations between oocyte yield, AMH (categorically grouped into quarters from 0-1 ng/mL and then 1 ng/mL increments until AMH > 4 ng/mL) and patient groups (FP and elective OC). Models were adjusted for age, BMI, smoking status, and gonadotropin usage. RESULTS: 10,040 cycles were analyzed including 648 FP and 9392 elective OC cycles. Results were noted for the following chromosomes: Total aneuploidy with NOA vs. OA, the aneuploidy rates did not differ significantly: 116 (38.16%) in NOA vs 83 (39.71%) OA embryos (p = 0.722). Statistical significant differences in aneuploidy between NOA and OA, respectively, were noted for the following chromosomes: Total aneuploidy in chromosome 13 (4.48% vs 1.91%, p = 0.028), Trisomy 13 (2.03% vs 0.64%, p = 0.037), Total aneuploidy in chromosome 17 (4.49% vs 1.28%, p = 0.004), Trisomy 17 (1.88% vs 0.21%, p = 0.022), Total aneuploidy in chromosome 22 (10.71% vs 6.38%, p = 0.015), and Monosomy 22 (5.35% vs 2.55%, p = 0.029). No other tested chromosomes displayed statistically significant differences in aneuploidy (including sex chromosomes) when comparing NOA to OA embryos.

CONCLUSIONS: Aneuploidy rates were not different between couples with NOA vs. OA undergoing PGT-A and rates were similar to other types of infertility. Some differences in aneuploidy were identified between specific chromosomes in NOA vs. OA, but this is likely insignificant clinically.

IMPACT STATEMENT: Type of azoospermia should not impact the decision to use PGT-A in couples undergoing IVF/ICSI with surgically extracted sperm.

SUPPORT: No financial support was received for this study.

O-217 10:45 AM Wednesday, October 26, 2022

TYPES AND RATES OF EMBRYONIC ANEUPLOIDY IN MEN WITH AZOOSPERMIA. Bijan Moshedi, M.D., 1 Seifeldin Sadek, MD, 2 Samad Jahandideh, PhD, 3 Eric A. Widra, M.D., 4 Kathleen Devine, MD, 1 Nicole K. Banks, M.D., 5 Eastern Virginia Medical School, Norfolk, VA; 2Shady Grove Fertility- Jones Institute, Norfolk, VA; 3Shady Grove Fertility, Washington D.C., DC; 4SG Fertility, Washington, DC.

OBJECTIVE: To study the types and rates of embryonic aneuploidy in men with nonobstructive (NOA) vs obstructive (OA) azoospermia.

MATERIALS AND METHODS: A retrospective chart review was conducted to analyze the rates and types of chromosomal aneuploidy that occurred in embryos from men with NOA and OA. The primary outcome was aneuploidy rate. Autologous PGT-A cycles performed using surgically extracted sperm for azoospermia from 2011 – 2020 were included. Analysis of affected chromosomes were limited to chromosomes included in PGT-A utilizing both fluorescence in situ hybridization (FISH) and next generation sequencing (13, 14, 15, 16, 17, 18, 21, 22, X, Y). Data was analyzed using SPSS software (IBM, Armonk NY). Categorical variables were analyzed using Fisher’s Exact Test, Chi-Square Analysis, or Spearman’s rank correlation, depending on sample size, distribution of variable, and type of variable. A two-tailed t-test or analysis of variance to determine a relationship between two groups for continuous variables.

RESULTS: In total 456 couples (265 NOA vs 191 OA) produced 1,161 embryos (691 NOA vs 470 OA). Overall rates of aneuploidy were not different 321 (46.45%) in NOA vs 224 (47.66%) OA embryos (p = 0.731). Even after excluding patients older than 35, the aneuploidy rates did not differ significantly: 116 (38.16%) in NOA vs 83 (39.71%) OA embryos (p = 0.722). Statistically significant differences in aneuploidy between NOA and OA, respectively, were noted for the following chromosomes: Total aneuploidy in chromosome 13 (4.48% vs 1.91%, p = 0.028), Trisomy 13 (2.03% vs 0.64%, p = 0.037), Total aneuploidy in chromosome 17 (4.49% vs 1.28%, p = 0.004), Trisomy 17 (1.88% vs 0.21%, p = 0.022), Total aneuploidy in chromosome 22 (10.71% vs 6.38%, p = 0.015), and Monosomy 22 (5.35% vs 2.55%, p = 0.029). No other tested chromosomes displayed statistically significant differences in aneuploidy (including sex chromosomes) when comparing NOA to OA embryos.

CONCLUSIONS: Aneuploidy rates were not different between couples with NOA vs. OA undergoing PGT-A and rates were similar to other types of infertility. Some differences in aneuploidy were identified between specific chromosomes in NOA vs. OA, but this is likely insignificant clinically.

IMPACT STATEMENT: Type of azoospermia should not impact the decision to use PGT-A in couples undergoing IVF/ICSI with surgically extracted sperm.

SUPPORT: No financial support was received for this study.

O-218 11:00 AM Wednesday, October 26, 2022

PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY IMPROVES LIVE BIRTH RATE PER TRANSFER IN MALE FACTOR INFERTILITY. John Rushing, M.D., 1 Tracy Truong, MS, 2 Randall Meacham, M.D., 3 Judy E. Stern, PhD, 1 Alex J. Polotsky, M.D., M.S., 4 University of Colorado Anschutz Medical Campus, Aurora, CO; 1Department of Biostatistics & Bioinformatics, Duke University Medical Center, Durham, NC; 3The University of Colorado School of Medicine, Aurora, CO; 4Dartmouth Health, Lebanon, NH.

OBJECTIVE: Pre-implantation genetic testing for aneuploidy (PGT-A) is performed to select euploid embryos for transfer, but outside of advanced maternal age, no clear benefit has been established. Recent studies reveal...
higher blastocyst mosaicism and aneuploidy rates in couples with severe male factor infertility undergoing IVF. Our goal was to determine whether PGT-A is associated with improved outcomes for patients with male factor infertility (MFI).

MATERIALS AND METHODS: The SART CORS database was queried for a retrospective cohort study of couples with reported MFI undergoing autologous oocyte IVF with ICSI in 2016-2018. Exclusion criteria were women >35 years, oocyte vitrification, embryo banking, PGT for known carrier, and gestational carrier cycles. Primary outcome was live birth per transfer (LBR). Secondary outcomes were pregnancy and clinical pregnancy per transfer, spontaneous abortion (SAB), and multiple births per transfer. Generalized estimating equation models were used to estimate odds of outcome stratified by 1 vs ≥2 embryos transferred controlling for partner’s age, infertility diagnoses, and blastocyst transfer.

RESULTS: 47,301 transfers were included, of which 9,591 (20.3%) utilized and 37,710 (79.7%) did not utilize, PGT-A. Analysis per transfer demonstrated that PGT-A resulted in a higher LBR (57.3% vs 48.1%), and higher adjusted odds for LBR (aOR 1.49, 95% CI 1.41-1.58) amongst those with single embryo transfers (SET). Among all transfers, those undergoing PGT-A had fewer multiple live births (7.3% vs 16.6%) likely due to more SET in the PGT-A cohort (SET 88% vs 59.8%). SAB rates did not differ (8% vs 8.2%). There were no significant differences in LBR per transfer when comparing fresh vs thawed sperm or surgically collected vs ejaculated sperm.

CONCLUSIONS: PGT-A is associated with improved outcomes including LBR per transfer and higher prevalence of SET leading to a decreased multiple delivery rate in couples with MFI and female age <35 years.

IMPACT STATEMENT: Male factor infertility can be an indication for PGT-A.

O-219 11:15 AM Wednesday, October 26, 2022

DEVELOPMENT OF A MACHINE LEARNING APPLICATION FOR INTRAOPERATIVE OBJECT DETECTION OF POSITIVE SEMINIFEROUS TUBULES IN MICRODISSECTION TESTICULAR SPERM EXTRACTION FOR NONOBSTRUCTIVE AZOOSPERMIA. Teppei Takeshima, M.D., Ph.D., MHDsc. Yokohama City University Medical Center, Yokohama, Japan.

OBJECTIVE: Approximately 1 in 100 men in the general population have azoospermia, and 80% of them have nonobstructive azoospermia (NOA). For couples with NOA who wish for a baby, the only effective treatment options are sperm retrieval by microdissection TESE (micro-TESE) and subsequent ICSI. However, the current sperm recovery rate is generally only 30-40%. Favorable seminiferous tubules that contain sperm are generally white and thicker in diameter than other tubules, and the success of sperm retrieval is largely dependent on the surgeon’s attentiveness and observational ability. The speedy and accurate retrieval of such tubules is thought to be the key to reducing damage to the testes and minimizing complications and aftereffects.

MATERIALS AND METHODS: From captured images of intraoperative videos, favorable seminiferous tubules with confirmed sperm presence are labeled with rectangles (bounding boxes) using the object detection annotation tool, and training is performed on more than 100 images using a combination of grid cells and rectangle analysis. The model was evaluated on validation data (still images) using evaluation metrics (precision, recall, and mean average precision (mAP)), and inference was performed on intraoperative images (still images) using evaluation metrics (precision, recall, mAP), and inference was performed on intraoperative data (still images) using evaluation metrics (precision, recall, mAP).

RESULTS: The object detection model created in the current study achieved relatively high prediction performance for still images, and was also able to infer positive tubules in intraoperative videos. We intend to perform data augmentation to create a more robust model and to perform inference on real-time video movies for clinical application to assist with genotype-specific tasks.

IMPACT STATEMENT: This is the first study of to use a machine learning object detection algorithm to detect intraoperative detection of positive tubules in micro-TESE.

SUPPORT: None

O-220 11:30 AM Wednesday, October 26, 2022

CLINICAL OUTCOMES OF MICRODISSECTION TESTICULAR SPERM EXTRACTION (MICRO TESE) AND INTRACYTOPLASMIC SPERM INJECTION (ICSI) IN NON-OBSTRUCTIVE AZOOSPERMIA (NOA) WITH THE HISTORY OF CRYPTORCHIDISM. Tomomoto Ishikawa, M.D., Ph.D., Kohei Yamaguchi, M.D., Ph.D., Yasuhiro Ohara, M.D., Masakazu Doshiba, M.D., Ph.D., Hidehiko Matusubayashi, M.D., Ph.D., Takumi Takeuchi, M.D., Ph.D., Reproduction Clinic Osaka, Osaka, Japan; Reproduction Clinic Tokyo, Tokyo, Japan.

OBJECTIVE: Undescended testes (UT) is associated with impairment of germ cell maturation and subsequent infertility in adulthood. The undescended testis is exposed to a higher temperature compared with the scrotal temperature and there is progressive Leydig and Sertoli cell atrophy. There have been very few studies of ICSI with a focus on, or large enough numbers to examine, the specific outcomes associated with male factor infertility. Improvement in sperm retrieval techniques including micro TESE and micromanipulation techniques, such as ICSI, has led to excellent fertilization and pregnancy outcomes of treatment cycles. The aim of this study is to assess the prevalence and the significance including sperm retrieval rate (SRR) by micro TESE and ICSI outcomes with embryonic development in NOA couples with the history of cryptorchidism.

MATERIALS AND METHODS: We evaluated SRR of micro TESE, two pronuclei (2PN) oocyte rates, blastocyst development rates, good-quality blastocyst (Grade 3BB and above on day 5 by the Gardner scoring) rates, and clinical pregnancy rates per embryo transfer (ET) in 44 NOA cases with the history of UT, 479 cases without past history (unexplained NOA; not including after orchidopexy, Klinefelter syndrome, cryptozoospermia, mumps orchitis, etc), and 118 cases of obstructive azoospermia (OA) between September 2013 and March 2022. Chromosomal analysis was performed on all patients on cultured lymphocytes from peripheral blood. Statistical analysis was performed using unpaired t-tests and chi-squared tests.

RESULTS: SRR of first attempt micro TESE in UT (30/44=68.2%) was higher than unexplained NOA (80/335=23.9%) (p<0.05). Spermatozoa were successfully retrieved in 8 of 14 (57.1%) UT group and 18 of 144 (12.5%) unexplained NOA who had previously undergone micro TESE with no sperm found. No correlation was found between serum FSH, LH, and T level with the success of sperm retrieval. Testicular volume and patient
age at orchidopexy also did not affect the SRR for micro TESE. 2PN oocytes, blastocysts development, and good-quality blastocysts rates were 55.8%, 55.2%, and 37.5% in UT, 57.8%, 47.0%, and 39.0% in unexplained NOA, and 64.0%, 50.8%, and 42.6% in OA, respectively. Clinical pregnancy rates per ET were 37.5% in UT, 30.0% in unexplained NOA, and 42.4% in OA. Significant difference was only observed in 2PN oocytes between unexplained NOA and OA (p<0.05) and clinical pregnancy between UT and unexplained NOA (p<0.05), and OA and unexplained NOA (p>0.01).

CONCLUSIONS: Micro TESE is particularly helpful for successful sperm retrieval in UT cases, additionally, in men with UT who have undergone previous attempts with negative results, a salvage micro TESE offers a more chance of finding sperm. In UT, the sperm retrieval from testicular tissue in micro TESE is a critical key to succeed for good clinical pregnancy.

IMPACT STATEMENT: This study shows a high impact in micro TESE and ICSI outcomes with embryonic development for the non-obstructive azoospermic couples with the history of cryptorchidism.

SUPPORT: None declared.

O-221 11:45 AM Wednesday, October 26, 2022

INFLAMMASOME IS ASSOCIATED WITH IMPAIRED FERTILITY DUE TO SPINAL CORD INJURY. Kajal Khodamoradi, PhD,1 Joginder Bidhan, MSC,2 Alexandra Dullea, MS,1 Juan Pablo De Rivero Vaccari, PhD,1 Emad Ibrahim, M.D., H.C.L.D 1University of Miami Miller School of Medicine, Miami, FL; 2Desai Sethi Urology Institute, Miller School of Medicine, University of Miami, Miami, FL.

OBJECTIVE: Spinal cord injury (SCI) affects around half a million new cases worldwide and 17,900 in the US every year (1,2). It occurs most often in young men at the peak of their reproductive health, resulting in severely impaired fertility. Most men with SCI have semen with normal sperm concentrations but have severely impaired sperm motility and viability.

The aim of this study was to understand the various mechanisms by which SCI contributes to male infertility, and to study the role of the inflammasome in male infertility in a rodent model of SCI.

MATERIALS AND METHODS: In this study, Sprague Dawley adult male rats (n = 14) were randomly divided into sham controls and SCI groups (each group contained 7 rats). A model of moderate contusive thoracic SCI (T9) was used in this study. Seminal vesicle and epididymal tissues were collected. Epididymal sperm parameters were analyzed by Computer Assisted Sperm Analysis (CASA). Seminal vesicle tissues were mechanically dispersed with a homogenizer, and the total protein was extracted. Quantitative detection of caspase-1 and IL-1β was performed using western blot analysis.

RESULTS: Our study results showed a significant decrease in sperm count, motility, viability and morphology in the SCI group compared to the control group (p<0.05). Western blot analysis showed evidence of inflammasome activation, as determined by cleavage of IL-1β and increased protein levels of cleaved GSDM-D in seminal vesicles of rats that were injured and sacrificed 14 days after SCI when compared to sham animals.

CONCLUSIONS: We conclude that contusive SCI has detrimental effects on sperm parameters and seminal vesicle tissues. Moreover, our results suggest that these effects are mediated by activating inflammatory processes that are mediated in part by the inflammasome and the inflammasome-mediated program cell death process of pyroptosis.

IMPACT STATEMENT: Better understanding of the mechanisms by which SCI induces detrimental effects on the reproductive system and fertility will provide necessary information for the management and treatment of reproductive complications in this population.

SUPPORT: The work focused on sperm dysregulation was supported in part by Inherent Bioscience’s National Science Foundation The Small Business Innovation Research (SBIR) Grant No. (2034014).

ORAL ABSTRACT SESSION: MENTAL HEALTH

O-223 10:45 AM Wednesday, October 26, 2022

PSYCHOSOCIAL OUTCOMES OF CHILDREN BORN VIA EMBRYO DONATION. Salomeh M. Safari, MD MS1, Seungho Lee, BS2,3, Joshua Mangels, BS2, Judy L. Madeira, Ph.D., J.D.4, Rebecca Flyckt, MD, John D. Gordon, M.D.5, Jeffrey Keenan, MD,6, Myirng Lee, Ph.D.,7 Paul Chungyu Lin, MD,8 Guido Pennings, Ph.D.,9 Craig Sweet, M.D.,10 Kimberly Tyson, B.S.,11 Steven R. Lindheim, M.D.,11,12 Susan Klock, PhD13 University Hospitals Cleveland Medical Center Case Western Reserve University, Beachwood, OH;1 University of Central Florida College of Medicine, Orlando, CT;1 Professor of Law, Bloomington, IN;4 University Hospitals Fertility Center/Case Western Reserve University, Beachwood;5 Southeastern Fertility, Knoxville, TN;6 University of TN Medical Center; 7 University of Texas Health Science Center at Houston, TX;8 Seattle Reproductive Medicine, Seattle, WA;9 Ghent University, Belgium;10 Embryo Donation International, P.L., Fort Myers, FL;11 Snowflakes Embryo Adoption Program, Colorado Springs, CO;12 University of Central Florida College of Medicine, FL;13 Northwestern University, Chicago, IL.

OBJECTIVE: The psychosocial adjustment of children born via embryo donation (ED) has yet to be investigated. The objective of this study was to assess parents’ perception of the psychosocial adjustment of their ED children.

MATERIALS AND METHODS: 60 fertile controls were used to identify the most epigenetically stable gene promoters in sperm. A stability threshold for each promoter in the genome was calculated and the most stable promoters were defined as the top 10th percentile of promoters with the lowest stability thresholds. Phase 2 of this study analyzed the DNA methylation pattern in sperm from 1331 men trying to conceive. For each semen sample the number of dysregulated promoters were counted. We defined a dysregulated promoter as a promoter that fell above a promoter stability threshold.

RESULTS: Three classes of patients emerged in our cohort of 1331 men based on the number of dysregulated promoters: Excellent, Poor, and Average sperm quality. In a blinded analysis there was a significant difference in pregnancy and live birth rates of men undergoing IUI between men in Poor and Excellent (p=0.0009*** and Poor and Average (p=0.0072**). In an average of 2.5 IUI cycles, men with Poor sperm quality had a 15.1% live birth rate versus 43.6% live birth rate in men with Excellent sperm quality. Interestingly, when men underwent IVF; there was no significant difference in pregnancy and live birth rates (p=0.811). Also, 80.4% of men with Poor sperm quality had normal sperm concentration and total motile count (TMC), Finally we found that the addition of age and total motile count improved our algorithm. Men with Poor sperm quality and low TMC had the lowest live birth rate while men with Excellent sperm quality and normal total motile count had the highest live birth rate.

CONCLUSIONS: Here we show a statistically significant correlation between the number of dysregulated promoters in sperm and live birth rates in men undergoing IUI but not in IVF, suggesting that the lower sperm quality can be overcome with IVF. Additionally, when incorporating age and TMC with the DNA methylation biomarker, the results become more refined.

IMPACT STATEMENT: After analysis of over 1300 semen samples, we introduce the discovery of an epigenetic biomarker that is predictive of sperm quality that when combined with the semen analysis support better treatment guidance and precision fertility care.

FERTILITY & STERILITY® e91
STUDY.

EMBRYO CRYOPRESERVATION: A QUALITATIVE UNDERWENT MEDICALLY INDICATED OOCYTE OR EXPERIENCES AND INTENTIONS OF PATIENTS WHO

O-224 11:00 AM Wednesday, October 26, 2022

that they have secure attachment to and acceptance of their children. have well-adjusted parent-child relationships and reassuring child psychosocial outcomes. Our preliminary data extends donation function well in terms of parent-child relationship quality, and child perceived parental acceptance.

CONCLUSIONS: Like oocyte and sperm donation, ED has resulted in the birth of many children. Studies suggest that families created through gamete donation function well in terms of parent-child relationship quality, and child behavioral and socio-emotional adjustment. Our preliminary data extends those findings by demonstrating that families created through ED also have well-adjusted parent-child relationships and reassuring child psychosocial outcomes.

IMPACT STATEMENT: Parents who have children via ED report that their children are well adjusted behaviorally and socio-emotionally, and that they have secure attachment to and acceptance of their children.

O-224 11:00 AM Wednesday, October 26, 2022

EXPERIENCES AND INTENTIONS OF PATIENTS WHO UNDERWENT MEDICALLY INDICATED OOCYTE OR EMBRYO CRYOPRESERVATION: A QUALITATIVE STUDY. Michelle J. Bayefsky, MD,1 Amani Sampson, B.A., M.S.,2 Jennifer K. Blakemore, M.D., M.S.c.,3 Mary Elizabeth Fino, M.D.,4 Gwendolyn P. Quinn, Ph.D. 5 NYU Langone Health, New York, NY, New Jersey Medical School, East Hanover, New Jersey, NY, NYU Langone Fertility Center, New York, NY, 6 NYU Langone Preliminary Fertility Center, New York, NY, 7 New York University School of Medicine, Department of Obstetrics and Gynecology, New York, NY.

OBJECTIVE: Current data suggest that many women who have frozen oocytes or embryos for medical indications have not returned to use their cryopreserved materials. We sought to learn more about the structural and cognitive experiences of these patients, including their goals for using their frozen materials.

MATERIALS AND METHODS: We conducted 42 interviews of cisgender women who had undergone oocyte or embryo cryopreservation for medical indications at an academic fertility center. Participants were invited to interview by email if they were <40 years old when they banked for a medical reason and froze between 1/2012 and 12/2021. Interviews were conducted in 2021-2022. Verbatim transcripts were created and thematic analysis was conducted using the constant comparison method.

RESULTS: Saturation was reached at 42 interviews. The median age of participants was 35 years (range 28-43) at interview and 31 yrs (range 28-43) at freezing. Thirty had a cancer diagnosis, 7 had non-cancer chronic medical conditions, and 5 were previvors with hereditary cancer susceptibility syndromes. Twelve banked embryos and 30 banked oocytes. The majority of women indicated a desire to use their frozen materials but many were unsure about how or when, 4 already used or were using, and 2 conceived naturally (Table 1). The freezing experience was described by the majority as highly emotionally challenging because they felt out of place among couples receiving infertility treatment and overwhelmed by the complex decisions to be made in a short time period. Common reported barriers to using frozen materials included: ongoing medical issues preventing pregnancy; need for a surrogate; lack of partner; cost; and desire for natural conception. Some were glad to have frozen to allow more time to meet a partner or were considering becoming single parents. Many previvors found the option to use pre-implantation genetic testing empowering.

CONCLUSIONS: The majority of women who have undergone oocyte or embryo cryopreservation for medical reasons reported a desire to use their frozen eggs or embryos but have been impeded by ongoing medical issues, the need for a surrogate, or lack of a partner.

IMPACT STATEMENT: As the first qualitative study on the reproductive outcomes of women who have undergone oocyte or embryo freezing for medical indications, this study sheds light on these patients’ unique barriers to using their frozen reproductive materials.

Table 1: Intentions regarding stored material

<table>
<thead>
<tr>
<th>Intentions</th>
<th>Number of Participants (%)</th>
</tr>
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<tbody>
<tr>
<td>Already used/using</td>
<td>4 (9.5%)</td>
</tr>
<tr>
<td>Plan to use in 1-4y</td>
<td>22 (52.4%)</td>
</tr>
<tr>
<td>Plan to use in 5-10y</td>
<td>8 (19.0%)</td>
</tr>
<tr>
<td>Plan to use in 10-20y</td>
<td>2 (4.8%)</td>
</tr>
<tr>
<td>Plan to donate to another person</td>
<td>2 (4.8%)</td>
</tr>
<tr>
<td>Plan to donate to research</td>
<td>5 (11.9%)</td>
</tr>
<tr>
<td>Unsure of plans</td>
<td>17 (40.5%)</td>
</tr>
<tr>
<td>Do not plan to use</td>
<td>2 (4.8%)</td>
</tr>
<tr>
<td>Other plans to use</td>
<td>5 (11.9%)</td>
</tr>
</tbody>
</table>

O-225 11:15 AM Wednesday, October 26, 2022

PSYCHOLOGICAL STRESS AND INFERTILITY: WHAT DO WOMEN IN MEDICINE BELIEVE? Jennifer B. Bakkensen, MD, Karishma Desai, BA, Eve C. Feinberg, MD, Angela K. Lawson, Ph.D. Northwestern University Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: Despite no rigorous research demonstrating a causal role of stress in infertility, those who struggle to conceive may experience self-blame due to a belief that stress causes infertility. This belief is important to understand among female physicians given their risk of infertility and their role in educating patients about causes of infertility. This study assesses the prevalence of and factors associated with this belief among female physicians.

MATERIALS AND METHODS: An electronic survey was distributed to female physicians via social media from March-April 2022. Demographic information and Likert-scale responses related to beliefs about psychological stress as a cause of infertility, pregnancy loss, poor pregnancy outcomes, and decreased fertility treatment success were collected. The association of demographic factors and the belief that stress causes each outcome was assessed using Chi square analysis.

RESULTS: A total of 741 female physicians completed the survey (mean age = 38.8 years, SD = 7.69). The most common specialties were obstetrics and gynecology (OB/GYN, 29.7%) and Internal Medicine (12.6%). Time since completion of training was 0-8 yrs (35.4%), 9-14 yrs (30.5%), and ≥15 yrs (29.0%). Most respondents were heterosexual (n = 670, 90.4%), married/partnered (n = 632, 85.3%), and had children (n = 496, 66.9%). A third (38%) had experienced infertility, 54.9% of whom used IVF to conceive.

Overall, 93.2% believed that psychological stress causes infertility at least “a little.” Similarly, 85.1%, 96.5%, and 94.7% believed that stress causes pregnancy loss, poor pregnancy outcomes, and decreased fertility treatment success, respectively. Women who experienced infertility were more likely to believe that stress causes infertility “a lot” (61.7% vs. 38.3%, p < .05). Women with 15+ yrs of training (15.5%) were less likely than women 0-8 yrs (43.2%) or 9-14 yrs (41.3%) out to believe that stress played a moderate role in poor pregnancy outcomes (p < .01). Having a child (77.4%) vs. no children (21.9%) was associated with the belief that stress has a moderate role in infertility (p < .05). OB/GYNs were less likely than those from other specialties combined to believe that psychological stress caused infertility, pregnancy loss, poor pregnancy outcomes, and decreased fertility treatment success “a lot” (p < .01). However, the majority of OB/GYNs believed stressed play at least a small role in each of the aforementioned reproductive experiences.

CONCLUSIONS: The belief that stress causes infertility and adverse pregnancy outcomes is prevalent among female physicians, particularly among those who have personally experienced infertility and have rarely observed it in their patients.
completed training. Although OB/GYNs appear less likely to harbor these beliefs, the high endorsement of stress as a causal role in reproductive experiences indicates the need for additional education about stress and fertility in medical training.

IMPACT STATEMENT: The majority of female physicians believe that stress causes infertility, which may cause unnecessary self-blame and emotional distress among physicians struggling to conceive.

SUPPORT: None

O-226 11:30 AM Wednesday, October 26, 2022

THE LIVED EXPERIENCE OF RECURRENT PREGNANCY LOSS ASSESSED BY PHOTO-ELICITATION INTERVIEW. Robyn K. Power, MD,1 Megan Hanson, B.S., M.B.A.,2 Amy Henderson Riley, DrPH,3 LaiQuannah Hason, BS, MA,4 Laura Sliifer, MPH,5 Bridget Huepfel, BA,6 Dana B. McQueen, M.D., M.A.S.1 1The University of Chicago, Chicago, IL; 2Recurrent Pregnancy Loss Association, Seattle, WA; 3Thomas Jefferson University; 4Reproductive Medicine Associates of New York, New York.

OBJECTIVE: The purpose of this study is to explore the lived patient experience of recurrent pregnancy loss (RPL) through qualitative interviews. Our aim is to understand the emotional impact of RPL and inform interventions to improve the patient experience.

MATERIALS AND METHODS: Institutional Review Board approval was obtained. Participants were recruited through patient advocate organizations via email list, social platforms, and snowball sampling. Guided by the photo-elicitation technique—a qualitative research approach developed in 1957—eligible participants were asked to submit five photos that would help them to explain their experience of miscarriage. Sixty minute interviews were then conducted through Zoom platform, with investigators using participants’ portfolios of images as an elicitation tool and stimulus to drive conversation. All interviews were audio recorded and transcribed verbatim. Interview transcripts were then analyzed to develop codes and group comparable text passages from different participants. Analysis involved a modified template approach, whereby coding was guided by an initial codebook that was modified in the process of data review via multiple coders from multidisciplinary backgrounds and using NVivo software. Codes were generated both deductively and inductively in order to capture all relevant themes and messages. Intercoder reliability was calculated to ensure coding accuracy and agreement.

RESULTS: There are a total of 22 study participants with a mean age of 34 and a mean of 3.8 previous pregnancy losses. The interviews and pictures identified important stressors women with RPL experience, namely mental health needs, fear, isolation, obsession, guilt, resentment, and jealousy. Interviews also highlighted key support structures (obstetricians, fertility specialists, emergency providers, ultrasonographers) that at times acted to both alleviate and enhance the burden of grief and overall experience. For example, one participant said, “I love my fertility doctor... she is my partner,” while others suggested areas for improvement, e.g., “the doctors need to understand that there is more to miscarriages than just the physical symptoms.”

CONCLUSIONS: RPL can be a complex experience that causes significant and lasting effects on the mental and physical health of people trying to conceive. There is currently a lack of adequate structure and support services to address the emotional burden. These findings demonstrate areas for improvement within current models of care and highlight action items to improve the patient experience in the future.

IMPACT STATEMENT: Patient-centered care is an increasingly important objective for many health systems, but it requires an understanding of the feelings, needs, and priorities of patients. Data describing the specific experience of RPL are limited. Thus, we need a more thorough understanding of the factors that shape patient experience to identify supportive interventions.

CONCLUSIONS: These data suggest that individuals who become first-time parents at or after age 40 do not report greater parental stress or lower social support relative to younger parents. However, they report a number of factors that delayed their start of parenting and believe that the optimal age to become a parent was 29.8 (SD = 4.3). P40s reported thinking about being around for their children’s life milestones (e.g. graduation, marriage, grandchild) less often than P30s or P20s, but reported more frequent concern about their children’s well-being. Children of P40s were on average six years old and twenty percent of them expressed worry “occasionally” about their parents’ lifespan. Partner factors (e.g. divorce, not having a partner, not being with the “right” partner, partner reluctance to have children) was a central theme in participants’ qualitative responses regarding reasons for delaying parenting.

CONCLUSIONS: Patient - centered care is an increasingly important object for many health systems, but it requires an understanding of the feelings, needs, and priorities of patients. Data describing the specific experience of RPL are limited. Thus, we need a more thorough understanding of the factors that shape patient experience to identify supportive interventions.
OBJECTIVE: At our institution, cryopreserved embryos remain in onsite storage for up to three years, after which point patients are given the option to transfer embryos to an offsite storage facility, donate them to research, or discard them. This study aimed to assess factors influencing patient decision-making regarding embryo disposition, primarily the use of preimplantation genetic testing (PGT) and donor gametes, and secondarily household income. It was hypothesized that patients using PGT or donor gametes will be more likely to maintain embryos in storage.

MATERIALS AND METHODS: A cross-sectional survey was sent to patients who had undergone an in vitro fertilization cycle in the preceding three years (1/2018 - 3/2021) with cryopreserved embryos in onsite storage. Untested embryos of sufficient quality from non-PGT cycles were considered usable and cryopreserved. Embryos from PGT-A, PGT-M and PGT-SR cycles were considered usable and cryopreserved only if eligible for transfer (euploid, unaffected or balanced, respectively). Logistic regression was used to model associations between disposition plan and use of PGT, donor gametes and household income.

RESULTS: Of the 1,496 eligible patients, 646 completed the survey for a 43% response rate. Median age was 35.0 years, 80% identified as White, 4% as Black/African American and 10% as Asian. Only 5% identified as Hispanic. Most subjects (88%) reported a household income >$100,000 per year. Donor gametes were used by 11% and 32% used PGT. Of those with usable embryos (n=584), 63% planned to keep embryos in storage, 7% planned to donate them to research, 2% planned to discard and 20% were unsure. Use of PGT was not associated with the decision to keep embryos in storage [63.6% vs 60.6%; RR 1.02 (0.89-1.16)], nor was the use of donor gametes [65.4% vs 52.2%; RR 0.80 (0.63 – 1.01)]. However, use of donor gametes was significantly associated with being unsure of disposition plan [RR 1.53 (1.02 - 2.31)]. Conversely, of those with unusable embryos identified via PGT (n=131), only 6% planned to keep embryos in storage, while 44% planned to donate them to research, 21% planned to discard and 28% were unsure. Household income <$100,000 vs ≥ $100,000 was not associated with the decision to keep embryos in storage [65.7% vs 63.5%; RR 0.97 (0.80-1.16)]. Of all respondents who plan to keep embryos in storage, 36% reported they will store them “for the foreseeable future.”

CONCLUSIONS: Most patients plan to keep usable embryos in storage, regardless of use of PGT or donor gametes. However, uncertainty towards embryo disposition is commonly reported, particularly among patients using donor gametes. Patients with unusable embryos identified via PGT were less likely to donate those embryos, suggesting a role for PGT in the decision-making process.

ORAL ABSTRACT SESSION: PATIENT EDUCATION AND SUPPORT/NURSING

O-229 10:45 AM Wednesday, October 26, 2022
THE INFLUENCE OF PATIENT EDUCATION LEVEL, PREGNANCY/BREASTFEEDING, AND INFERTILITY TREATMENT ON PERCEPTIONS OF THE COVID-19 VACCINE: A MIXED METHODS STUDY. David Joseph Eggert, DO.1 Cassandra Roxane Krier, Medical Student.1 Kate D. Schoyer, MD.2 Kristina Kaljo, PhD.1 Stephanie Gunderson, M.D.2 Medical College of Wisconsin, Wauwatosa, WI; 2Medical College of Wisconsin, Milwaukee, WI.

OBJECTIVE: To elucidate fertile patient perceptions of the novel COVID-19 vaccine as it pertained to fertility treatments and future pregnancies.

MATERIALS AND METHODS: This was an IRB approved, single center mixed methods survey study. A 60-question survey was administered assessing patient perceptions regarding the novel COVID-19 vaccine as it pertained to their fertility care and future fertility treatment. The survey was offered to a total of 760 patients undergoing fertility evaluation and treatment, 192 responded (25% response rate). Fischer exact or McNemar exact tests were performed depending on quantitative data distribution. Responses to the open-ended questions were analyzed using inductive content analysis to generate qualitative themes.

RESULTS: Quantitative: Of the 192 respondents most were white females, holding private insurance, with a college degree. Participant willingness to accept the COVID-19 vaccine was analyzed in conjunction with various demographic variables to determine trends between these variables and vaccine acceptance. Respondents’ age, marital status, income level and insurance status did not correlate with perceived willingness to accept the COVID-19 vaccine. However, respondents who reported having a college education were more likely to consider the COVID-19 vaccine when it became available to them (No Degree= 5/16 (31.3%), College Degree= 76/104 (73.1%), Post-graduate Degree= 57/67 (85.1%), N=187, P<0.001). When asked if pregnancy or breastfeeding impacted respondents’ willingness to consider the COVID-19 vaccine 79 (43.9%) responded yes, while 101 (56.1%) responded no or unsure. When participants’ responses were stratified by the number of previous completed fertility treatments (either embryo transfers or intrauterine inseminations), there was a statistically significant trend of increasing willingness to receive the COVID-19 vaccine during a pregnancy or while breastfeeding (1 Treatment= 53/135 (39.2%), 2 treatments= 19/37 (51.3%), 3 treatments= 66/100(60%), N=180).

Qualitative themes included participants’: fear of the unknown due to existing perceptions, beliefs, and mistrust; interpretations of medical knowledge and self-generated benefit-risk assessments, and desire for provider guidance and mindful communication.

CONCLUSIONS: This study suggests that despite identified hesitancy of the COVID-19 vaccine, patients with higher levels of education and those who completed >2 infertility treatments were more willing to consider the COVID-19 vaccine, even with pregnancy or breastfeeding in mind. Patients unwilling to receive the vaccine reported mistrust in healthcare, lack of communication with providers, and medical misunderstanding while formulating benefit-risk assessments.

IMPACT STATEMENT: This study highlights the ongoing hesitancies regarding COVID-19 vaccination in patients seeking infertility evaluation and those undergoing treatment. Higher quality patient-provider communication is essential for infertility patients with a less than a college degree and for patients in the early stages of their fertility journey.

O-230 11:00 AM Wednesday, October 26, 2022
WHO ARE THE PATIENTS’ OPINIONS CONCERNING THE USE OF “ADD-ONS” ON REPRODUCTIVE MEDICINE? A SURVEY OF IVF PATIENTS. Daniela Braga, PhD.1 Amanda Souza Setti, MSc.1 Mauro Bibancos De Rose, PhD.2 Assumpto Iaconelli, Jr., MD.3 Edson Borges, Jr., PhD3 1Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil; 2Fertility Medical Group, Sao Paulo, Brazil.

OBJECTIVE: In vitro fertilization (IVF) ‘add-ons’ are adjunct treatments used in addition to standard IVF protocols, in attempts to improve success rates. However, the benefits of add-ons are often not supported by high-quality evidence. Despite that, many infertile patients are willing to try anything that might help them improve their chances of having a baby. Therefore, the use of add-ons has been widespread, leading to extensive debate and discussion. The goal for the present study was to evaluate the intention to use add-ons to increase the chance of success, among infertile patients, who have already started or will start an IVF treatment.

MATERIALS AND METHODS: This online-platform survey was performed in a private university-affiliated IVF center from October 2021 to January 2022. Female participants were invited via WhatsApp and e-mail, with a cover-letter outlining the survey and a link to access. Six hundred and twenty participants were split into two groups: those who have yet to start their treatments (n=160) or those who have already started it (n=460). Information on demographic data were collected. In addition, women were asked if they would accept to try add-ons therapies, despite there being no clinical evidence supporting its efficiency, and if yes, they were asked when: ‘‘from the beginning of the treatment, or only if they had negative results with the purely conventional technique before’’. Generalized linear models followed by Bonferroni post hoc test were used to compare the answers between groups.
RESULTS: Mean age was 38.5 ± 5.5 years-old (median: 39.0 years-old). There was no significant correlation between patients age and their intention to use add-ons (OR, 0.988; C.I.: 0.933 – 1.047, p=0.688). Most patients (93.5%) stated they would try some add-ons to increase their chances of success, even with no scientific evidence. Among them, the most of the time they would try it on the beginning of the treatment (76.5%), while 23.5% of the patients would try it only if they had a negative result before. When the answers of patients who are yet to start their treatments were compared with those who have already started the treatment, we observed that those who are already involved in the treatment process are more willing to try something else when compared with those who have not yet started their treatments (97.6% vs 84.1%, p<0.001).

CONCLUSIONS: Add-on treatments are well accepted by most infertile patients, especially those who have already started their IVF treatments.

IMPACT STATEMENT: Add-on have generated much discussion in the last decade. A particular concern is that there are no scientific evidence supporting the efficacy of most add-ons and whether an add-on causes unanticipated harms or worsens treatment outcomes. There is a need for transparent information about interventions for IVF patients, a vulnerable population, including uncertainties and risks, to support their decisions regarding the use of certain adjunctive therapies.

SUPPORT: N/A

O-232 11:30 AM Wednesday, October 26, 2022
THE EFFECT OF MEDIA AIDS IN GENETIC CARRIER SCREENING EDUCATION AMONG INFERTILITY PATIENTS. Megan R. Sax, MD,1 Crystal Dupont, M.D.,2 M.S.2 Anthony Leonard, PhD,2 Kurt R. Peterson, DO,1 Suruchi Thakore, MD,3 University of Cincinnati Medical Center, West Chester, OH;2 University of Cincinnati College of Medicine, Cincinnati, OH;3University of Cincinnati, Cincinnati, OH.

OBJECTIVE: To evaluate the effect of educational videos on the utilization of preconception genetic carrier screening in infertility patients.

MATERIALS AND METHODS: From November 2021 through February 2022, patients presenting for infertility consult at the University of Cincinnati Center for Reproductive Health were randomly assigned to the video arm or in-person counseling arm for education on preconception genetic carrier screening. The video arm consisted of five 2-3 minute videos within the patient education web application EngagedMD, while in-person counseling was completed by providers at the time of appointment. Surveys were completed by all patients and providers at the end of the appointment.

Chi square, Fisher's exact test, and Wilcoxon tests were used to compare the video vs in-person counseling study arms with the primary outcome being completion of genetic carrier screening. Groups were compared on experience and interpretation of counseling. Finally, logistic regression was used to adjust for the clinic attended by the patient. The study alpha was a two-tailed p = 0.05, unadjusted for multiple tests, and all analyses were conducted using SAS software.

RESULTS: A total of 73 patients were enrolled: 42 in the video arm and 31 in the in-person counseling arm. Patients who completed video counseling prior to their new patient appointment were significantly more likely to proceed with genetic carrier screening (78.6%) than were those receiving only counseling in the office (41.9%), p-value 0.003. The survey response rate was 100% for patients and providers. The positive effect of the educational videos was maintained when adjusted for clinic (p=0.003).

Patients who completed EngagedMD videos were perceived to have a better understanding of the purpose of genetic carrier screening as evidenced by the “teach-back” method (p=0.07). Providers noted a significantly decreased demand on counseling time when videos were used (p <0.001).

Of the patients not enrolled (n=190) due to exclusion criteria, only 16.8% (n=32) completed genetic carrier screening.

CONCLUSIONS: The use of patient education videos increases utilization of preconception genetic carrier screening and is an acceptable alternative to in-person provider counseling for patients and providers.

IMPACT STATEMENT: Counseling regarding preconception genetic carrier screening is strongly recommended by many women’s health organizations. Patient education videos are not inferior to provider counseling and do not compromise patient and provider satisfaction. Educational videos viewed prior to new patient appointments will allow more time for directed counseling.

O-233 11:45 AM Wednesday, October 26, 2022
OBSTETRIC OUTCOMES OF FERTILITY PATIENTS WITH PELVIC PAIN DISORDERS. Samantha Lauren Estvez, M.D.,1 Caroline Gellman, MD,2 Atossa Ghofranian, MD,3 Tamar Alkon-Meadows, MD,4 Carlos Hernandez-Nieto, MD,4 Dmitry Gounko, B.S., M.A.,1 Joseph A. Lee, BA,1 Jenna Friedenthal, MD,2 Alan B. Copperman, MD3 Icahn School of Medicine at Mount Sinai, New York, NY;2Reproductive Medicine Associates of New York, New York, NY.
OBJECTIVE: Previous research has shown vaginismus to be an independent risk factor for cesarean delivery (CD). CD is associated with increased maternal and neonatal morbidity compared with vaginal deliveries; despite this, the rate of CD continues to rise. The American College of Obstetricians and Gynecologists' (ACOG) consensus statement of 2010 and subsequently updated in 2018 recommend a VCU/TE biopsy for a higher rate of CD compared with controls (59.8% vs. 49.2% p = 0.003). Patients with a history of PPD had a higher rate of CD compared with controls (3.4 vs 3.2 vs. 12.0, CI 95%; 1.06-2.02). Patients in the PPD group had significantly higher diagnosis of anxiety disorders (115±21.9 vs. 55±31.6, p< 0.009) and use of anxiolytics (17±3.2 vs. 12±6.9, p< 0.03) as compared to controls. The prevalence of chronic hypertension was significantly higher in patients with PPD (6±3.4 vs 5±1.0, p<0.02). Patients with a history of PPD had a higher rate of CD compared with controls (59.8% vs. 49.2% p=0.01). Additionally, after adjusting for age, BMI, AMH, duration of infertility, and fertility diagnosis, there was a significant association between having a diagnosis of PPD and increased odds of having a CD (aOR= 1.5, CI 95%; 1.06-2.20).

CONCLUSIONS: Patients with PPDs have significantly greater odds of CD, higher rates of anxiety disorders, and increased use of anxiolytics compared to patients without a history of pelvic pain.

IMPACT STATEMENT: REIs could serve as a point of intervention and referral for patients with PPDs. Pelvic physical therapy, emotional support, and mode of delivery in women with vaginismus or localised provoked pain disorders (PPDs).

MATERIALS AND METHODS: The study included all nulliparous patients undergoing assisted reproductive technology (ART) treatment at a single academic fertility center who had a live birth from 2012-2020. Cases included all patients diagnosed with PPDs. A 3:1 ratio propensity score matched population of patients without PPDs was included as a control group. Patients were matched by age, body mass index (BMI), and anti-Müllerian hormone (AMH). Baseline demographics were collected and included age, BMI, marital status, duration of infertility, AMH, history of anxiety disorders, use of anxiolytics, and obstetrical outcomes. Exclusion criteria were pregnancy outside of treatment, fibroids, Müllerian anomalies, and prior uterine surgery. Comparative statistics were performed using chi-square and students t-test where appropriate. A multivariate regression analysis was conducted to evaluate the association between PPDs and mode of delivery. A total sample size of 170 patients per group was calculated in order to detect a 15% difference is CD rates with an 80% power (α=0.05).

RESULTS: 174 patients who reported a history of a PPD were compared to 575 controls. Demographic characteristics were comparable among groups. Significant differences were found in the duration of infertility among groups with PPD patients reporting a longer duration of infertility (18.9±2.0 vs 14.0±1.4 vs p = 0.003). Patients in the PPD group had significantly higher diagnosis of anxiety disorders (115±21.9 vs. 55±31.6, p< 0.009) and use of anxiolytics (17±3.2 vs. 12±6.9, p< 0.03) as compared to controls. The prevalence of chronic hypertension was significantly higher in patients with PPD (6±3.4 vs 5±1.0, p<0.02). Patients with a history of PPD had a higher rate of CD compared with controls (59.8% vs. 49.2% p=0.01). Additionally, after adjusting for age, BMI, AMH, duration of infertility, and fertility diagnosis, there was a significant association between having a diagnosis of PPD and increased odds of having a CD (aOR= 1.5, CI 95%; 1.06-2.20).

CONCLUSIONS: Patients with PPDs have significantly greater odds of CD, higher rates of anxiety disorders, and increased use of anxiolytics compared to patients without a history of pelvic pain.

ORAL ABSTRACT SESSION: PREIMPLANTATION GENETIC TESTING 2

O-234 12:00 PM Wednesday, October 26, 2022

PATIENT OPINION SURVEY ON POSITIVE AND NEGATIVE ASPECTS OF TELEMEDICINE. Marcela Cullere, PhD, Marcelo Herran, Sr, BAcc, Cesar Sanchez Sarmiento, PhD 1. NASCENTIS. ESPECIALISTAS EN FERTILIDAD Y GENETICA REPRODUCTIVA, Argentina; 2. NASCENTIS. ESPECIALISTAS EN FERTILIDAD Y GENETICA REPRODUCTIVA, CORDOBA, Argentina.

OBJECTIVE: The COVID-19 pandemic completely changed health care protocols. During the strict quarantine stage, telemedicine became the preferred strategy for doctors and patients to solve routine controls and consultations. Currently the pandemic is ending, some countries have declared COVID-19 endemic, and the time has come to make decisions regarding the continuity of this communication system between doctors and patients. We aimed to determine the assessment made by Argentine patients about telemedicine, to analyze which are the factors that justify their preference and to inquire about their motivation to continue using it.

MATERIALS AND METHODS: A mixed-type questionnaire of 17 questions was designed (segmentation and questions about preferences of use, reasons why they use/do not use the tool, predisposition to continue using it) that was distributed to different sectors of society through social networks. The survey was answered by people of both sexes over 16 years of age from 17 provinces of Argentina. All responses were collected using the SurveyMonkey platform and analyzed using calculation programs and statistical tools (Excel, Statistica 8.0) and the results processed using graphic programs (Excel, Power Point, Sigma Plot).

RESULTS: A total of 491 responses were obtained, 77.39% were women, mostly between 21 and 40 years old (49.49%). 59.27% stated that they had used telemedicine during the pandemic, valuing the experience on average 4/5. Those who evaluated the experience as positive, indicated that the main advantage was comfort (78.6%), followed by the greater speed in obtaining the consultation (49.0%) and the low impact on their economy (40.4%). When the experience was negative, the major factors were discomfort during the consultation due to the video call (37.04%), doctor’s lack of punctuality (37.40%) and the general feeling that being present improves the quality of care (27.32%). Of all those surveyed, 83.51% stated that they would like telemedicine to be permanently installed.

CONCLUSIONS: In general, the majority of patients value the telemedicine experience as positive and consider that it would be useful to maintain it over time as a definitive alternative for medical consultations. These results are useful for designing an attention care strategy in health institutions, considering the preferences of patients to achieve better care and communication with them.

IMPACT STATEMENT: Considering the patient experience is important to ensure the highest possible quality of care provided in health institutions.
NF-κB was identified in this study has been reported to play a role in activating genes discovered in this analysis. The SHARPIN E3 ubiquitin ligase that increased expression in blastocoel fluid-conditioned media (from euploid blastocysts) from advanced maternal age patients compared to younger patients.

Additionally, this study identified BCL2-Like 12 which is known to be part of the linear ubiquitin chain assembly complex (LUBAC). This gene is associated with increased expression of the anti-apoptotic gene BCL2-Like 12. Taken together, these findings suggest that inhibition of apoptosis may be taking place during preimplantation embryo development, and this anti-apoptotic activity is enhanced in embryos from advanced maternal age patients.

OBJECTIVE: This retrospective study assessed gene expression using RNA-Seq of blastocoeel fluid-conditioned media from euploid ICSI-generated embryos to identify genes associated with advanced maternal age patients.

MATERIALS AND METHODS: Blastocoel fluid-conditioned media was obtained following biopsy (ploidy status via NextGen sequencing) of ICSI-generated day-5 blastocysts. Media samples selected for RNASeq were from 24 euploid blastocysts where 9 were from patients age 35 or older. RNA was extracted (Zymo Quick-RNA Microprep Kit) and libraries prepared (Takara Bio SMART-Seq Stranded Kit). Following Illumina NextSeq500 sequencing, sequences were aligned to the human genome, reads counted and gene expression determined (~50 million reads). After quality control, the total gene count was 24,347. DESeq2 was used to test for differential gene expression. Raw read counts were normalized across all samples. Wald test statistic was used to compare between age groups. Adjusted false-discovery rate (FDR) p-value < .05 were considered as statistically significant for the differential expressed genes. Normalized counts were further used in Gene set enrichment analysis (GSEA) and KEGG pathway analyses for functional annotation.

RESULTS: This study identified 21 genes in blastocoeel fluid-conditioned media (from euploid blastocysts) from advanced maternal age patients with a statistically significant increase (p<0.05) in expression compared to conditioned media from patients under age 35. Genes identified included those that encode ubiquitin ligases. One of these ubiquitin ligases is SHARPIN, which is known to be part of the linear ubiquitin chain assembly complex (LUBAC). Additionally, this study identified BCL2-Like 12 which is an anti-apoptotic gene that is known to inhibit caspases responsible for apoptosis.

CONCLUSIONS: This study uncovered a group of genes that exhibit increased expression in blastocoeel fluid-conditioned media (from euploid blastocysts) from advanced maternal age patients compared to younger patients. Ubiquitin ligases and genes associated with apoptosis were among those identified. There is a potential mechanistic link between at least two genes discovered in this analysis. The SHARPIN E3 ubiquitin ligase that was identified in this study has been reported to play a role in activating NF-κB to increase expression of anti-apoptotic genes. This study revealed increased expression of the anti-apoptotic gene BCL2-Like 12. Taken together, these findings suggest that inhibition of apoptosis may be taking place during preimplantation embryo development, and this anti-apoptotic activity is enhanced in embryos from advanced maternal age patients.

Further study is needed to determine if this enhancement in anti-apoptotic activity is associated with unsuccessful implantation outcomes.

IMPACT STATEMENT: Uncovering specific gene expression patterns in blastocoeel fluid-conditioned media obtained from euploid embryos that are associated with patients of advanced maternal age provides insight into the molecular events that may be altered or adjusted as patients age.

SUPPORT: Prisma Health Transformative Research Seed Grant.

THE IMPORTANCE OF RETROSPECTIVE DATA ANALYSIS IN GENETIC COUNSELLING FOR PGT-SR – MATERNAL AGE IS MORE SIGNIFICANT THAN REARRANGEMENT TYPE. Colleen A. Lynch, BSc MSc PhD,1 2 Olivia Whiting, BSc MSc,3 Jennifer Sloan, B.SC., M.S.C.,4 Elizabeth Cameron, M.S.,5 Leoni Xanthopoulou, Ph.D.,4 Tony Gordon, PhD,4 Darren K. Griffin, DSc4 CooperSurgical Fertility Solutions;1 University of Kent;2 University of Kent, Canterbury, United Kingdom;3 CooperSurgical;4 CooperSurgical, Trumbull, CT;5 London, United Kingdom;6 COOPERGENOMICS, London, United Kingdom.

OBJECTIVE: Analysis of real-life clinical data to build a robust guide for genetic counselling of PGT-SR patients, including information on the availability of embryos for transfer and cycle outcomes.

MATERIALS AND METHODS: Between April 2015 and December 2021, 2831 trophoderm samples underwent PGT-SR via next generation sequencing (24 chromosome analysis). Karyotypes were reviewed prior to case acceptance to confirm all imbalances were within the resolution of the test, with a minimum size of detection of 5MB. Cases with smaller imbalances required in-house confirmation of detection of the imbalance in DNA of an affected individual. Embryos were classified according to the rearrangement (balanced/unbalanced) and according to chromosomes not involved in the rearrangement (euploid/aneuploid/mosaic). Data from the different types of chromosome rearrangement were compared and results were analysed by sex of the carrier, maternal age and day of biopsy. Incidental aneuploidy (chromosomes not involved in the rearrangement) and mosaicism were examined for evidence of interchromosomal effect. Cycles with at least one embryo available for transfer was calculated in each group and sub-group. The two-tailed Fisher’s exact test was used for statistical analysis. IVF centres were contacted to provide cycle outcome data.

RESULTS: Data was collated for 1814 trophoderm samples. The proportion of Euploid/Balanced samples for reciprocal translocations was significantly lower than the Robertsonians (p<0.0001) and inversions (p=0.0219), correlating to Robertsonians having a significantly higher chance of having at least one embryo available for transfer (p=0.0225). However, advanced maternal age (≥37yrs) was shown to have a more significant impact on the availability of embryos for transfer in the reciprocal group (p<0.0001) and Robertsonian group (p=0.0031). The sex of the carrier of the rearrangement only impacted the Robertsonian group, producing more unbalanced embryos from maternal carriers, but not impacting the overall proportion of cycles with embryos for transfer. Increasing maternal age increased the rate of incidental aneuploidy and reduced the proportion of cycles with embryos for transfer across all groups. Day of biopsy did not appear to impact on cycles and no evidence of interchromosomal effect or unparental disomy was observed. Data collection on the remaining 1017 samples continues, and outcome data is awaited from participating clinics.

CONCLUSIONS: Despite many publications on chromosome rearrangements focussing on the type of rearrangement and expected segregation patterns, analysis of real-life clinical data demonstrates maternal age to be the most significant factor in PGT-SR treatment cycles. This data has increased the ability and confidence of our genetic counselling team to provide patient and cycle specific information. In turn, the genetic counselling team perceives increased confidence from patients in real-life clinical data.

IMPACT STATEMENT: Maternal age is more significant than the type of chromosome rearrangement in PGT-SR cycles.
MATERIALS AND METHODS: Prior to running cases, genes and mutations associated with one or more monogenic disorders were confirmed by externally provided mutation reports at the time of patient enrolment. Valid mutation reports confirmed both the mutation status of parent(s) and associated segregation in the proband(S). Clinical cases with no such reports were excluded. This retrospective study includes clinical cases for PGT-M by Karyomapping between 2014 and 2021 at three CooperSurgical laboratories in New Jersey, Michigan, and London. In cases with applicable mutations (point mutations, small mutations) direct mutation analysis using Sanger sequencing was also performed concurrently. PGT-M cycles subsequently run between 2015-2021 from case preparations were included for analysis of the accuracy of Karyomapping.

RESULTS: A total of 8615 cases confirmed by pre-case work up as suitable for Karyomapping were retrospectively analysed. This included 912 unique disorders; 197 cases required preparation for more than one monogenic disorder and 15 cases were excluded due to absence of mutation reports. A total of 4082 unique, direct mutations were identified in affected parents, with 73% of cases eligible for direct mutation analysis of embryos (n=6361), either exclusively or in addition to linkage analysis. Linkage analysis alone was required for 2314 case preparations intending to test for expansion disorders, microdeletions, microduplications, translocations and HLA matching. A single nucleotide change was the most common mutation identified (n=2912) followed by deletions (n=812), duplications (n=234), insertions (n=65) and indels (n=59) respectively. The 8615 PGT-M cases resulted in 14,606 cycles of PGT-M by Karyomapping between 2015 and 2021. Karyomapping gave an accurate diagnosis of the disease status of the embryo in 100% of cases, as reported to the reference laboratory.

CONCLUSIONS: Karyomapping is a highly accurate methodology for PGT-M, applicable to all 912 monogenic disorders tested; it also could expand into chromosome disorders. By performing comparative analysis with the “gold standards” of direct mutation analysis and linkage analysis, we demonstrate its veracity in all cases tested. The inherent advantages of its universality, manifested in a near eliminated work up time compared to older methods (typically 4 to 8 weeks in CooperSurgical laboratories but up to one year elsewhere) make it a far more attractive option for patients.

IMPACT STATEMENT: As a result of this study, the largest reported so far, we are confident of informing patients that Karyomapping is at least 99% accurate for PGT-M and, with work-up times near eliminated, it represents a far less stressful and timely experience for patients seeking PGT-M.

O-240 12:00 PM Wednesday, October 26, 2022

UPDATE ON THE INTERNATIONAL REGISTRY OF MOSAIC EMBRYO TRANSFERS. Manuel Viotto, PhD
Zouves Foundation for Reproductive Medicine.

OBJECTIVE: To understand the potential and risks associated with mosaic embryo transfers by analyzing a large body of data composed of PGT-A results and associated clinical outcomes.

MATERIALS AND METHODS: Numerous participating clinics and centers contributed data on clinical outcomes of mosaic embryo transfers (n=1,741) and a control group of euploid embryo transfers (n=11,691). The assembled registry was analyzed and differences were evaluated statistically by t-test or chi square test.

RESULTS: Embryos classified as ‘mosaic’ by NGS-based PGT-A under PGDIS guidelines have decreased likelihood of achieving implantation compared to euploid embryos (46.7% vs. 56.4%; p<0.05), as well as ongoing pregnancy/live birth (36.8% vs. 49.8%; p<0.05 ). Conversely, mosaic embryos have a higher risk of spontaneous abortions (24.7% vs. 9.0%; p<0.05). Features of mosaicism detected with PGT-A dictate the success rate of mosaic embryo transfers, with ‘low’ mosaicins performing better than ‘high’ mosaicins, and ‘segmental’ mosaicins being preferable over mosaicins involving whole chromosomes. On average, babies born from mosaic embryo transfers are indistinguishable from babies from euploid embryos (n=415 matched newborn pairs), judging by weight at birth (6lb 9oz vs. 7lb 12oz; p=n.s.), length of gestation (38w1d vs. 38w2d; p=n.s.), and routine physical inspection by neonatologist (no gross abnormalities in babies from mosaic embryos, n=415). A combined 356 prenatal tests (48 CVS, 71 NIPT, 237 amniocentesis) in pregnancies from mosaic embryo transfers were largely normal. The mosaicism detected at the embryonic stage by PGT-A was resolved in prenatal testing in only two out of 249 pregnancies (0.8%).

CONCLUSIONS: The international registry of mosaic embryo transfers continues to grow in sample size, in turn increasing the power of analysis. The results show that embryos of the mosaic category have lower implantation rates and higher miscarriage rates compared to embryos of the euploid category. Furthermore, features of mosaicism (level and type) correlate with different outcomes and should be considered during clinical embryo management. Data from prenatal tests indicate that in the vast majority of cases, chromosomal mosaicism identified at the blastocyst stage by PGT-A is resolved during a pregnancy, likely via the self-corrective mechanisms that have been described in the literature. The two cases in which mosaicism persisted need to be considered when explaining the risk of mosaic embryo transfers to patients and advising them on performing prenatal testing.

IMPACT STATEMENT: The findings of the mosaic embryo transfer registry can help educate the management and selection of embryos in the clinic. Mosaic embryos can be considered for transfer, with the understanding that they have lower likelihood of achieving a pregnancy and live birth. The features of mosaicism should be weighed up to prioritize mosaic embryos according to their chances of implantation. In the vast majority of cases, mosaicism is resolved during the pregnancy, and babies from mosaic embryo transfers are indistinguishable from babies from euploid embryo transfers.
OBJECTIVE: A Reproductive Tissue Engineering (REPROTEN) approach has been proposed to sequentially mimic in vitro folliculogenesis (iF) and meiotic maturation. To this aim, 3D culture of ovine ovarian follicles are performed on PCL-patterned electrospun scaffolds to recapitulate the native ovarian matrix by enabling long-term cultures without affecting 3D-matrix and meiotic competence.

RESULTS: 3D PCL-patterned scaffolds were able to synchronously sustain follicle and oocyte growth with high viability (88.2%), approximately 72% of antrum differentiation and 1.9-fold change increase of CYP19A1 expression (PA vs. EA, p<0.0001). Furthermore, a greater resumption of meiosis was obtained under the intrafollicular maturation protocol (intrafollicular vs. conventional IVM: 26.7% vs. 23.0% for germinal vesicle breakdown, p=0.0012) even if the incidence of Metaphase II was independent of the IVM protocol adopted (intrafollicular vs. conventional IVM: 64% vs. 68% Metaphase II, p=0.0572).

CONCLUSIONS: Reproductive biomimetic scaffolds are promising tools to design tissue engineering approaches targeted to innovate iF. The present results confirmed that PCL-patterned electrospun scaffolds can mimic the native ovarian matrix by enabling long-term cultures without affecting 3D-morphic properties with pattern formation. To functionally test how the BM shapes em-

OBJECTIVE: To assess the full preimplantation embryo developmental competence of identical replicates of both male and female gametes.

MATERIALS AND METHODS: Copies of oocytes were initiated by parthenogenetic activation of metaphase II oocytes from B6D2F1 mice by ionomycin. The male counterparts were generated by injecting B6D2F1 spermatozoas into enucleated ooplasts. Haploid constructs of both sexes were cultured to blastocysts, and haploid stem cell lines (haESCs) were derived.

In a different cohort, haploid blastomeres at the 8-cell stage were used as identical copies of female gametes by nuclear transfer into recipient ooplasts to generate putative artificial oocytes. These artificial oocytes were inseminated with wildtype mouse spermatozoa to generate conceptuses. Similarly, 8-cell haploid androgenetic blastomeres were fused with an intact oocyte as a male genome donor. Both types of constructs were cultured in a time-lapse system and compared with control ICSI conceptuses. Ploidy was assessed on the haploid blastomeres and the derived stem cell lines.

RESULTS: Parthenogenetic activation was performed on 129 oocytes and generated 119 (92.2%) constructs with a female pronucleus. Androgenetic counterparts were generated from piezo-ICSI on 375 ooplasts and yielded 317 (84.5%) constructs with a male pronucleus. The pronuclear decondensation for both haploid experimental constructs was comparable to the controls at 90.7%. However, compared to the blastocyst development rate of the controls at 80.8%, haploid female and male embryos yielded blastocysts at rates of 27.8% and 11.2%, respectively (P<0.0001). A total of 5 parthenogenetic and 3 androgenetic haploid stem cell lines were derived, and 80% of cells karyotyped maintained haploidy.

In a different cohort, haploid embryos of parthenogenetic and androgenetic origins were cultured up to the 8-cell stage at a respective rate of 76.4% and 59.3%. A total of 105 putative oocytes generated from 15 replicated oocytes yielded a fertilization rate of 88.6% (93/105) and an eventual blastocyst rate of 76.6% (71/93). For the male counterparts, a total of 145 biparental constructs were generated from 21 androgenetic embryos and 88 (60.7%) blastocysts were achieved. All reconstructed embryos retained morphokinetics that were similar to control conceptuses.

CONCLUSIONS: Haploid embryos of both sexes can achieve full preimplantation development and generate haploid stem cell lines with retained haploidy. In our model, a single haploid embryo stemmed from a single gamete can yield 4–5 embryos with retained preimplantation development and identical haplotype.

IMPACT STATEMENT: Male and female genomes from a respective spermatozoon or oocyte can be replicated using our proposed technique; resulting embryonic cells can be used for reproductive applications. Once our technique is optimized in humans, it can be used to investigate gamete heterozygosity for inherited disorders.

SUPPORT: None.
RESULTS: Single-cell RNA sequencing revealed that genes for components of the BM are highly upregulated in the hypoblast, and 3D super-resolution imaging confirmed that there is a LAMININ+ BM that lies between the OCT4+ epithelial and the GATA6+ hypoblast. This BM is present at 7 dpf and at 9 dpf, indicating that it is formed during the peri- to post-implantation transition. Strikingly, the BM exhibits spatially heterogeneous patterns during post-implantation stages. This heterogeneity occurs before signs of AP axis formation becomes evident. By manipulating the BM in the mouse pre-gastrulating embryos, we demonstrated that this heterogeneity in the BM shapes the collective cell migration event that establishes the AP axis. Following disruption of the BM, aberrant migration of anterior-specifying cells leads to mislocalization of posterior features such as the primitive streak. Using 3D quantitative imaging analyses to define cell behaviors, we showed that the BM informs collective cell migration by tuning tissue fluidity during morphogenesis.

CONCLUSIONS: Our results showed that the BM exhibits spatial heterogeneity during peri- to post-implantation embryogenesis, and that this heterogeneity informs the formation of the AP axis. These results reveal a conserved mechanism in which the extracellular mechanical anisotropy shapes body axis determination in pre-gastrulating embryogenesis.

IMPACT STATEMENT: We discovered a novel mechanism by which extracellular cues regulate pattern formation at critical stages in early pregnancy. Our findings identify morphogenetic indicators that could be applied when evaluating the developmental potential of an embryo.

O-244 11:30 AM Wednesday, October 26, 2022
EVALUATION OF CRISPR/Cas9-INDUCED DNA BREAK REPAIR OUTCOMES IN MOUSE AND HUMAN EMBRYOS. Bieke Bekkert, M. Sc.,1 Annekatrien Boel, PhD,1 Lisa De Witte, M. Sc.,1 Gwenwy Cosmans, M. Sc.,1 Susana M. Chuva De Sousa Lopes, PhD,1 Bjorn Menten, Prof. PhD,1 Bjorn Heindryckx, Prof. Ph.D.1 Ghent University;2 Ghent University;3 Leiden University Medical Center, Leiden, Netherlands.

OBJECTIVE: Comparison of the DNA repair outcomes following CRISPR/Cas9 gene editing in mouse and human, aiming for the correction of a male infertility-causing Plcz1 mutation.

MATERIALS AND METHODS: For mouse, we employed a previously described homozygous Plcz1 knock-out model (Plcz1<sup>Δ129yw</sup>). For human, sperm of a patient experiencing fertilization failure after routine ICSI, harboring a heterozygous PLCZ1 mutation (c.136-1G>C), was utilized. For both mouse and human, a CRISPR/Cas9 guideRNA molecule was designed that specifically recognized the respective mutant allele. The guideRNA-Plcz1 complex and a repair template harboring the wild type Plcz1<sup>Δ129lw</sup> sequence was injected into the oocyte. To overcome fertilization failure, AOA was applied during ICSI. At the eight-cell stage, a number of embryos were dissociated in individual blastomeres. For the remaining embryos, after a culture period of maximal 4 to 6 days in mouse and human, respectively, the DNA was extracted and analyzed with targeted and genome-wide sequencing techniques.

RESULTS: In both mouse and human, CRISPR/Cas9 editing did not affect embryonic development. In mouse, assessing the target region, 24% (5/21) of the obtained blastocysts still contained the unedited Plcz1<sup>Δ129yw</sup> allele, 24% (5/21) harboured additional indel mutations and 52% (11/21) contained the wild type sequence. Template use could be identified in (27%) 3/11 of the embryos. In neither the obtained blastocysts nor the additional indel mutations, 52% (11/21) contained the wild type sequence. Template use could be identified in (27%) 3/11 of the embryos. In none of these alleles, repair template use was observed. We showed that the BM informs collective cell migration by tuning tissue fluidity during morphogenesis.

RESULTS: In both mouse and human, CRISPR/Cas9 editing did not affect embryonic development. In mouse, assessing the target region, 24% (5/21) of the obtained blastocysts still contained the unedited Plcz1<sup>Δ129yw</sup> allele, 24% (5/21) harboured additional indel mutations and 52% (11/21) contained the wild type sequence. Template use could be identified in (27%) 3/11 of the embryos. In none of these alleles, repair template use was observed. We showed that the BM informs collective cell migration by tuning tissue fluidity during morphogenesis.

CONCLUSIONS: Our results showed that the BM exhibits spatial heterogeneity during peri- to post-implantation embryogenesis, and that this heterogeneity informs the formation of the AP axis. These results reveal a conserved mechanism in which the extracellular mechanical anisotropy shapes body axis determination in pre-gastrulating embryogenesis.

IMPACT STATEMENT: We discovered a novel mechanism by which extracellular cues regulate pattern formation at critical stages in early pregnancy. Our findings identify morphogenetic indicators that could be applied when evaluating the developmental potential of an embryo.

O-245 11:45 AM Wednesday, October 26, 2022
DE NOVO GAMETES GENERATED IN A NOVEL THREE-DIMENSIONAL CULTURE SYSTEM TO CREATE EMBRYOS CAPABLE OF FULL PREIMPLANTATION DEVELOPMENT. Mary McKnight, B.S., Philip Xie, B.S., Zev Rosenwaks, M.D., Gianpietro D. Palermo, M.D., Ph.D.2 Weill Cornell Medicine, New York, NY;3 The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To obtain de novo male gametes capable of supporting full preimplantation development utilizing a novel three-dimensional (3D) culture system.

MATERIALS AND METHODS: Male mouse embryonic stem cells (mESCs) were cultured on a gelatin-coated 6-well plate with fibroblasts in monolayer and later spherified by resuspension in a sodium alginate solution and dropped in a calcium chloride solution. Spheres of mESCs were submerged in specifically designed conditioned medium containing Activin A, bFGF, and KSR for 3 days to encourage differentiation into blastocyst-like cells, followed by medium containing BMP4, LIF, SCF, EGF, and retinoic acid for up to 36 days to encourage differentiation into male germ-like cells. Cells were assessed for germ cell differentiation biomarkers and injected into oocytes on days 15, 22, 29, and 36, as normal spermatogenesis occurs in 30 days. Assessed markers included DAZL (spermatogonium), VASA (primary spermatocyte), BOULE (post-meiotic secondary spermatocyte), and acrosin (spermaticid). Differentiated cells with diameters of approximately 7 mm were injected into oocytes and activated by calcium ionophore. Fertilized conceptuses were monitored in a time-lapse incubator comparing to a control cohort of embryos generated by piezo-ICSI using mature epididymal spermatozoa.

RESULTS: Advancement into in vitro spermatogenesis was exhibited on day 3 by the expression of DAZL in 20% and VASA in 15% of spermatids. On day 10, DAZL and VASA were reassessed and increased to 45% and 52%, respectively; post-meiotic biomarkers BOULE and acrosin were manifested in a scant number of cells at 2% and 1%, respectively. On day 15, VASA expression plateaued at 17%, BOULE expression peaked at 10%, and acrosin reached 5%. At the fourth assessment on day 22, expression of VASA increased slightly to 19%, BOULE decreased to 8%, and acrosin peaked at 7%. On day 29, VASA expression peaked at 20%, BOULE expression dropped to 2%, and acrosin expression remained stable at 7%. On day 36, VASA expression remained at 13%, and BOULE and acrosin expression fell drastically to 0% and 1%, respectively. The control cohort attained 89.2% fertilization and 77.8% blastocyst rates. Generated putative post-meiotic cells on days 15, 22, 29, and 36, equivalent to BOULE- and VASA-expressing cells of approximately 7 mm in diameter, were injected into oocytes. Following chemical activation by calcium ionophore, fertilization was achieved at rates of 35.0%, 61.1%, 81.8%, and 75.0%, respectively. Respective blastocyst rates according to the time intervals were 5.0%, 6.7%, 36.4%, and 8.3%.

CONCLUSIONS: Our novel 3D differentiation model can generate competent gametes to support full pre-implantation development and can obviate the need for final germ cell maturation through allo-xenogeneic transplantation.

IMPACT STATEMENT: If the results are reproducible and the ability to obtain healthy offspring is confirmed, this method may represent a feasible model for achieving neogametogenesis in humans.
EXPLORING THE ROLE OF CONNECTIVE TISSUE GROWTH FACTOR (CTGF) IN THE ANGIOGENESIS OF ENDOMETRIOSIS. Monica Chung, MD,1 William Gibbons, MD,2 Xiaoming Guan, MD, PhD,3 Sang Jun Han, PhD 3 Baylor College of Medicine, Houston, TX; 2Baylor College of Medicine, Dept of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Houston, TX; 3Baylor College of Medicine, Dept of Obstetrics and Gynecology, Division of Minimally Invasive Gynecologic Surgery, Houston, TX. Published Online September 22, 2015.10.034. PMID:26544941; PMCID: PMC4640214.

Tsai SY, Tsai MJ, DeMayo FJ, O’Malley BW. Estrogen Receptor beta1 (ERβ) modulated endometriosis.2015.10.034. PMID:26544941; PMCID: PMC4640214.

OBJECTIVE: This study aims to define the role of connective tissue growth factor (CTGF) in the angiogenesis of estrogen receptor beta (ERβ) modulated endometriosis.

MATERIALS AND METHODS: Normal endometria were isolated from the endometrium of leiomyoma patients, and endometriotic tissue were isolated from ectopic lesions of patients with endometriosis. Primary human endometrial stromal cells were developed from the isolated normal endometria and ectopic lesions. Immortalized human endometrial epithelial cell lines (IHEECs) and immortalized human endometrial stromal cell lines (IHESCs) were generated from human endometrial cells obtained from surgically excised ovarian endometrioma specimens. Myc-FLAG tagged human connective tissue growth factor (CTGF) was subcloned into the pcDH-CMV vector, a mammalian lentiviral expression vector. Stable CTGF overexpressing IHEECs and IHESCs were generated by transduction with the lentivirus carrying the CTGF expression unit.

RESULTS: Western blotting with primary human endometrial stromal cells revealed that CTGF, HIFα1, and ERβ were elevated in endometriotic stromal cells compared to normal endometrial stromal cells. Immunohistochemistry analysis showed that ectopic lesions had higher levels of CTGF than normal endometrium. Western blot analysis validated CTGF expression from the pcDH-CMV-CTGF clone and confirmed CTGF overexpression in IHEECs and IHESCs.

CONCLUSIONS: The generation of CTGF overexpressing IHEECs and IHESCs may mimic human endometriotic lesions due to the high levels of CTGF found in mice endometriotic lesions. These recombinant cell lines are excellent tools to further explore the molecular etiology of CTGF-mediated angiogenesis in endometriosis progression both in vivo and in vitro.

IMPACT STATEMENT: Diagnosis and treatment of endometriosis are challenging, given the limited knowledge of specific cellular and molecular pathways defined in this disease. Patients often experience systemic side effects with current medical therapy, and recurrence of endometriosis is common after discontinuation of medications or after surgical resection. Prior studies in our lab discovered ERβ’s pivotal role in the pathogenesis and progression of endometriosis and CTGF’s direct and functional interaction with ERβ. Furthermore, CTGF is elevated in endometriotic stromal cells and higher levels of CTGF are exhibited in ectopic lesions when compared to normal endometrium. Given these recent findings and CTGF’s known essential role in angiogenesis, CTGF has the potential to stimulate human endothelial cells and promote the growth of endometriotic lesions. Thus, CTGF may be a potential target for anti-angiogenesis therapy in treating endometriosis.

SUPPORT: This work was supported by grant funding from NICHD (R01 HD098059-01A1).

REFERENCES:

ORAL ABSTRACT SESSION: REPRODUCTIVE ENDOCRINOLOGY

ELEVATED ANTI-MULLERIAN HORMONE LEVELS ARE NOT ASSOCIATED WITH PRETERM DELIVERY AFTER IN VITRO FERTILIZATION OR OVULATION INDUCTION. Anne E. Kim, MD,1 Michael K. Simoni, MD,2 Ashni Nadguda, MD,1 Nathan C. Koelper, MPH,3 Anuja Dokras, MD, PhD1 1Hospital of the University of Pennsylvania, Philadelphia, PA; 2Penn Fertility Care, Philadelphia, PA; 3Reading Hospital - Tower Health, Reading, PA; 4UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, Philadelphia, PA.

OBJECTIVE: Prior studies suggest that elevated anti-Müllerian hormone (AMH) levels are associated with an increased risk of preterm birth (PTB) in patients with polycystic ovary syndrome (PCOS) after assisted reproductive technology. AMH may reflect uterine development or hormonal milieu, thus leading to the proposed risk of PTB. We investigated the association between AMH and risk of PTB in a larger cohort of patients who underwent either in vitro fertilization (IVF) or ovulation induction (OI) with intrauterine insemination at a US academic fertility center.

MATERIALS AND METHODS: We performed a retrospective cohort study of all live, singleton births from patients who underwent IVF or OI from 2010-2020. Review of the medical records confirmed all clinical outcomes.

RESULTS: First- and second-trimester serum analytes were analyzed from 100 unassisted and 233 IVF pregnancies. When comparing unassisted vs. IVF pregnancies, there were differences in the following analytes: PAPP-A (1.14±0.72 vs. 0.86±0.58, p<0.01), AFP (1.04±0.37 vs. 1.11±0.55, p<0.05), and uE3 (0.94±0.27 vs. 1.03±0.33, p<0.01). While changes in PAPP-A were observed in pregnancies using either conventional IVF or intra-cytoplasmic sperm injection (ICSI), changes in AFP and uE3 were only seen in those that utilized ICSI. Lower PAPP-A levels were seen following both fresh embryo(s) transferred was only associated with changes in uE3 (p=0.02).

CONCLUSIONS: ART interventions are associated with changes to maternal serum analytes when compared to infertile women who conceived without ART. ICSI and frozen transfer were associated with changes in more serum analyte categories compared to fresh transfer, respectively.

IMPACT STATEMENT: Among infertile women, ART is associated with significant changes to maternal serum analytes. Our results may provide insights into which treatment intervention(s) may exert the most impact on early pregnancy and placental development.

SUPPORT: Supported by the Eunice Kennedy Shriver National Institute of Child Health & Human Development Grant No. R01 HD084380-05

REFERENCES:

ELEVATED ANTI-MULLERIAN HORMONE LEVELS ARE NOT ASSOCIATED WITH PRETERM DELIVERY AFTER IN VITRO FERTILIZATION OR OVULATION INDUCTION.
information, including indication of PTB. Pregnancies with oocyte donation, gestational carrier, multiple gestation, and delivery prior to 20 weeks gestation were excluded. Among PCOS and non-PCOS patients, serum AMH values were compared in women who delivered at full term to those who delivered preterm. Total study duration was 10 days with treatments ABCDE being administered with one or two doses of the vaccine (-0.01 day, 95% CI -0.05 to 0.03 and -0.01 day, 95% CI -0.06 to 0.03, respectively), as was the case in unvaccinated patients (0.05 days, 95% CI -0.02 to 0.12). While participants who reported a COVID infection were noted to have a shorter first cycle after infection (-0.07 days, 95% CI -0.11 to -0.02), this difference was not clinically significant. There were no observed associations between AMH quartiles and PTB. Additional studies are needed prior to counseling patients regarding their risk of PTB based on serum AMH levels.

CONCLUSIONS: Our results demonstrate that elevated AMH levels were not associated with an increased risk of PTB in both PCOS and non-PCOS patients who conceived after IVF or OI. Our findings call into question the significance of AMH level and risk of PTB, particularly in PCOS patients.

IMPACT STATEMENT: Detailed review of obstetric records in the largest PCOS cohort studied in the US did not demonstrate an association between elevated AMH levels and PTB. Additional studies are needed prior to counseling patients regarding their risk of PTB based on serum AMH levels.

SUPPORT: None.

O-249 11:15 AM Wednesday, October 26, 2022

PHARMACOKINETIC (PK) STUDY OF ORAL LEUPROLIDE DELIVERY WITH OVAREST® ACHIEVES DRUG LEVELS EXCEEDING THOSE OF APPROVED INJECTABLE PRODUCTS. Gary A. Shangold, M.D., Arkady Rubin, Ph.D., Thomas Daggs, M.B.A., John Vrettos, Ph.D., Andrejs Rasums, B.S., Angelo Consalvo, B.S., Nicola Skeet, B.S., MS, Sreeja Polpully Variam, M.S., Kalpana Ramakrishnan, Ph.D., Paul Shields, Ph.D., Enteris BioPharma Inc, Boonton, NJ, ARSTAT Inc, Berkeley, CA, University of California San Francisco, San Francisco, CA. OBJECTIVE: To assess the PK profile of our oral dosage form of leuprolide (Ovarest®) as a bridge to historical data for highly effective injectable leuprolide products. Specific goals: evaluate PK profiles and dose-proportionality of single doses from 40 - 120 mg, evaluate dose-proportionality of daily dosing regimens from 80 - 120 mg/day, compare QD to BID dosing, and further quantify known food effects of Ovarest.

MATERIALS AND METHODS: We conducted an open label, 5-period, single-sequence crossover study to evaluate the safety and PK profile of 2 tablet strengths and 2 dosing regimens of Ovarest® following an overnight fast in 22 healthy female volunteers in a Clinical Pharmacology Unit. Three regimens were administered under fasting conditions, 4 hrs before breakfast and 4 hrs after dinner: A - Ovarest 40 mg BID; B - Ovarest 60 mg BID; C - Ovarest 120mg QD. Ovarest 60 mg BID was also administered closer to feeding: D - 2 hrs before breakfast and 2 hrs after dinner, E - 1 hr before breakfast and 1 hr after dinner. Frequent blood sampling occurred for 36 hrs after dosing. Total study duration was 10 days with treatments ABCDE administered sequentially with 36- to 48-hr wash-out intervals.

RESULTS: 22 subjects were enrolled and dosed, and 21 subjects completed the study; 1 subject discontinued after her fourth treatment. AUCs, Cmax, and trough levels were calculated for each subject for each treatment period. Total daily exposure (AUC0-24) following fasting 60 mg BID (Treatment B) was 1.4 times that of fasting 40 mg BID (A), indicating approximate dose proportionality within this range. Total daily exposure following 60 mg BID with 4-hr dose-feeding interval (B) was 1.7 and 2.0 times greater than when administered with a 2-hr (D) and 1-hr interval (E), respectively, reflecting significant time-dependent food effects on PK metrics. Following a maximal dose of 120 mg QD (C), the 24-hr mean Cmax was 230 ng/mL, occurring at a median Tmax of 3.0 hrs, and the mean AUC0-24 was 535 ng*hr/mL, both well exceeding corresponding values measured on day 1 in our previous studies with Lupron Depot 3.75 mg im (Cmax 17.5 ng/mL, AUC 82 ng*hr/mL) or Lupron 1 mg sc (Cmax 59.4 ng/mL, AUC 163 ng*hr/mL). Frequently reported Treatment Emergent Adverse Events (TEAEs) across all treatment groups were headache (14-27%), dizziness (7-13%) and nausea (0-13%). Study drug was generally well tolerated, with 65 of 76 (85.5%) AEIs associated with mild, and no severe or serious AEIs. Safety issues were observed for clinical lab results or changes in vital signs.

CONCLUSIONS: Results confirm oral delivery of leuprolide levels expected to be within established therapeutic ranges. Leuprolide oral tablets in women dosing in 80 to 120 mg appear to be safe, well tolerated, and roughly dose proportional. Compared to proprietary Enteris data and published historical data, Ovarest delivered more drug than highly effective injectable leuprolide formulations.

IMPACT STATEMENT: PK and safety results support further development of Ovarest as a differentiated alternative to current dosage forms of the GnRH agonist leuprolide eliminating the need for potentially painful injections.

SUPPORT: This study was funded in its entirety by Enteris BioPharma Inc.

O-250 11:30 AM Wednesday, October 26, 2022


OBJECTIVE: To evaluate whether receiving a COVID-19 vaccine or infection with COVID-19 had an impact on the length of menstrual cycles in women of reproductive age.

MATERIALS AND METHODS: Cross-sectional, nationwide study of reproductive age females users of the menstrual tracker app Glow. All participants were aged 18-55 and lived in the United States. From 3/022 to 4/722, participants who had at least 6 months of continuous app use prior to and after April 2021 (defined as logging of menstrual cycle data) were invited to participate in a short questionnaire asking about vaccine status, COVID infection status, and symptoms around the time of vaccination and/or infection. This study was approved by the University of California IRB.

RESULTS: Out of 218,977 eligible individuals, 11,591 completed the study. 10,922 (representing 269,278 cycles) were included. Some patients were excluded due to not having 6 cycles of data before or after the vaccine or infection and for reporting hormonal birth control use. 75% received two doses of the vaccine (60% Pfizer-BioNTech, 34% Moderna, and 7% J&J), 5% received one dose (63% Pfizer-BioNTech, 37% Moderna, and 1% J&J), and 20% were unvaccinated. There was no change in menstrual cycle length after one or two doses of the vaccine (-0.01 day, 95% CI -0.05 to 0.03 and -0.01 days, 95% CI -0.06 to 0.03, respectively), as was the case in unvaccinated patients (0.05 days, 95% CI -0.02 to 0.12). While participants who reported a COVID infection were noted to have a shorter first cycle after infection (-0.07 days, 95% CI -0.11 to -0.02), this difference was not clinically significant. There were no differences in months 2-6 after infection, or in average cycle length in the 6 months after infection. Of note, whether a patient was symptomatic or asymptomatic with vaccination or infection did not meaningfully impact the menstrual cycle length; well exceeding corresponding values.

CONCLUSIONS: The COVID-19 vaccine and COVID-19 infection do not result in meaningful menstrual cycle changes compared to unvaccinated or uninfected individuals, respectively.

IMPACT STATEMENT: This is the largest study to date to describe that the COVID-19 vaccine and COVID-19 infection do not appear to result in menstrual cycle changes and adds to the body of literature supporting the safety of the COVID-19 vaccine.

SUPPORT: No financial support.
O-252 11:45 AM Wednesday, October 26, 2022

RELATIONSHIP OF ANTITHYROID ANTIBODIES AND TSH TO INFERTILITY PHENOTYPES AND OUTCOMES. Aimee M. Seungdamrong, M.D.,¹ Labna Pal, MBBS,² Satu Kuokkanen, MD, PhD,³ Harry Lieman, MD,⁴ Robert A. Wild, MD, MPH, Ph.D,¹ Fangbi Sun, MPH,⁴ Heping Zhang, PhD,⁴ Michael P. Diamond, MD,⁴ Richard S. Legro, M.D.,⁴ Nanette Santoro, MD,⑤ ¹Yale University, Orange, ²NYU Langone,Minola, NY, ³Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY, ⁴Oklahoma University Health Sciences Center, Oklahoma City, OK; ⁵Yale University School of Public Health, New Haven, CT; ⁶Medical College of Georgia at Augusta University, Augusta, Ga; ⁷Penn State College of Medicine, Hershey, PA; ⁸University of Colorado School of Medicine, Aurora, CO.

OBJECTIVE: To determine the prevalence of subclinical hypothyroidism and thyroid peroxidase antibodies (TPOs) in women participating in Reproductive Medicine Network (RMN) trials with polycystic ovary syndrome (PCOS) and unexplained infertility (UI), and to link thyroid indices to reproductive phenotype and outcomes.

MATERIALS AND METHODS: Secondary analysis of data from 2 NIH funded RMN trials: Pregnancy in Polycystic Ovary Syndrome II (PPCOS II; N=750) and Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation (AMISG, N=900). TSH and TPOs were analyzed as continuous and categorical variables. A TSH cutoff of 2.5 and 4.0 uIU/ml were used; for TPOs a cutoff of 55 IU/ml was used. Associations were examined for the entire combined cohort as well as by diagnosis. Outcomes evaluated were characteristics of the sample (ovarian reserve, androgenicity, demographics and biometry) and conception, clinical pregnancy (CP), pregnancy loss (PL) and live birth (LB). Data are shown as median [IQR].

RESULTS: The means of TSH and TPOs did not differ between PCOS and UI patients nor did the prevalence of TSH >4 or TPOs >55 IU/ml. In the combined cohort, BMI (28.7 [23.4, 36.8] vs 30.4 [23.8, 35.1]), AMH (3.4 [1.7, 6.3] vs. 3.0 [1.4, 6.3]), AFC (26.0 [16.0, 41.0] vs. 23.0 [14.0, 41.0]), FSH and HgbA1c did not differ by TPO status. CP (28.5 vs. 20.3) was related to TPOs (p=0.036), but this association did not remain after adjustment for age, TSH, and BMI. In PCOS women, BMI (35 [27.4, 41.7] vs 35.1 [31.8, 42.2]), AMH (6.1 [3.6, 10.1] vs 7.3 [4.4, 12.6]), AFC (40 [27.8] vs 44 [32.5, 62.5]), FSH and HgbA1c did not differ by TPO status. Neither conception, CP, nor LB were related to TPO status. CP (28.5 vs. 20.3) was related to TPOs (p=0.036), but this association did not remain after adjustment for age, TSH, and BMI. In PCOS women, BMI (35 [27.4, 41.7] vs 35.1 [31.8, 42.2]), AMH (6.1 [3.6, 10.1] vs 7.3 [4.4, 12.6]), AFC (40 [27.8] vs 44 [32.5, 62.5]), FSH and HgbA1c did not differ by TPO status. Neither conception, CP, nor LB were related to TSH and TPOs. In both the combined cohort and in women with PCOS, TSH was higher in those with TPOs >55 IU/ml (2.2 uIU/ml vs 1.7 uIU/ml p<0.001).

CONCLUSIONS: In this well characterized sample of women with both UI and PCOS, we found no relationship between TSH and elevated TPOs, clinical phenotypes, or pregnancy outcomes. Women with PCOS with TPOs >55 IU/ml had higher, though normal TSH.

IMPACT STATEMENT: Elevated TSH or TPO’s were not related to clinical phenotypes or pregnancy outcomes in women with UI or PCOS.

Supported by R25 HD 57573.

O-252 12:00 PM Wednesday, October 26, 2022

NEUREGULIN 1 REGULATES CUMULUS-OOCYTE DIFFERENTIATION DURING IVM AND IMPROVES POST-IVF EMBRYO DEVELOPMENT. Thaisy Tello Dellaqua, Ms.¹, Mario Mignini Renzini, MD,² Mariabeatrice Dal Canto, B.Sc., Ph.D.,³ José Buratini, DVM, Ph.D.⁴ ¹Sao Paulo State University, Botucatu, Brazil; ²Biogenesi Reproductive Medicine Centre, Monza, Italy; ³BIOGENESI Reproductive Medicine Centre, Monza, Italy.

OBJECTIVE: Although its application has been restricted to specific patient profiles, in vitro maturation (IVM) of germinal vesicle oocytes may represent an alternative to reduce infertility treatment cost and risk/discomfort. The bovine IVM model has been particularly valuable to improve our comprehension about the regulation of cumulus-oocyte maturation, as well as to develop IVM strategies for sub-fertile women. Gradual instead of abrupt activation of the ovarulatory cascade during IVM has been proposed to enhance nuclear-cytoplasmic synchrony and cumulus-oocyte communication, thus favoring development towards metaphase II. Here, we used the bovine IVM/IVF model to assess the effects of neuregulin 1 (NRG1), an EGF-like factor that modulates EGF signaling and thus the activation of the ovarulatory cascade, on oocyte nuclear maturation dynamics, cumulus expansion, expression of mRNAs regulating these processes and on post-IVF embryo development.

MATERIALS AND METHODS: Bovine cumulus-oocyte complexes (COCs) were aspirated from 2-8mm follicles of slaughterhouse ovaries, pooled in groups of 20-25 and subjected to IVM in TCM containing physiological concentrations of FSH, IGFI and steroids (‘IVM Follicular System’; 200 ng/100 ml). AREG in the absence or presence of IVM/mL NRG1 for 6, 9, 12, 20, and 24 h. Oocyte chromatin/meiotic status was assessed by fluorescence microscopy following Hoechst staining at each time-point. Expansion degree and cumulus mRNA expression (real time RT-PCR) were assessed after 24 h of IVM. Embryo production rates and embryo cell number (fluorescence microscopy/Hoechst) were assessed after standard IVF using frozen semen of a single bull/batch and embryo culture for 7 days. All experiments were done in 5 replicates. Data in percentages were arcsine transformed and all the data were first tested for normality (Shapiro-Wilk test) before assessing treatment effect with the t-Student test.

RESULTS: At 6h of IVM, NRG1 decreased the percentage of oocytes undergoing germinal vesicle breakdown (GVBD; 52.24 ± 4.70 vs. 70.37 ± 5.10; P = 0.02; NRG1 vs. Control group, respectively), without altering later meiotic dynamics or the percentage of oocytes achieving Metiosis II at the end of culture. NRG1 did not affect cumulus expansion, but increased the percentage of expanded and hatched blastocysts (39.31 ± 2.56 vs. 32.60 ± 1.03; P = 0.03), as well as blastocyst total cell number after IVF/IVC (202.30 ± 10.52 vs. 169.18 ± 10.55; P = 0.03). NRG1 decreased EGRF (0.82 ± 0.05 vs. 1.00 ± 0.03; P = 0.02) while increasing that of NPR2 (1.64 ± 0.22 vs. 1.03 ± 0.13; P = 0.04) and PTX3 (5.73 ± 2.74 vs. 1.19 ± 0.24; P = 0.04) mRNA levels at 9h, and TNPAP6 (1.77 ± 0.23 vs. 0.82 ± 0.04; P = 0.02) mRNA abundance at 20h of IVM.

CONCLUSIONS: This is the first study suggesting a modulatory role for NGR1 during the activation of the ovarulatory cascade, preventing precocious nuclear maturation and favouring oocyte developmental competence in a mono-ovulatory species.

IMPACT STATEMENT: The present data contribute for a better understanding of oocyte biology, while constituting valuable references to improve IVM/IVF outcomes.

ORAL ABSTRACT SESSION: REPRODUCTIVE IMMUNOLOGY

O-253 10:45 AM Wednesday, October 26, 2022

ENDOMETRIAL IMMUNE CELL RATIOS IN RECURRENT PREGNANCY LOSS (RPL) PATIENTS. Rumiana Ganeva, MSc,¹ Dimitar Parvanov, PhD,¹ Maria Handzhiyska, MSc,¹ Margarita Ruseva, MSc,¹ Nina Vidolova, MSc,¹ Veselina Moskova-Doumanova, assoc., prof.,¹ Dimitar Metodiev, M.D.,¹ Georgi Stamenov, MD/PhD.¹ Nadezhda Women’s Health Hospital, Sofia, Bulgaria; ²Sofia University “St. Kliment Ohridski, Sofia, Bulgaria.

OBJECTIVE: Although there are many causes of recurrent pregnancy loss (RPL), it is frequently associated with immunological dysregulation. Various immune deviations in the Natural Killer (NK) levels and T cell subpopulations (T helpers (Th) and T killers (Tk)) were found in the peripheral blood of RPL women. However, the endometrial immune cell composition and their local quantities could be more indicative for the condition of the immunune tolerance towards the developing foetus. The objective of this study was to compare the endometrial immune cell ratios between repeated pregnancy loss (RPL) patients and control group of women with history of full-term delivery.

MATERIALS AND METHODS: Endometrial tissue from 60 patients with RPL, defined as two or more miscarriages before 24 weeks of gestational age, and control patients with history of full-term delivery were selected from the hospital tissue bank. All samples were obtained by regular diagnostic biopsy during mid-luteal phase of the menstrual cycle from unstimulated IVF patients without endometrial pathologies. The endometrial samples were immunohistochemically stained with antibodies against Th cells (CD4, IS649, Dako), Tk cells (CD8, CD040, Quartett) and NK cells (CD56, A00121, ScyTek) using novelink polymer detection system (RE7280-K, Leica) according to the manufacturers instructions. The immune cell quantities were evaluated by microscopic observation in multiple tissue areas. Results were presented as median and range. Mann-Whitney U test was performed with SPSS v.21. P<.05 was considered significant.
RESULTS: The median percentages of Th and Tcd cells in the RPL and the control groups did not show significant difference (0.17%, 0.01-0.73 vs. 0.19%, 0-1.05, respectively, p=0.63 and 0.41%, 0.02-1.38 vs. 0.37%, 0.06-1.85, respectively p=0.78). Although not statistically significant, there was a trend toward lower percentage of NK cells in the RPL group compared to the controls (0.35%, 0.11-1.03 vs. 0.47%, 0.11-3.15, respectively p=0.06). When the immune cell ratios between RPL and the control group were compared, it turned out that neither Th/Tc ratio (0.33, 0.06-1.91 vs. 0.44, 0.05-2.11, respectively) nor NK/Tc ratio (1.97, 0.57-3.00 vs. 2.49, 0-3.00, respectively) differed significantly (p>0.05). However, the NK/Tc ratio was significantly lower in the RPL group when compared to the controls (0.72, 0.19-2.17 vs. 1.24, 0.33-5.36, p<0.01).

CONCLUSIONS: The endometrial immune composition of RPL patients differs significantly from the controls in the Tk/NK ratio. This is evidence for the importance of the mutual regulation of the cytotoxic immune cells in the endometrium. Local immune imbalance could lead to pathological conditions inconsistent with pregnancy.

IMPACT STATEMENT: This study helps to identify the key players in the building of the decidua immune tolerance required during pregnancy. The deviation in the Tk/NK ratio could be indicative for the immune dysfunction of the endometrium and should be properly managed by cell therapies to form favourable environment for the developing foetus.

SUPPORT: N/A

REFERENCES: N/A

O-254 11:00 AM Wednesday, October 26, 2022

PREDICTION AND DIAGNOSIS OF REPRODUCTIVE FAILURE BASED ON NKp46 EXPRESSION IN ENDO- METRIAL OR DECIDUAL NK CELLS. - Assashi Fukui, MD, PhD. Shinichiro Saeki, MD, PhD, Ryu Takeyama, MD PhD, Ayano Yamaya, MD, PhD Hyogo Medical University, Nishinomiya, Hyogo, Japan.

OBJECTIVE: Natural Killer (NK) cells are the most abundant immune cells at the time of implantation and early stage of pregnancy in uterine endometrium and decidua. NK cells have important roles in the achievement and maintenance of pregnancy. NKp46, an NK cell receptor, is involved in cytokotoxicity and cytokine production. We have previously reported the lower expression of NKp46 on uterine and peripheral blood NK cells in women with reproductive failures, such as repeated implantation failures or recurrent pregnancy loss (RPL). This study aimed to evaluate the NKp46 expression on endometrial (eNK) and decidual NK (dNK) cells. We also aimed to determine whether NKp46 can be used to detect immunological abnormalities in women with reproductive failures.

MATERIALS AND METHODS: Uterine endometrium was obtained using an endometrial sampler from women with reproductive failures (n=81) during the mid secretory phase of the menstrual cycle. Decidual tissue was mechanically disrupred during the mid secretory phase of the menstrual cycle. Decidual tissue ing an endometrial sampler from women with reproductive failures (n=88) and failed (n=81) abortions. Uterine endometrium or decidual tissue was mechanically disrupted and failed (n=81) abortions. Uterine endometrium or decidual tissue was mechanically disrupted and failed (n=81) abortions. Uterine endometrium or decidual tissue was mechanically disrupted and failed (n=81) abortions.

RESULTS: For eNK cells, the NKp46 threshold was determined via ROC curve analysis based on pregnancy outcome after 1-year follow-up. The pregnancy threshold for the expression of NKp46 of eNK cells was 60.5% with 52.9% sensitivity and 92.3% specificity. For dNK cells, proportions of NKp46+ dNK cells were significantly lower in the RPL women with genetically normal pregnancies than in controls (p<.01). The NKp46 threshold was also determined via ROC curve analysis based on pregnancy outcome after 1-year follow-up. The pregnancy threshold for the expression of NKp46 of dNK cells was 75.3% with 61.5% sensitivity and 84.6% specificity. The median percentage of NKp46+ dNK cells was 86.5%, showing 83.3% sensitivity and 100% specificity.

CONCLUSIONS: RPL patients with immunological abnormalities have decreased NKp46 expression and dysfunctional cytokine production. IMPACT STATEMENT: NKp46 expression on both eNK and dNK cells could be an effective biomarker for reproductive failure with immunological abnormalities.

SUPPORT: This work was supported by JSPS KAKENHI (Grant Number JP16K11078 and JP21K09504).

O-255 11:15 AM Wednesday, October 26, 2022

EXOGENOUS LEPTIN TREATMENT ALTERS THE TESTICULAR IMMUNE MICROIMMUNE-ENVIRONMENT. - Himanshu Arora, B.S.C., M.S.C., PH.D., Deepa Seetharam, PH.D, Alexandra Dullea, M.S., Ranjith Ramasamy, M.D., Fakih Firdaas, PhD 1University of Miami Miller School of Medicine, Miami, FL; 2Postdoc.

OBJECTIVE: In men, Leydig cells (LCs) are the primary source of testosterone (T) production. Dysfunction of the LC can lead to T deficiency and male hypogonadism. The development of LCs is influenced by the paracrine factors released by the testicular microenvironment (TME). In our recent study, we demonstrated using cells isolated from human testis biopsies that Leptin, a paracrine factor secreted by TME, is critical for Leydig stem cell (LSCs) differentiation into Adult Leydig Cells (ALD), and subsequent T production. However, one of the limiting aspects of our findings was the lack of intact testicular immune microenvironment in-vitro conditions. This study focuses on overcoming this limitation by evaluating the effect of different doses of Leptin in an intact testicular immune microenvironment.

MATERIALS AND METHODS: We selected a murine model (C57/BL6 mice purchased from Jackson Laboratory) to conduct the study. Mice (n=5 per group) were subjected to intraepididymal Leptin injections at concentrations of 0mg (control), 10 microgram or 100micrograms. Mice were injected with Leptin every day for 10 days. After treatment, mice were euthanized, and blood was collected from the tail and was processed for complete blood count (CBC) profiling and hormonal (T, LH, and FSH) profiling. unstained sections from testis were subjected to immunohistochemistry to study Leptin induced changes on the expression of LEPR (Leptin receptor), hedgehog signaling markers (GLI, SMO), ADL markers (LHR and B3HSD).

RESULTS: The CBC profiling data was notable for a significant difference between the control and leptin 10ug in the number of neutrophils, lymphocytes, monocytes, and platelets. The control group had a significantly higher concentration of these cell types compared to the leptin 10ug group (p<0.05). Interestingly, when comparing control to the 100ug group, the only significantly different blood values were monocytes and eosinophils, with a higher concentration present in the 100ug group. While there was no significant difference in the amount of red blood cells between the groups, mean corpuscular hemoglobin concentration (MCHC) was significantly altered with increased in both the 10ug and 100ug groups. The hormonal data showed that LH was significantly elevated in leptin 10ug group when compared to control group (p<0.05). Moreover, IHC results also highlighted significant changes in the expression of DHH signaling, LEPR and ADL expression post Leptin treatments.

CONCLUSIONS: The findings suggest that low dose of leptin have a significant impact not only on the levels of LH, but importantly also on the markers of immune microenvironment. Therefore, future studies will focus on exploring the differential impact that low doses of leptin might have on several of the immune markers in testicular microenvironment.

IMPACT STATEMENT: This is the first study of its kind to evaluate impact of exogenous Leptin treatment in intact testicular immune microenvironment. Further research will open new doors to the use of Leptin as a personalized medicine for men with testosterone deficiency.

SUPPORT: Supported by the Clinician Scientist Development award from American Cancer Society and NIH health grant RO1 DK130991 to RR and Research Scholar Award from American Urological Association to HA.

O-256 11:30 AM Wednesday, October 26, 2022

DIFFERENCES IN MENSTRUAL CYKOTINE PROFILES OF WOMEN WITH AND WITHOUT UTERINE FIBROIDOS. - Zainub Dhanani, AB, Norma Jimenez Ramirez, BS, Jennifer Nguyen, BS, Yael Rosenberg Hasson, PhD, Sara Naseri, MD, Diana Atashroo, MD, Deirdre A. Lum, MD, Bertha Chen, MD Stanford University School of Medicine, Stanford, CA; 2Stanford University, Stanford, CA.

CONCLUSIONS: The menstrual cytokine profiles of women with uterine fibroids differ from those without fibroids, with lower expression of pro-inflammatory cytokines and higher expression of anti-inflammatory cytokines. This finding may have implications for the pathogenesis and treatment of uterine fibroids.
OBJECTIVE: Uterine fibroids are often associated with pelvic discomfort, abnormal uterine bleeding, and urinary symptoms but the cause of these symptoms remains unclear. We hypothesize that these may be due to changes in uterine/endometrial cytokines induced by fibroid growth and that these cytokines may be excreted in menstrual blood. A recent study analyzed menstrual blood of healthy women to understand the cytokine profile of normal menstrual blood, however, no such studies have been conducted on women with fibroids. Hence, we sought to examine differences in menstrual blood cytokine expression for women with and without fibroids.

MATTERIALS AND METHODS: Menstrual samples were collected from seven women on the first heavy day of the period using a modified menstrual pad with an embedded dried blood sample collection strip. Inclusion criteria included having no known gynecological disease besides fibroids, use of a non-intrauterine form of birth control, no smoking history, and being between the ages of 20-40. Four control samples from healthy patients in the same age group with no known history of gynecological disease, no smoking history, and no intra-uterine form of birth control use were also obtained. Samples were extracted and run on a H48plex immunoassay and analyzed for cytokine expression.

RESULTS: We found notable trends in the expression of the following five immune markers: G-CSF, IL-1a, IL-1b, IL-6, and VEGF-A. Patients in the fibroid group had higher average expression levels of these cytokines compared to the control group, with the exception of IL-1b, where patients in the fibroid group had decreased levels of cytokine expression compared to the control group.

CONCLUSIONS: Our findings indicate that there are differences in the menstrual cytokine expression of women with and without fibroids. These differences suggest that immune mechanisms may be associated with the differential symptoms experienced by patients with fibroids during menses. Our pilot study is limited by the small sample size but the data suggest that menstrual blood cytokine profiles can be used to study uterine fibroid pathophysiology. Larger studies of menstrual cytokines in patients with fibroids are necessary to better understand these results and their possible implications.

IMPACT STATEMENT: The observed differences in menstrual cytokine expression amongst women with and without fibroids indicate a need for further investigation into the role of immune modulation in uterine fibroids and may offer potential targets for future therapies for fibroid-related symptoms.

REFERENCES:

O-257 11:45 AM Wednesday, October 26, 2022

DISTINCT CYTOKINE SECRETION PROFILES UPON IMMUNOMODULATION OF PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMC) WITH INFN AND HCG

FERON TAU (IFNT) AND HUMAN CHORIONIC GONADOTROPIN (HCG), Margarita Ruseva, MSc, Dimitar Parvanov, PhD, Rumiana Geneva, MSc, Maria Handzhyska, MSc, Nina Vidolova, MSc, Dimitar Metodiev, M.D., Georgi Stamenev, MD/PhD Nadezhda Women’s Health Hospital, Sofia, Bulgaria.

OBJECTIVE: Uterine administration of PBMC has been shown to improve endometrial receptivity and has become routine practice in assisted reproduction. Modulation of these cells’ activity with various trophoblast-derived signals is an active area of research. The present study aimed to investigate and compare the effect of immunomodulation with IFNt and HCG on the cytokine secretion from cultivated PBMC.

MATERIALS AND METHODS: Heparinized whole blood samples (17 ml) were collected from healthy pregnant female patients. Following Pancoll (P0460100, PanBiotech) gradient centrifugation for 25 min at 400G PBMC were collected from theuffy coat, washed and suspended in 1.5ml RPMI medium (E15842, APP), containing 1% FCS (GHSA125, LifeGlobal). Cells were incubated either alone (control), with 500IU IFNt (NBP261440, Novus) or with 10IU hCG (BTHOR250, Biotang) for 24 hours at 37°C. The PBMC medium was used to measure tumor necrosis factor alpha (TNFa), interleukin-6 (IL6), interleukin-4 (IL4) and interleukin-10 (IL10) via sandwich enzyme-linked immunosorbent assay (CSBE04740h, CSBE04638h, CSBE04633h and CSBE04593h, Cusabio, respectively). Cytokine concentrations are reported as median and range and compared between groups via Wilcoxon rank test.

RESULTS: Incubation with IFNt had suppressive effects on the secretion of both pro-inflammatory cytokines – resulting in markedly reduced TNFa concentration (17.1 (1.2-86.2) pg/ml) compared to 24h control (96.8 (18.3-384.9) pg/ml; p<0.001) and hCG treated cells (76.1 (21.9-478.7) pg/ml; p=0.001); there was also no difference in IL10 concentration between the two immunomodulators (p=0.05). IFNt caused a considerable increase in IL4 concentration (25.1 (5.2-260.2) pg/ml) compared to 24h control (13.5 (5.196.5) pg/ml; p=0.03) and a notable albeit insignificant increase compared to hCG induced incubation (16.4 (4.6-178.2) pg/ml; p=0.05). HCG-treated and non treated cells did not differ in IL4 secretion (p=0.05).

CONCLUSIONS: Supplementation of PBMC culture medium with IFNt but not hCG reduces the secretion of TNFa and IL6 increases that of IL4. In contrast, the concentration of IL10 is not significantly altered following exposure to either of the studied modulators. Thus, IFNt seems to induce a more advantageous PBMC modulation.

IMPACT STATEMENT: In clinical practice PBMC for uterine use is either untreated or activated with hCG. These findings indicate a potential benefit of optimizing established protocols by using compounds which induce more favorable cytokine secretion profiles. This may further improve clinical outcomes of patients with recurrent implantation failure.

O-258 12:00 PM Wednesday, October 26, 2022

ASSOCIATION BETWEEN CYTOKINE LEVELS IN BLOOD PLASMA AND PBMC CULTURE MEDIA. Rumiana Geneva, MSc, Dimitar Parvanov, PhD, Maria Handzhyska, MSc, Margarita Ruseva, MSc, Dimitar Metodiev, M.D., Georgi Stamenev, MD/PhD Nadezhda Women’s Health Hospital, Sofia, Bulgaria.

OBJECTIVE: Intrauterine administration of human chorionic gonadotropin (hCG) activated peripheral blood mononuclear cells (PBMC) has positive effect on embryo implantation in repeated implantation failure patients. This effect is mainly caused by the PBMC cytokine production. The aim of this study was to find association between the tumor necrosis factor alpha (TNFa), interleukin 6 (IL6), interleukin 4 (IL4) and interleukin 10 (IL10) plasma levels and their respective concentrations in the media of cultivated PBMC alone or treated with hCG.

MATERIALS AND METHODS: Plasma and PBMCs were isolated from 8 ml of whole blood from 20 healthy women. PBMCs were collected after gradient centrifugation using Pancoll (60100, Biotech). PBMC (1x106 cells/ml) suspended in RPMI medium (E15842, APP) with 1% FCS (GHSA125, LifeGlobal) were incubated alone or with 10 IU hCG (HOR-250, Biotang) for 24h at 37°C.

Concentrations of TNFa, IL6, IL4 and IL10 in the blood plasma and the PBMC media were measured by sandwich enzyme-linked immunosorbent assay (CSBE04740h, CSBE04638h, CSBE04633h and CSBE04593h, Cusabio, respectively) according to the manufacturers’ instructions.

Cytokine alteration in the cultivated PBMC media was presented as fold change from their respective plasma levels. Statistical analyses were performed using SPSS V21.

RESULTS: The median plasma cytokine levels were: 2.1 (0.55-4.3) pg/ml for TNFa; 0.1 (4.3) pg/ml for IL6; 11.7 (1.7-780.4) pg/ml for IL4 and 1.8 (0.2-326.4) pg/ml for IL10.

The cytokines fold changes from their plasma levels after PBMC cultivation alone or with hCG activation were: 19 (0.8618) and 20.1 (0.665) for TNFa; 8380.0 (232.17818) and 7011.2 (447.172275) for IL6; 1.1 (0.1-17.4) and 0.1 (0.1-14.4) for IL4 and 1.3 (0.1-169.4) and 3.1 (0.2-190.8) for IL10, respectively. Wilcoxon signed ranks test showed no differences in the fold changes of the cytokine concentrations between the untreated and hCG treated PBMC media (p=0.05).

Spearman analysis revealed significant negative correlation between the IL10 plasma levels and its fold change in both untreated and hCG treated PBMC samples (R=-0.696; p<0.001) and R=-0.615; p<0.001, respectively). This trend was also observed for IL4 plasma levels and its fold change in both untreated and hCG treated PBMC media (R=-0.859, p<0.001 and R=-0.841, p<0.001, respectively).

Plasma levels of TNFa and IL6 did not show any correlation with their respective fold changes in the PBMC media (p=0.05).
CONCLUSIONS: In this study hCG treatment of PBMC did not have significant effect on the cytokine secretion when compared to the untreated PBMC. The increase of the studied anti-inflammatory cytokines after PBMC cultivation, either with or without hCG activation, is negatively related to their respective plasma levels.

IMPACT STATEMENT: The anti-inflammatory cytokine plasma levels could serve as an indicator of the PBMC cytokine secretion ability with or without activation with hCG. Knowledge on the PBMC cytokine secretion could improve the future research on the exact mechanisms of how the PBMC treatment favours embryo implantation.

SUPPORT: N/A

References: N/A

O-259 10:45 AM Wednesday, October 26, 2022


OBJECTIVE: Biomarkers can change the way we diagnose and manage women with a possible ectopic pregnancy (EP). After initial discovery, candidate biomarkers must demonstrate good discrimination from disease and control using a clinically available high quality validated assay prior to widespread implementation.

MATERIALS AND METHODS: With initial discovery data, we developed a pool of 26 biomarker candidates for pregnancy location and viability using a combination of agnostic proteomic screening or hypothesized putative biological function. We first assessed assay performance (functional sensitivity, range, recovery/linearity, intra-assay precision, and trend) using serum from two pools of women with early pregnancy. We then screened the pool of markers using Enzyme-linked immunosorbent assays (ELISA) in a case-control study among patients with definitive intrauterine pregnancy (IUP) n=70, pregnancy loss (SAB) n=70 or EP (n=70). Ability to discriminate outcome was assessed by Area Under the Curve (AUC) with 95% Confidence Intervals, measures of central tendency with two-sample t-tests, and visual plots.

RESULTS: Three candidate markers demonstrated unacceptable assay performance. Of the remaining 23 biomarkers, seven had an AUC >0.6 and/or statistically significant difference in measure of central tendency for discrimination of pregnancy viability (IUP vs. EP and SAB) and location (EP vs. SAB and IUP).

CONCLUSIONS: Many biomarkers have been proposed but few are validated. Through careful iterative analysis we have successfully honed a pool of novel candidates leading to 7 markers that may predict pregnancy viability and 7 overlapping markers that may predict location. Our next step will be to validate the use of these markers in combination.

IMPACT STATEMENT: By improving detection of ectopic pregnancy, biomarkers can facilitate noninvasive intervention, reduce morbidity, and avoid detrimental intervention from misdiagnosis.

O-260 11:00 AM Wednesday, October 26, 2022

APPLICATION OF A MULTIPLEX PLATFORM TO IDENTIFY NOVEL BIOMARKERS FOR PREGNANCY LOCATION AND VIABILITY. Iris TIENLYNN. Lee, M.D., Nathan C. Koelper, MPH, Courtney A. Schreiber, M.D., Suneeta Senapati, MD, MSCE, Mary Sammel, D.Sc., S.C.D., Kurt T. Barnhart, MD, MSCE, UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, PHILADELPHIA, PA; UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, PHILADELPHIA, PA; UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, PHILADELPHIA, PA; UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, PHILADELPHIA, PA; UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, PHILADELPHIA, PA.

OBJECTIVE: To identify novel biomarkers to distinguish ectopic pregnancy (EP), spontaneous abortion (SAB), and viable intrauterine pregnancy (IUP) using a high throughput multiplex platform.

MATERIALS AND METHODS: We conducted a case-control study including EPs, SABs, and viable IUPs. Serum was obtained from patients presenting for early pregnancy assessment. Using the Olink Proteomics multiplex proximity extension assay, serum concentrations of 1012 candidate biomarkers were compared between cases and controls, with separate comparisons for pregnancy location (EP versus SAB + early IUP) and viability (SAB versus early + late viable IUP). The discriminatory ability of a given biomarker was determined by the area under receiver operating characteristic curve (AUC).

RESULTS: We included 13 EPs, 89 SABs, and 27 viable (13 early, 14 late) IUPs. Twenty markers (2% of all tested) had an AUC of 0.8: 18 for pregnancy location and 2 for viability. For pregnancy location, most markers were lower in EP but 3 were higher: thyrotropin subunit beta (TSHB), carbonic anhydrase 3 (CA3), and probable ATP-dependent RNA helicase (DDX58). Some proteins such as Pappalysin-1 had been previously explored as biomarkers for pregnancy outcome, while others had not. Markers were

### Top Biomarkers

<table>
<thead>
<tr>
<th>Location (EP vs. IUP and SAB)</th>
<th>Biologic Mechanism</th>
<th>AUC</th>
<th>p value</th>
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<tr>
<td>PSG9</td>
<td>Trophoblast function</td>
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<td>PSG3</td>
<td>Trophoblast function</td>
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<tr>
<td>PSG1</td>
<td>Trophoblast function</td>
<td>0.621</td>
<td>0.019</td>
</tr>
<tr>
<td>Location (EP vs. IUP and SAB)</td>
<td>Biologic Mechanism</td>
<td>AUC</td>
<td>p value</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-------------------</td>
<td>-----</td>
<td>---------</td>
</tr>
<tr>
<td>PSG9</td>
<td>Trophoblast function</td>
<td>0.871</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PSG1</td>
<td>Trophoblast function</td>
<td>0.867</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IGFBP1</td>
<td>Endometrial function, cell migration</td>
<td>0.758</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>KISS1</td>
<td>Trophoblast function, cell adhesion</td>
<td>0.705</td>
<td>0.001</td>
</tr>
<tr>
<td>PSG3</td>
<td>Trophoblast function</td>
<td>0.644</td>
<td>0.021</td>
</tr>
<tr>
<td>NOTUM</td>
<td>Trophoblast function, cell signaling</td>
<td>0.613</td>
<td>0.064</td>
</tr>
<tr>
<td>PARVB</td>
<td>Cell adhesion, differentiation</td>
<td>0.604</td>
<td>0.155</td>
</tr>
</tbody>
</table>
implicated in pathways including cell migration, immune regulation, and angiogenesis among others.

CONCLUSIONS: We identified novel biomarkers for pregnancy location and viability. Further work is needed to elucidate their physiological roles and to validate biomarker assays in the clinical setting.

IMPACT STATEMENT: Serum biomarkers may offer a noninvasive technique to differentiate between EP and IUP as well as to predict pregnancy viability.

RESULTS: We identified 1,941 RPL patients (age: mean 34.1, standard deviation 5.8), and 1,941 control patients (age: mean 34.1, standard deviation 5.4). Of 1,401 clinical phenotypes analyzed, 169 phenotypes are significantly (adjusted p-value < 0.05) associated with RPL, including 49 that are also significant prior to first loss (denoted with *). Our findings include known associations: congenital anomalies of genital organs* (OR = 7.07), cervical insufficiency*y (OR = 4.11), primary hypercoagulable state (OR = 3.33), diabetes mellitus (OR = 3.31), hypothyroidism (OR = 1.51), and pituitary hyperfunction (OR = 4.15). Controversial or previously unreported associations include: ovarian dysfunction* (OR = 5.39), polycystic ovarian syndrome* (OR = 2.20), infertility* (OR = 3.44), irregular menstrual cycle/breastfeeding* (OR = 2.27) and endometriosis (OR = 1.87). Intriguingly, we also found several pain-related associations: nonspecific chest pain* (OR = 1.44), pain in joint* (OR = 1.50), pain in limb* (OR = 1.45), and migraine (OR = 1.52).

CONCLUSIONS: Using EHR data, we identified both well-known phenotypes and intriguing phenotypes associated with RPL, including many that are related to reproductive health or pain. Future directions include clinician chart review, integration of procedure and medication data, evaluation of differences in length or depth of EHR records between cohorts, prediction models based on data prior to first loss, and causal inference approaches for quantifying modifiable targets for prevention of RPL. This is an exciting step in leveraging big data for deep phenotyping of RPL and opens up new avenues for further study.

IMPACT STATEMENT: Uncovering novel hypotheses about RPL etiology could lead to more personalized reproductive diagnoses and treatment opportunities for RPL patients, with the aim of achieving successful pregnancies.

SUPPORT: This material is based upon work supported by the National Science Foundation Graduate Research Fellowship Program under Grant No. 2038436. Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the National Science Foundation.
OBJECTIVE: There is controversy surrounding the utility of in vitro fertilization (IVF) and preimplantation genetic testing for aneuploidy (PGT-A) as a treatment for women with recurrent pregnancy loss (RPL). We hypothesized that in women with RPL, the addition of PGT-A would improve the probability of live birth per cycle start in the first embryo transfer following retrieval. This study aims to evaluate the impact of PGT-A on IVF outcomes among women with RPL in the United States (US).

MATERIALS AND METHODS: This was a Society for Assisted Reproductive Technology (SART) Registry Retrospective Cohort Study. Institutional Review Board approval was obtained. The first IVF cycle between 2016 and 2020 among women with RPL as their only SART diagnosis were included. All banking cycles and cycles utilizing donor oocytes or gestational carriers were excluded. Live birth rates were compared between IVF cycles utilizing PGT-A and cycles without PGT-A. The primary outcome was the live birth rate per cycle start. Only the first embryo transfer (fresh or frozen) was used for outcome calculations. A secondary analysis was performed to stratify by age and to compare miscarriage rates. Miscarriage rate was calculated as biochemical and clinical pregnancy losses per pregnancy. Continuous variables were compared with a student’s-t-test and categorical variables with a Chi-square. A multi-variable analysis was performed to assess the independent contribution of PGT-A and control for confounders, including patient age, anti-mullerian hormone level, ethnicity and geographic region.

RESULTS: A total of 3951 first IVF cycles among women with an isolated diagnosis of RPL were included, 1656 cycles in which no embryos underwent PGT-A and 2295 cycles in which all embryos underwent PGT-A. Embryo transfers were performed in 66.7% (1104/1656) of cycles without PGT-A and 72.8% (1670/2295) of cycles with PGT-A (P<0.0001). The live birth rate per cycle start was 24.2% (400/1656) in cycles without PGT-A and 41.0% (942/2295) in cycles with PGT-A, (P<0.0001). When analyzed on a per transfer basis, the live birth rate per transfer was 36.23% (400/1104) in transfers without PGT-A and 56.41% (942/1670) in transfers with PGT-A (P<0.0001). The miscarriage rate was 36.5% (240/657) in cycles without PGT-A and 23.18% (287/1238) in cycles with PGT-A, P<0.0001. After controlling for confounders, the live birth rate per cycle start was significantly higher in cycles that utilized PGT-A (OR=1.8, 95% CI 1.5, 2.1, P<0.0001).

CONCLUSIONS: Among women undergoing IVF in the US with an isolated diagnosis of RPL, there is a significantly higher live birth rate per cycle start in cycles that utilize PGT-A. The use of PGT-A in women with RPL undergoing IVF results in a significantly lower miscarriage rate (23% vs 37%).

IMPACT STATEMENT: The use of PGT-A does result in a higher live birth rate per cycle start among women with RPL undergoing IVF in the US.

0-263 11:45 AM Wednesday, October 26, 2022
THE ADENO STUDY: ADENOMYOSIS IN DUTCH WOMEN AND ITS EFFECT ON NEONATAL AND OBSTETRIC OUTCOMES: A RETROSPECTIVE POPULATION-BASED STUDY. Connie Odette Rees, MD, MSc,1 Huib Van Vliet, MD, PhD,1 Albertus Siebers, PhD,2 Michelle Westerhuis, MD, PhD,1 Aleida G. Huppelschoten, MD, PhD,1 Benedictus Christiana Schoot, MD, PhD,1 1Department of Gynaecology and Obstetrics, Catharina Hospital Eindhoven, Eindhoven, Netherlands; 2PALGA, Houten, Netherlands.

OBJECTIVE: To retrospectively investigate prevalence of adverse obstetric and neonatal outcomes in women with histopathologically proven adenomyosis compared to the general (Dutch) population.

MATERIALS AND METHODS: Design: Retrospective population-based cohort study
Women with pregnancy outcomes in the Dutch national Perined registry, who also received a histopathological diagnosis of adenomyosis (post-hysterectomy) between 1995 to 2018, as registered in the Dutch national pathological registry, were included. Pregnancy outcomes of 7,925 women with a histopathological diagnosis of adenomyosis were compared to 4,615,803 women without adenomyosis. Adjusted Odds Ratios (aOR, 95% CI) were calculated. Outcomes were corrected for: maternal age, parity, ethnicity, year of registered birth, induction of labour, hypertensive disorders in pregnancy, multiple gestation and low socioeconomic status.

RESULTS: Women with adenomyosis had an aOR of 1.37 (95% CI 1.25-1.50) for hypertensive disorders, an aOR of 1.37 (95% CI 1.25-1.51) for preeclampsia, and an aOR of 1.15 (95% CI 1.07-1.25) for small-for-gestational-age. They had an aOR of 1.54 (95% CI 1.41-1.68) for neonatal perinatal death, an aOR of 1.24 (95% CI 1.21-1.27) for failure to progress in labour, an aOR of 1.28 (95% CI 1.10-1.48) for placental reten- tion and an aOR of 1.23 (95% CI 1.10-1.38) for postpartum haemorrhage.

CONCLUSIONS: We conclude that women with adenomyosis show an increased prevalence of a variety of adverse obstetric outcomes, specifically hypertensive disorders of pregnancy, small-for-gestational age, failure to progress in labour and placental retention. This seems to confirm the theory that uterine placental invasion and contractile function in labour may be impaired in women with adenomyosis.

IMPACT STATEMENT: Up to now, this is the largest study which investigates the impact of adenomyosis on obstetric outcomes, and it is the first study which uses the golden standard of adenomyosis diagnosis by histopathology. We suggest that results with (suspected) adenomyosis form a group at higher risk of obstetric complications, and thereby could be seen as having high-risk pregnancies.

SUPPORT: None.

0-264 12:00 PM Wednesday, October 26, 2022
ALTERATIONS OF X-CHROMOSOME INACTIVATION (XCI) IN PREDISPOSITION TO RECURRENT PREGNANCY LOSS (RPL): A TRANSCRIPT LEVEL STUDY IN THE NORTHEAST INDIAN POPULATION. Natasha Khashyap, M.Sc.,1 Chandana Ray Das, MD, Ph.D.,2 Ratul Dutta, MD,1 Anjuma Begum, M.Sc.,1 Sujoy Bose, M.Sc., Ph.D.,4 Purabi Deka Bose, M.Sc., Ph.D.1 1MBBT Department, Cotton University, Guwahati, Assam, India; 2Gauhati Medical College and Hospital, Guwahati, India; 3Down Town Hospitals, Guwahati, India; 4Gauhati University, Guwahati, India; 5MBBT Department, Cotton University, Guwahati, India.

OBJECTIVE: Recurrent pregnancy loss (RPL) affects 1-5% of reproductive age women, with a prevalence of 7.46% in the Indian population. Although the role of genetic modifications of the X-chromosome has been associated with idiopathic RPL in some populations, no such study is available in the Indian context. This study, therefore, aims to elucidate the role of alterations in the transcript levels of genes associated with X-chromosome inactivation (XCI) as a cause for predisposition to RPL.

MATERIALS AND METHODS: RPL patients who had undergone three or more spontaneous miscarriages (N=21) and medically terminated pregnancies (MTP) cases (n=35) were enrolled for this study. Transcript level study of X-inactive specific transcript (XIST), TSIX (reverse of XIST) and X-active specific transcript (XACT) was carried out in the product of conception (P0Cs) collected from the MTP and RPL cases, with informed consent. The expression of these genes in XIST-associated cases was studied using Real Time PCR using beta actin as an internal control. Correlation analysis for these genes was also carried out using SPSS statistical software.

RESULTS: The differential expression data showed that XIST non-coding RNA (ncRNA) was downregulated in the RPL cases as compared to the MTP cases (0.09 ± 0.13 folds); although an upregulation was observed in two cases. In these two cases, further analysis was carried out for TSIX and XACT ncRNA expression (which works anti-sense to XIST), and an upregulation of at least one of these two factors was observed in these two cases. Additionally, the TSIX ncRNA expression was also downregulated (0.92 ± 0.7 folds) in the RPL cases, while the XACT ncRNA was upregulated (1.59 ± 1.5 folds) in the RPL cases compared to the controls. Bivariate correlation analysis also shows a significant negative correlation between the expression of XIST and TSIX ncRNA (P<0.01) in the RPL cases.

CONCLUSIONS: The downregulation of XIST ncRNA with a subsequent upregulation of its antagonists is indicative of a skewed XCI at the transcript level in the RPL cases. The results are therefore suggestive of a possible deregulation in the critical X-chromosome inactivation (XCI) process which in turn may have a detrimental role in RPL pathogenesis.

IMPACT STATEMENT: This study elucidates the possible role of alterations in the critical process of XCI in RPL predisposition in the ethnically distinct Northeast Indian population. The genetic factors associated with XCI therefore play an important role in RPL and can be targeted through therapeutic interventions to enable a sub-group of RPL patients to carry a pregnancy to term.
OBJECTIVE: To evaluate the risk of GDM in singleton pregnancies conceived via infertility treatment and examine the influence of race/ethnicity and pre-pregnancy BMI.

MATERIALS AND METHODS: We utilized the US vital records data of singleton stillbirths and live births (delivered between 20-44 weeks' gestation) from 2015-2020. We examined the risk of GDM by infertility treatment type after bifurcation into two groups: (i) those that used fertility-enhancing drugs, artificial insemination, or IUI; and (ii) those that used assisted reproductive technology (ART). Women diagnosed with diabetes prior to pregnancy were excluded. We then examined if the infertility treatment-GDM association was modified by maternal race/ethnicity and pre-pregnancy BMI. Associations were expressed as risk ratio (RR) and 95% confidence intervals (CI), derived from log-linear models following adjustment for potential confounders.

RESULTS: Of the 21,943,384 singleton births (2015-2020), 1.5% (n=318,086) received an infertility treatment. The GDM risk was 11.0% (n=34,946) and 6.5% (n=1,398,613) among any type of infertility treatment and spontaneous conceptions, respectively (Table 1). The risk of GDM was modestly increased for fertility-enhancing drugs compared to ART, and this risk was especially apparent for Non-Hispanic White women (RR 1.29, 95% CI 1.29, 1.41) and Hispanic women (RR 1.35, 95% CI 1.29, 1.41). Pre-pregnancy BMI did not modify the infertility treatment-GDM association overall, and within strata of race/ethnicity.

CONCLUSIONS: A timely diagnosis and management of GDM is paramount importance due to its well-known associations with several poor obstetric and neonatal outcomes. Infertility treatment is associated with an increased risk of developing GDM across all races and this association is more apparent with fertility-enhancing drugs. The persistently higher risk of GDM among women that seek infertility treatment, irrespective of pre-pregnancy weight classification, deserves attention.

Table 1. Risk of GDM in Relation to Infertility Treatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Births</th>
<th>GDM: n (%)</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous conceptions</td>
<td>21,625,298</td>
<td>1,398,613 (6.5)</td>
<td>1.00 (Reference)</td>
</tr>
<tr>
<td>Any infertility treatment</td>
<td>318,086</td>
<td>34,946 (11.0)</td>
<td>1.24 (1.23-1.26)</td>
</tr>
<tr>
<td>ART</td>
<td>188,380</td>
<td>20,577 (10.9)</td>
<td>1.18 (1.17-1.20)</td>
</tr>
<tr>
<td>Fertility-enhancing drugs</td>
<td>132,954</td>
<td>118,330 (89.0)</td>
<td>1.28 (1.27-1.30)</td>
</tr>
</tbody>
</table>

IMPACT STATEMENT: Infertility treatment should be considered an independent risk factor for the development of GDM, and special attention should be given to those receiving fertility-enhancing drugs. Infertility specialists must be vigilant with preconception counseling to ensure that all patients, regardless of race/ethnicity or pre-pregnancy BMI, are adequately tested for GDM early in pregnancy.
O-268 11:15 AM Wednesday, October 26, 2022

WEIGHT CHANGES IN GRAVIDAE CONCEIVING WITH ASSISTED REPRODUCTIVE TECHNOLOGIES (ART) IN MULTIPLE PREGNANCIES. Alexa M. Sassin, MD,1 Haleh Sanghi-Haghpeykar, PhD,2 Kjersti M. Aagaard, MD, PhD2 Houston, TX;3 Baylor College of Medicine, Houston, TX.

OBJECTIVE: The amount of weight gained during pregnancy can have immediate and long-term effects on the future health of the pregnant person and their offspring. However, longitudinal prospective datasets which allow for interrogation of pre-pregnancy weight, weight change throughout pregnancy, and weight at time of delivery over multiple ART pregnancies are sparse. We sought to examine how these variables vary from pregnancy to pregnancy in gravidae who have conceived more than once with ART.

MATERIALS AND METHODS: A 2-hospital, single academic institution, population-based database comprised of over 60,000 participants with pregnancy data incorporating Aug 2011 to Jan 2022 was employed. We extracted all singleton deliveries, selecting only for pregnancies conceived with ART including ovulation induction, intracytoplasmic sperm injection, in vitro fertilization, and intratuterine insemination. From this group, participants with two ART deliveries in the database were selected as the study sample of interest (n=109 subjects, 218 deliveries). Pre-pregnancy weight, weight at delivery, pre-pregnancy body mass index (BMI), and BMI at delivery were identified. Changes in weight during pregnancy were subsequently calculated. Pre-pregnancy weights were used to identify whether patients achieved the recommended ranges of weight gain based on the ACOG Opinion on weight gain during pregnancy. Statistical analysis was performed using a generalized linear mixed method. A p value <0.05 was considered statistically significant.

RESULTS: We found a significant difference in pre-pregnancy weight (pounds) from the first ART pregnancy (145.7 ± 3.7) to the second ART pregnancy (149 ± 3.7) (p=0.007) as well as a significant difference in weight at delivery from the first pregnancy (174.9 ± 3.5) to the second pregnancy (177.6 ± 3.5) (p=0.01). However, there was no difference in the total weight change from the first pregnancy (29.2 ± 1.3) to the second (28.3 ± 1.5) (p=0.52). Additionally, we found a significant change in pre-pregnancy BMI (kg/m²) from the first ART pregnancy (24.2 ± 0.59) to the second ART pregnancy (24.9 ± 0.59) (p=0.009). There were no differences in the percentages of patients who were “below” (24.8% vs 22.9%), “within” (37.6% vs 41.3%), or “above” (37.6% vs 35.8%) the recommended weight gain for their first versus second ART pregnancy respectively (p=0.92).

CONCLUSIONS: Gravidae’s pre-pregnancy weight, pre-pregnancy BMI, and weight at delivery all increase significantly with each subsequent ART pregnancy. However, the overall rates of achieving the recommended weight gain did not change from the first to second ART pregnancy. Future studies are needed to evaluate how weight changes with subsequent ART pregnancies beyond a second ART pregnancy, and whether initial weight loss or limited inter-pregnancy weight gain could render beneficial impact on maternal or neonatal outcomes.

IMPACT STATEMENT: In women who have achieved more than one ART pregnancy, there is a statistically significant difference in pre-pregnancy weight, weight at delivery, and pre-pregnancy BMI from the first to second pregnancy.

SUPPORT: Women’s Reproductive Health Research program NIH/NICHD K12 HD103087.


O-269 11:45 AM Wednesday, October 26, 2022

THE IMPACT OF OBESITY AND ADIPOSETIS ON ANTI-MULLERIAN HORMONE (AMH) LEVELS IN A LATINA/LATINX POPULATION. Samantha B. Schon, M.D., M.S.,1 Charley Jiang, M.S.,2 Ali A. Bazzi, M.D.,3 Felix Valbuena, Jr., M.D.,1 Donna D. Baird, Ph.D.,2 Erica E. Marsh, M.D., MSCI, FACOG1 Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI;2 MD/MSCR candidate, Ann Arbor, MI;3 University of Michigan, Ann Arbor, MI;4Community Health and Social Services (CHASS) Center, Detroit, MI;5National Institute of Environmental Health Sciences, NIH, Durham, NC.

REFERENCES: ISO 110 ASRM Abstracts Vol. 118, No. 4, Supplement, October 2022
OBJECTIVE: Research suggests that obesity has an adverse effect on ovarian reserve, as assessed by AMH. Previous studies have explored this association predominantly in Caucasian non-Hispanic and African American cohorts. Additionally, studies have predominantly utilized BMI to categorize patients as having obesity. The objective of this study was to examine the association of obesity/adiposity with AMH in a Latina/Latinx population using multiple measures of obesity/adiposity.

MATERIALS AND METHODS: This cross-sectional study utilized data from the Environment, Leiomyomas, Latinas, and Adiposity Study (ELLAS). ELLAS is a prospective longitudinal cohort study conducted in Michigan following Latina/LatinX females for 5 years. All participants were between the ages of 21-50 at time of consent and data from the first study visit was utilized for analysis. Anthropometric measurements, bioelectrical impedance analysis (BIA) and serum AMH (pico-AMH assay, Ansh Labs, Webster, TX) were included in the analysis. The effects of BMI and waist/hip ratio (w/h) on AMH were assessed as both continuous and categorical outcomes. The impact of adiposity including fat percentage, and visceral fat percentage on AMH was also assessed as a continuous variable. Statistical associations were determined using Chi-square, Wilcoxon rank-sum and linear or logistic regression as appropriate.

RESULTS: A total of 720 women are enrolled in ELLAS. 603 completed the first study visit and had BMI, w/h and AMH data available. BIA data was available on 571 participants. The mean age of study participants was 37.4 ± 6.95 years. The mean BMI of the study population was 30.1 ± 7.67 kg/m², with 470 (78%) of participants classified as having obesity by BMI (BMI ≥ 30 kg/m²). BMI was significantly associated with AMH (β=-0.055 p=0.014), however, this association was no longer significant after adjusting for age. Similarly, percent body fat and visceral fat percentage were also negatively associated with AMH (β=-0.058 p=0.013, and β=-0.256 p<0.001), however this association did not hold after adjusting for age.

CONCLUSIONS: Among a cohort of Latina/LatinX females, obesity and adiposity as assessed by BMI, waist/hip circumference and percent body fat were not associated with AMH. These findings demonstrate the importance of study population in considering the impact of obesity on AMH levels and highlights the need for additional studies in diverse populations.

IMPACT STATEMENT: In contrast to findings in populations who self-identify as White or African American, obesity as assessed by BMI, waist/hip and percent body fat is not associated with AMH in this Latina/Latinx cohort of reproductive aged females.

Table 1:

<table>
<thead>
<tr>
<th>Reproductive outcome</th>
<th>Group A (BMI &lt; 30 kg/m²) (n= 297)</th>
<th>Group B (BMI ≥ 30 kg/m²) (n= 179)</th>
<th>p value</th>
<th>Adjusted p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live Birth Rate</td>
<td>52.5%</td>
<td>49.2%</td>
<td>0.50</td>
<td>0.78</td>
</tr>
<tr>
<td>Clinical Pregnancy Rate</td>
<td>65.0%</td>
<td>66.5%</td>
<td>0.80</td>
<td>0.20</td>
</tr>
<tr>
<td>Miscarriage Rate</td>
<td>18.1%</td>
<td>23.5%</td>
<td>0.20</td>
<td>0.02</td>
</tr>
</tbody>
</table>
E-PAPER ABSTRACT SESSION: 1

P-1 6:30 AM Monday, October 24, 2022

CAN MORPHOKINETIC PARAMETERS REFLECT BLASTOCYST PLOIDY STATUS? A PROSPECTIVE STUDY. Manar Hozyen, MSc;1 Amr Elshimy, BSc;2 Eman Mohammad Hasanen, BSc;3 Hanan Ahmed Alkhdher, MBBC;4 Hosam H. Zaki, M.B.B.CH., M.D., M.SC. 1Ganin Fertility Center IVF lab, Cairo, Egypt; 2Ganin IVF lab Director, Cairo, Egypt; 3Clinical Embryologist, Cairo, Egypt; 4Ganin IVF lab Director, Cairo, Egypt.

OBJECTIVE: To determine if there is a relation between the morphokinetic parameters and ploidy status of blastocysts.

MATERIALS AND METHODS: A prospective study of 389 blastocysts from 132 ICSI couples at a private center from December 2021 to March 2022. Cases are eligible if they planned to do PGT-A for their blastocyst from 132 ICSI couples at a private center from December 2021 to March 2022. All embryos were cultured in Mii° time-lapse incubators under the same conditions. Morphokinetic annotations were done manually, and PGT-A was done using next generation sequencing. Data were analyzed using SPSS v23.

RESULTS:

<table>
<thead>
<tr>
<th>Euploid n = 191</th>
<th>Aneuploid n = 136</th>
<th>Low mosaic n = 24</th>
<th>High mosaic n = 38</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Morphokinetic annotations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tPB2 (time of polar body extrusion)</td>
<td>3.6±1.2</td>
<td>3.5±1.3a</td>
<td>4.2±1.1b</td>
<td>3.8±1.4</td>
</tr>
<tr>
<td>tPA (time of 2PN appearance)</td>
<td>12.2±3.8</td>
<td>11.7±3.8</td>
<td>12.9±3.8</td>
<td>11.9±4.2</td>
</tr>
<tr>
<td>tPN (time of PN fading)</td>
<td>22±4.8</td>
<td>23.2±3.4</td>
<td>22.1±3.7</td>
<td>22±5.3</td>
</tr>
<tr>
<td>t2 (time to 2 cell)</td>
<td>26.1±4</td>
<td>26.2±3.3</td>
<td>25.7±3.1</td>
<td>26.9±4.4</td>
</tr>
<tr>
<td>t3 (time to 3 cell)</td>
<td>36.4±9.1</td>
<td>36.8±5.4</td>
<td>33.4±7.1</td>
<td>37.2±7.1</td>
</tr>
<tr>
<td>t4 (time to 4 cell)</td>
<td>39.1±6.5</td>
<td>39.6±5.4</td>
<td>37.3±5.6</td>
<td>39.7±5.2</td>
</tr>
<tr>
<td>t5 (time to 5 cell)</td>
<td>50.4±9.6</td>
<td>51.5±8.4</td>
<td>47.9±10.3</td>
<td>51.6±9</td>
</tr>
<tr>
<td>t6 (time to 6 cell)</td>
<td>54.1±8.4</td>
<td>54.9±8.5</td>
<td>52±9.9</td>
<td>55.5±8.5</td>
</tr>
<tr>
<td>t7 (time to 7 cell)</td>
<td>58.9±10.4</td>
<td>60.4±11.3</td>
<td>56.8±13.1</td>
<td>59.1±10.6</td>
</tr>
<tr>
<td>t8 (time to 8 cell)</td>
<td>66.8±11.1</td>
<td>67.5±11.9</td>
<td>66.9±14.7</td>
<td>67.7±12.6</td>
</tr>
<tr>
<td>tS (time to start compaction)</td>
<td>79.8±15.1</td>
<td>69.5±14.9</td>
<td>97±19.8</td>
<td>80.8±15</td>
</tr>
<tr>
<td>tM (time to morula)</td>
<td>91.9±12.2</td>
<td>92.9±12.1</td>
<td>97.3±12.7</td>
<td>93.8±13.3</td>
</tr>
<tr>
<td>tSB (time to start blasting)</td>
<td>104.4±11.3a</td>
<td>106.9±10.3</td>
<td>108.4±11.4b</td>
<td>108±11.4b</td>
</tr>
<tr>
<td>tB (time to full blastocyst)</td>
<td>114±11.6a</td>
<td>117±11.4b</td>
<td>117.4±12.5b</td>
<td>117±8.7b</td>
</tr>
<tr>
<td>tEB (time to expanded blastocyst)</td>
<td>120.8±11.4</td>
<td>124±11.1</td>
<td>120.1±11.3</td>
<td>127±12.3</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation. n: number of embryos. *significant difference p ≤0.05 between a and b

2. Additional dynamic annotations

| Abnormal fertilization (0.1/3PNs) | 7/191 (3.6%) | 10/136 (7.3%) | 2/24 (8.3%) | 4/38 (10.5%) | 0.10 |
| Fragmentation (>5%) | 78/191 (40.8%) | 47/136 (34.5%) | 11/24 (45.8%) | 10/38 (26.3%) | 0.11 |
| Multinucleation at 2 cell | 85/191 (44.4%) | 51/136 (37.5%)a | 8/24 (33.1%) | 21/38 (55.2%)b | 0.05* |
| Multinucleation after 2 cell | 17/191 (8.9%)a | 31/136 (22.7%)b | 2/24 (8.3%) | 5/38 (13.1%) | >0.00* |
| Direct cleavage | 7/191 (3.6%)a | 16/136 (11.7%)b | 0/24 | 1/38 (2.6%) | 0.004* |
| No polar body extrusion | 5/191 (2.6%)a | 10/136 (7.5%)b | 0/24 | 0/38 | 0.04* |

Data are percentages. *significant difference p ≤0.05 between a and b

CONCLUSIONS: Our results showed a strong relationship between some morphokinetic parameters and the ploidy status of embryos. Hence, morphokinetics may help in selecting embryos to be tested for ploidy.

IMPACT STATEMENT: Combining morphokinetics with PGT-A will have financial implications for programs that charge per embryo rather than a cohort of embryos, to select embryos that are more likely to be euploid.

P-2 6:30 AM Monday, October 24, 2022


OBJECTIVE: To assess ERICA, a machine learning software, as a tool of predictive value with potential to distinguish the blastocyst with the highest probability of euploidy.

V ol. 118, No. 4, Supplement, October 2022
MATERIALS AND METHODS: A total 1890 blastocyst images from a single clinic were evaluated by ERICA (IVF 2.0 LTD, UK) from March 2021 to February 2022 and considered for this study. All embryo images were captured 5 or 6 days after fertilization before biopsy using regular micromanipulation techniques. The blastocyst was frozen after trophectoderm biopsy for preimplantation genetic testing for aneuploidy (PGT-A). Images from mosaic embryos and images not meeting evaluation criteria were excluded.

Cycles with both euploid and aneuploid embryos were assessed by the normalized Discounted Cumulative Gain (NDCG), where a value of 1 would be the perfect ranking (all euploids with a better ranking than aneuploids).

RESULTS: After applying the inclusion and exclusion criteria, 110 embryos from 60 cycles subject to PGT-A remained. The overall euploidy rate was 44.5% in this dataset and the mean patient’s age at the moment of the oocyte retrieval for autologous oocytes was 37.7.

Amongst cycles with both euploid and aneuploid embryos (17 cycles, 46 embryos, euploidy rate of 52.2%), the probability of finding a euploid embryo on top of the ranking according to ERICA was 70.6%, and an aneuploid at the bottom was 76.5%, regardless of the label assigned to the embryo. Additionally, the mean NDCG for these cycles was 0.88.

CONCLUSIONS: Using the ERICA algorithm, it was possible to predict the embryo with the highest prognosis for euploidy a positive predictive value for euploidy estimated at 70.6% on top of the ranking is for now good enough to guide embryologists during the embryo selection process in those cases where PGT-A was not performed.

NDCG is currently considered as the best metric to assess ranking algorithms, and the reported performance is robust. A larger sample will always be a moving target we should aim for to evaluate performance of any AI through time.

IMPACT STATEMENT: This tool represents a potentially significant advantage in helping embryologists when prioritizing the order to transfer embryos and to choose the best embryo with the highest euploidy probability, saving time spent on annotation, no time-lapse or when invasive biopsy is not possible or desirable.

SUPPORT: New Hope Fertility Center.
COMBINED USE OF ARTIFICIAL INTELLIGENCE (AI) ALGORITHMS FOR EVALUATING EMBRYO VIABILITY AND EMBRYO GENETICS IMPROVES SELECTION OF EMBRYOS LEADING TO CLINICAL PREGNANCY. Sonya M. Diakiw, PhD.1 Jonathan MM. Hall, PhD.2 Matthew VerMilyea, PhD.3 Adelle Yun Xin Lim, M.S.C.1 Ashleigh Storr, PhD.1 Rebecca Matthews, PhD.6 Tuc Van Nguyen, PhD.7 Don Perugini, PhD.1 Michelle Perugini, PhD.1 CAI Wen Chan, BA Sc.1 Life Whisperer Diagnostics Inc (a subsidiary of Presagen), San Francisco, CA; 2 Life Whisperer Diagnostics Pty Ltd (a subsidiary of Presagen), Adelaide, SA, Australia; 3 Ovation Fertility, Austin, TX; 4 Alpha IVF & Women’s Specialists, Fertile Asia Malaysia; 5 Fertility Science, Glencelg, SA, Australia; 6 ORM Fertility, Portland, OR; 7 Life Whisperer Diagnostics Pty Ltd (a subsidiary of Presagen), Adelaide, Australia; 8 Life Whisperer Diagnostics Inc (a subsidiary of Presagen), San Francisco.

OBJECTIVE: To determine if a non-invasive AI algorithm for evaluating the likelihood of embryo euploidy (genetics AI) improves selection of viable embryos when used in combination with an AI for evaluating the likelihood of clinical pregnancy (viability AI).

MATERIALS AND METHODS: 1149 embryo images with matched clinical pregnancy outcomes (fetal heartbeat at first scan) were retrospectively obtained from 7 IVF clinics in the USA, Australia, and Malaysia. 670 embryos were known to be euploid using pre-implantation genetic testing for aneuploidies (PGT-A); the remaining 479 embryos had not been biopsied for PGT-A screening.

All images were analyzed by 2 independent AI algorithms developed previously. The ability to select viable embryos was evaluated using a simulated cohort ranking method, also developed previously. In brief, embryo images from different patients were randomized to thousands of simulated embryo cohorts. Embryos in each cohort were ranked according to predicted likelihood of embryo viability, with performance reported as the average number of cycles needed to select an embryo leading to pregnancy.

RESULTS: Both viability and genetics AI scores independently correlated with clinical pregnancy rate (p<0.0001). AI scores significantly correlated with each other (R² = 0.4079), but increasing genetics scores identified a higher proportion of pregnancies when applied to embryos of similar viability scores (>5/10), ranging from 46.3% to 64.7% for genetics scores of >3/10 and >9/10, respectively.

Simulated cohort analyses showed that viability score alone reduced the number of cycles needed to achieve pregnancy by ~20% compared to random ranking. However, when pre-selecting embryos above a genetics score threshold in each cohort, then ranking these embryos according to viability score, the cycles needed to achieve pregnancy were further reduced by up to 5.4% (for genetics scores >9/10). Improvement over Gardner-based ranking almost doubled when pre-selecting embryos with genetics scores >9/10.

Interestingly, the genetics AI only improved ranking of embryos on the subset of embryos which had not been screened using PGT-A; no further improvement was observed on the subset of known euploid embryos.

CONCLUSIONS: Pre-selection of embryos using the genetics AI improved subsequent ranked and selection of viable embryos using the viability AI, with fewer cycles needed to achieve pregnancy. This was only true when ploidy status was unknown, suggesting that the genetics AI may be used in a similar manner to PGT-A to pre-select embryos that are likely to be euploid followed by morphology-based selection for transfer.

IMPACT STATEMENT: Euploid embryos display improved clinical outcomes over mosaic/aneuploid embryos, such as higher pregnancy rates and reduced miscarriages. However, randomized controlled trials have not demonstrated a consistent benefit for PGT-A, possibly due to biopsy damage or misinterpretation of PGT-A results. Alternative non-invasive methods for evaluation of embryo ploidy, like the genetics AI, may improve outcomes when used with other methods for embryo evaluation and selection.

REFERENCES:


OBJECTIVE: To assess deep learning algorithms to predict implantation in vitro fertilization while improving performance of the CNN models trained on embryo images with high variance.

MATERIALS AND METHODS: We retrospectively collected single static images of 1,741 day 5 blastocysts from 1,008 patients who underwent embryo transfer at a single in vitro fertilization (IVF) clinic between January 2015 and March 2021. The images were collected from standard optical light microscopes and matched with pregnancy data such as gestational sac (G-sac) and fetal heartbeat (FHB). We built two convolutional neural network (CNN) models with different pregnancy outcomes; G-sac and FHB, and compared the accuracy and the area under the receiver-operating curve (AUROC). We also observed high variance in visual properties such as color, brightness and contrast as the embryo images were taken under various environments. We applied the MixUp data augmentation method known to maintain the performance of models trained on datasets with high variance. The dataset was split into a training set and a test set with a ratio of 8:2.

RESULTS: The AUROCs of the CNN models predicting G-sac and FHB were 0.78 and 0.72, respectively. After MixUp augmentation, the AUROCs improved to 0.80 and 0.79, respectively. The accuracies of the CNN models predicting G-sac and FHB were 0.75 and 0.63. After applying MixUp, the accuracies went up to 0.75 and 0.68, respectively.

CONCLUSIONS: The CNN models built based on day 5 embryo images successfully predicted G-sac and FHB with high accuracy. Overall, the performance of the G-sac prediction model was better than that of the FHB model. It is expected that non-embryo factors like uterus and immunology become more important as pregnancy advances. Further study to include non-embryo factors in the CNN model may improve the predictive model. We also acknowledge that a high variance in images can reduce performances of the CNN models. In this study, we demonstrated that data augmentation methods like MixUp can improve the performance of the models using images in high variance. The limitation of this study is that it was a retrospective study performed on embryo image data from a single IVF clinic. Cross validation using training data from one clinic and test data from another clinic is warranted.

IMPACT STATEMENT: In this study, we demonstrated that the CNN model successfully predicted clinical pregnancy with high accuracy. However, the further pregnancy advances, the more factors influence the maintenance of pregnancy. To improve the prediction models, further studies are required to identify additional non-embryo factors to include in the models.

REFERENCES:

MATERIALS AND METHODS: This study included 16479 blastocysts with PGT-A results from 5165 treatments across 13 clinics from 2014 to 2021. 6769 blastocysts were euploid and 8168 were aneuploid. All embryos were incubated in time-lapse incubators for a minimum of 5 days. Embryos were split into training (80%) and testing (20%) on the level of euploidy. In this study, we investigated if AI models could be used to prioritize and reduce the number of blastocysts requiring PGT-A testing to attain at least one euploid blastocyst per treatment.

OBJECTIVE: PGT-A testing is time consuming and expensive. Recent AI models have been used to predict ploidy status using embryo images or time-lapse videos with area under the curve (AUC) between 0.62 and 0.75, indicating further advancement in the field. The purpose of the current study was to assess the performance of the AI models in determining the genetic status of embryos using PGT-A entirely, but may help select which blastocysts to test in order to achieve a desired number of euploids. In this study, we investigated if AI models could be used to prioritize and reduce the number of blastocysts requiring PGT-A testing to attain at least one euploid blastocyst per treatment.

RESULTS: The test set AUC for ploidy prediction was 0.681 (n=3470). Euploid rates ranged from 4% (n=139) for low AI scores to 71% (n=139) for high AI scores. By prioritizing 20% of all PGT-A tests with the embryo-level strategy, 54.8% (n=608) of all treatments were unaffected, meaning PGT-A would be carried out on the same blastocysts as previously. In 35.1% (n=389) of all treatments, only aneuploid blastocysts were deprioritized. In 6.0% (n=67) of all treatments, some but not all euploid blastocysts were deprioritized. And in 4.1% (n=45) of all treatments, the only available euploid blastocyst (45 in total) was deprioritized, thus requiring subsequent testing. With this strategy, affected treatments were reduced by 1.4 biopsies.

REFERENCES:

ARTIFICIAL INTELLIGENCE CAN BE USED AS A GUIDE TO SELECT WHICH BLASTOCYSTS TO BIOPSY AND TEST FOR PGT-A. Mikkel Fly Fly Kragh, PhD,1 Jens Rimestad, M.Sc.,1 Jacob Theilgaard Lassen, M.Sc.,2 Martin Johansen, PhD,1 Francesca Buhr, B.Sc.,2 Jørgen Berntsen, M.Sc.1 1Vitrolife A/S, Viby J, Denmark; 2Vitrolife, Inc., San Francisco, CA.

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REFERENCES:

FERTILITY & STERILITY® e115
on average. By deprioritizing 20% of all PGT-A tests with the treatment-level strategy, 81.6% (n = 905) of all treatments were unaffected, 5.5% (n = 61) had only aneuploids deprioritized, 12.2% (n = 135) had some but not all euploids deprioritized, and 0.7% (n = 8) had all available euploid blastocysts (12 in total) deprioritized. Affected treatments were reduced by 3.4 biopsies on average.

CONCLUSIONS: Using AI models to deprioritize PGT-A testing on treatment-level, 20% of all tests could have been avoided, with only 0.7% of all treatments resulting in incorrectly deprioritizing all available euploid blastocysts.

IMPACT STATEMENT: In order to achieve a desired number of euploid blastocysts, PGT-A test prioritization with AI should be based on entire cohorts and not individual blastocyst scores. This strategy may reduce clinical resources and treatment costs, especially for patients with many blastocysts.

P-10 6:30 AM Monday, October 24, 2022

CAN CHLOE EQ³⁴, AN AI-BASED EMBRYOLOGIST ASSISTANT TOOL, AUTOMATICALLY PREDICT WHETHER AN EMBRYO WILL BLASTULATE, BE UTILISED AND/OR IMPLANT?

Claire Miret Lucio, MSc, Marta Lozano, MSc, Adriana Brualla Mora, MSc, Anat Sakov, PhD, Cristina Hickman, PhD, Juana Crespo, Valencia, Spain; Fairtility, London, United Kingdom; Embryotools, Barcelona, Spain; Fairtility, United Kingdom

OBJECTIVE: To compare automatic annotations, pronucleate (PN) detection, blastulation & utilisation prediction by CHLOE EQ³⁴ (FAIRILITY, an AI-based embryologist assistant tool) and experienced embryologists.

MATERIALS AND METHODS: A retrospective cohort study (June 2021 to March 2022) of 2851 time-lapse cultured embryos from 309 patients. Embryos were annotated by experienced embryologists, & automatically by CHLOE. Manual & automatic morphokinetic annotations and PN count were compared to establish strength of agreement using intra-class correlation (ICC). CHLOE’s efficacy of prediction of blastulation (by end of culture & by 116hpi) was assessed using AUC as the efficacy metric. Embryo utilisation was compared with ranking by CHLOE.

RESULTS: All morphokinetic parameters demonstrated a very strong (ICC: tSB = 0.93 n = 1246; tB = 0.93 n = 1059; tEB = 0.8 n = 656) or strong (ICC: tPN = 0.69 n = 2165; t2 = 0.64 n = 2201; t3 = 0.76 n = 2307; t4 = 0.61 n = 1730; t5 = 0.77 n = 1707; t8 = 0.68 n = 1612; tM = 0.78 n = 1367) level of agreement, with none showing moderate, weak or very weak agreement. PN agreement between embryologists and CHLOE was 91% (2360/2591).

CHLOE agreed with experienced embryologists in the determination of normal (2PN) fertilization in 94% of 2PNs as established by experienced embryologists (2095/2223), demonstrating a high level of agreement.

CHLOE Blast Score was predictive of overall blastulation (AUC = 0.83; sensitivity = 0.69; specificity = 0.78, p < 0.001) as well as blastulation by 116hpi (AUC = 0.82; sensitivity = 0.65, specificity = 0.85, p < 0.001). CHLOE embryo ranking was predictive of embryo utilization (AUC = 0.79; sensitivity = 0.76, specificity = 0.67). Out of the 297 embryos ranked 1 by CHLOE, most (91%) were transferred or frozen; a lower utilization proportion was observed for embryos ranked 3 or more (49%, p < 0.001).

CONCLUSIONS: CHLOE automatic annotation of embryos; determination of cell number, assessment of stage of embryo development, and determination of number of PNs were comparable to human manual annotations. Moreover, CHLOE accurately predicted blastulation and embryo utilisation on day 2 (as early as 30hpi) as well as on day 3. Embryos ranked by CHLOE are in agreement with embryo utilisation decisions made by experienced embryologists.

IMPACT STATEMENT: Automatic assessment of embryos cultured in time-lapse and direct integration between CHLOE, the time-lapse incubator and the electronic medical record (EMR) provides opportunities for automatic data-capture directly from the source: saving embryology time, reducing transcription error risks; improving the fluidity of information between stakeholders and improving transparency in operational intelligence through automatic and live KPI monitoring. CHLOE-supported clinics can increase the number of cycles capacity per embryologist with the potential to reduce operational costs and make IVF treatment more financially accessible.

CHLOE provides a time-efficient, objective tool to support the embryologist in clinical decision-making, with the potential to optimize success, cost and emotional burden to our patients.

E-POSTER ABSTRACT SESSION: 2

P-11 6:30 AM Monday, October 24, 2022

CAN CHLOE (AN AI-BASED EMBRYOLOGIST ASSISTANT) AUTOMATICALLY PREDICT ON DAY 3 WHETHER AN EMBRYO WILL BECOME A BLASTOCYST, BE UTILISED AND/OR IMPLANT?

Jose Teruel, MSc, Clara Miret Lucio, MSc, Marta Lozano, MSc, Marina Benavent, MSc, Maria Escriba, MSc, Amparo Garcia, MSc, Juana Crespo, Medical Director, Nuno Costa Borges, PhD, Francisco Marco-Jimenez, Sr., PhD, Cristina Hickman, PhD, Adriana Brualla Mora, MSc, Noam Bergelson, B.Sc, Gloria Calderon, PhD, Equipo Juana Crespo, Valencia, Spain; Juana Crespo, Valencia, Spain; Embryotools, Barcelona, Spain; Universitat Politècnica de València, Valencia, Valencia, Spain; Fairtility, London, United Kingdom; Fairtility, Spain.

OBJECTIVE: To compare automatic annotations, pronuclei (PN) detection, blastulation and utilisation prediction by CHLOE (FAIRILITY, an AI-based embryologist assistant tool) and experienced embryologists.

MATERIALS AND METHODS: A retrospective cohort study (between June 2021 and March 2022) of 2851 time-lapse cultured embryos from 309 patients. All embryos were annotated by experienced embryologists (CONTROL), and automatically by CHLOE (TREATMENT). Manual and automatic morphokinetic annotations and PN count were compared to establish strength of agreement using intra-class correlation (ICC). CHLOE’s efficacy of prediction of blastulation (by end of culture and by 116hpi) was assessed using AUC as the efficacy metric. Embryo utilisation was compared with ranking by CHLOE.

RESULTS: All morphokinetic parameters showed a very strong (ICC: tSB = 0.93 n = 1246; tB = 0.93 n = 1059; tEB = 0.8 n = 656) or strong (ICC: tPN = 0.69 n = 2165; t2 = 0.64 n = 2201; t3 = 0.76 n = 2307; t4 = 0.61 n = 1730; t5 = 0.77 n = 1707; t8 = 0.68 n = 1612; tM = 0.78 n = 1367) level of agreement, with none showing moderate, weak or very weak level of agreement.

The PN agreement between embryologists and CHLOE was 91% (2360/2591). CHLOE(Blast) agreed with the experienced embryologist in the determination of normal (2PN) fertilization in 94% of the 2PNs established by experienced embryologists (2095/2223), demonstrating a high level of accuracy.

CHLOE Blast Score was predictive of overall blastulation (AUC = 0.83; sensitivity = 0.69; specificity = 0.78, p < 0.001) as well as blastulation by day 5 (at 116hpi; AUC = 0.82; sensitivity = 0.65, specificity = 0.85, p < 0.001).

CHLOE-generated embryo ranking was predictive of embryo utilisation (AUC = 0.79; sensitivity = 0.76, specificity = 0.67). Out of the 297 embryos ranked 1 by CHLOE, most (91%) were transferred or frozen; a lower utilization proportion was observed for embryos ranked 3 or more (49%, p < 0.001).

CONCLUSIONS: CHLOE automatic annotation of human embryos; determination of number of cells, assessment of stage of embryo development, and determination of number of PNs were comparable to human manual annotations. Moreover, CHLOE accurately predicted blastulation and embryo utilisation on day 2 (as early as 30hpi) as well as on day 3. Embryos ranked by CHLOE are in agreement with embryo utilisation decisions made by experienced embryologists.

IMPACT STATEMENT: Automatic assessment of embryos cultured in time-lapse and direct integration between CHLOE (FAIRILITY), the time-lapse incubator and the electronic medical record (EMR) provides opportunities for automatic data-capture directly from the source: saving embryology time, reducing transcription error risks; improving the fluidity of information between stakeholders and improving transparency in operational intelligence through automatic and live KPI monitoring. CHLOE-supported clinics can increase the number of cycles capacity per embryologist with the potential to reduce operational costs and make IVF treatment more financially accessible.
TRANSPARENT PREDICTION OF BLASTULATION, PLOIDY AND IMPLANTATION: AN INTERNATIONAL MULTISITE VALIDATION AT SIX INDEPENDENT CLINICS. Assaf Ben-Meir, MD,1 Clara Miret Lucio, MSc,2 Marta Lozano, MSc,3 Rabi Ahmed-Odia, MSc,4 Semra Kahraman, Prof. MD,5 Yesim Kurtmepe Colakoglu, MSc,6 Hakan Kadir Yelke, MSc,7 Triantafilos Triantafillou, PhD,8 Emilio Gomez, PhD,9 Danilo Cimadomo, PhD,10 Adelle Yun Xin Lim, MSc,11 Adriana Brualla Mora, MSc,12 Iris Har-Vardi, PhD,13 Anat Sakov, PhD,1 Cristina Hickman, PhD14 1Fairtility, Israel; 2Juana Crespo, Valencia, Spain; 3Embryologist, Valencia, Spain; 4CRGH, London, United Kingdom; 5Istanbul Memorial Sisli Hospital, Istanbul, Turkey; 6Istanbul Memorial Hospital, Istanbul, Turkey; 7Memorial Sisli Hospital, Istanbul, Turkey; 8IASO, Greece; 9TAHE, Spain; 10Clinica Valle Giulia, GeneraLife IVF, Rome, Italy; 11Alpha IVF & Women’s Specialists, Petaling Jaya, Malaysia; 12Fairtility, Sant Cugat Del Valles, Barcelona, Spain; 13Fairtility, Beer-Sheva, Israel; 14Fairtility, London, United Kingdom.

OBJECTIVE: To assess the ability of CHLOE EQ™ (Fairtility) to predict blastulation, utilization, ploidy & implantation at 6 independent clinics.

MATERIALS AND METHODS: Time-lapse videos from 4603 embryos, 627 cycles, 6 clinics, 4 countries were retrospectively assessed using CHLOE: a transparent AI tool that supports embryologists in making clinical decisions from time-lapse videos. CHLOE combines a plethora of machine learning algorithms, three of which were trained to predict embryo utilization (CHLOE BLAST score, CHLOE RANK) and implantation (CHLOE EQ score) from as early as 30hpi. Logistic regression assessed the efficacy of prediction of blastulation (by 116hpi) Overall 4266, p<0.001). CHLOE ranking was predictive of embryo utilization (AUC=0.68; 0.68-0.71, n=4719, p<0.001). CHLOE EQ score was predictive of ploidy (AUC=0.86; 0.84-0.93, n=4266, p<0.001). CHLOE ranking was predictive of embryo utilization. CHLOE EQ score is predictive of both ploidy and implantation.

RESULTS: Overall, BLAST score was predictive of blastulation (AUC=0.86; 0.84-0.93, n=4266, p<0.001). CHLOE ranking was predictive of embryo utilisation (AUC=0.68; 0.68-0.71, n=4719, p<0.001). CHLOE EQ score was predictive of ploidy (AUC=0.76, n=4266, p<0.001) and implantation (AUC=0.76, n=535, p<0.001).

Prediction of:

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<td>5</td>
<td>2453</td>
<td>&lt; 0.001</td>
<td>0.68</td>
<td>0.71</td>
<td>0.71</td>
<td>0.59</td>
<td>0.31</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>109</td>
<td>&lt; 0.001</td>
<td>0.67</td>
<td>0.78</td>
<td>0.57</td>
<td>0.88</td>
<td>0.46</td>
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</tbody>
</table>

CONCLUSIONS: CHLOE BLAST score at 68hpi is predictive of blastulation & utilization. CHLOE ranking is predictive of embryo utilization. CHLOE EQ score is predictive of both ploidy and implantation.

IMPACT STATEMENT: The ability to accurately and consistently predict blastulation, utilisation, ploidy and implantation potential as early as 30hpi instantaneously is essential towards improving personalised care, enhancing the management of patient expectations, managing blastocyst biopsy and vitrification workload later in the week, determining which embryos to prioritise for biopsy, transfer and cryopreservation, ensuring viable embryos are not discarded and determining the best embryo transfer strategy for each individual embryo for each individual patient.

FERTILITY & STERILITY®

P-12 6:30 AM Monday, October 24, 2022

WHY SPEND TIME DOING MANUAL ANNOTATIONS WHEN CHLOE EQ™’S AUTOMATIC ANNOTATIONS ARE COMPARABLE TO THAT OF EXPERIENCED EMBRYOLOGISTS? A MULTI-CENTRE COMPARATIVE STUDY. Adriana Brualla Mora, MSc, Amy Barrie, PhD, Rachel Smith, BSc,4 Alison J. Campbell, PhD, Clara Miret Lucio, MSc, Marta Lozano, MSc, Semra Kahraman, Prof. MD, Yesim Kurtmepe Colakoglu, MSc, Anat Sakov, PhD, Iris Har-Vardi, PhD, Assaf Ben-Meir, MD., Cristina Hickman, PhD Fairtility, Spain; 2CARE Fertility Group; 3CARE Fertility, Nottingham, Nottingham, United Kingdom; 4Juanas Crespo, Valencia, Spain; 5Istanbul Memorial Sisli Hospital, Istanbul, Turkey; 6Istanbul Memorial Hospital, Istanbul, Turkey.

OBJECTIVE: To assess the agreement between manual and CHLOE EQ™ morphokinetic annotations.

MATERIALS AND METHODS: Time-lapse videos from 5402 embryos from 1092 patients from 3 clinics from 3 countries (UK N=328 cycles; Spain N=309 cycles; Turkey N=455 cycles) were annotated manually by experienced embryologists and by CHLOE EQ™ (Fairtility). CHLOE EQ™ is a transparent AI tool that supports embryologists in making clinical decisions from time-lapse videos. The agreement between manual and CHLOE EQ™ annotations were quantified using Concordance Correlation Coefficient (CCC) for each morphokinetic event, as well as through a confusion matrix.
RESULTS: Overall, the level of agreement across all morphokinetic parameters was at least strong (tPNF, t2, t3, t4, t6, t7, t8, t9, tM, tEB), if not very strong (t5, tSB, tB). Across all 3 clinics, the level of agreement for all morphokinetic parameters assessed was at least strong.

<table>
<thead>
<tr>
<th>Degree of Agreement with experienced embryologists</th>
<th>Clinic 1</th>
<th>Clinic 2</th>
<th>Clinic 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>tPNF 0.77 Strong</td>
<td>0.92</td>
<td>0.69</td>
<td>0.91</td>
</tr>
<tr>
<td>t2 0.73 Strong</td>
<td>0.86</td>
<td>0.64</td>
<td>0.91</td>
</tr>
<tr>
<td>t3 0.79 Strong</td>
<td>0.81</td>
<td>0.76</td>
<td>0.88</td>
</tr>
<tr>
<td>t4 0.65 Strong</td>
<td>0.7</td>
<td>0.61</td>
<td>0.78</td>
</tr>
<tr>
<td>t5 Very Strong</td>
<td>0.82</td>
<td>0.77</td>
<td>0.85</td>
</tr>
<tr>
<td>t6 0.79 Strong</td>
<td>0.82</td>
<td>0.74</td>
<td>0.85</td>
</tr>
<tr>
<td>t7 0.69 Strong</td>
<td>0.74</td>
<td>0.63</td>
<td>0.85</td>
</tr>
<tr>
<td>t8 0.68 Strong</td>
<td>0.67</td>
<td>0.68</td>
<td>0.72</td>
</tr>
<tr>
<td>t9 0.69 Strong</td>
<td>0.71</td>
<td>0.61</td>
<td></td>
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<tr>
<td>tM 0.78 Strong</td>
<td>0.77</td>
<td>0.78</td>
<td>0.78</td>
</tr>
<tr>
<td>tSB 0.92 Very Strong</td>
<td>0.9</td>
<td>0.93</td>
<td>0.91</td>
</tr>
<tr>
<td>tB 0.91 Very Strong</td>
<td>0.88</td>
<td>0.93</td>
<td>0.92</td>
</tr>
<tr>
<td>tEB 0.79 Strong</td>
<td>0.82</td>
<td>0.48</td>
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</table>

CONCLUSIONS: CHLOE EQU™ automatic annotation of human embryos is comparable to human manual annotations. This finding was found to be consistent in three different independent clinics, suggesting that the algorithm, which was blindly tested without prior training, can be generalised across different clinics worldwide.

IMPACT STATEMENT: The ability to automatically annotate time-lapse embryos using AI algorithms such as CHLOE EQU™ presents an opportunity to save precious embryologist time whilst increasing the granularity and immediacy of data captured to support clinical and operational decision making in an IVF clinic. The automatic annotation further provides an international morphokinetic language, resolving inter and intra operator variation.

P-15 6:30 AM Monday, October 24, 2022

IS INTELLIGENT DATA ANALYSIS-SCORE (IDA-SCORE) A USEFUL TOOL IN DAILY ROUTINE IVF LABORATORY PRACTICE TO SELECT EMBRYOS? Solmaz Sarandi, MD,1 Julie Labrosse, MD,2 Yasmine Boumerdassi, M.D.,1 Vincent Puy, MD,1 Michael Grynberg, M.D., Ph.D.,1 Christophe Sifer, M.D,5 Jean Verdier, Bondy, France, France.

OBJECTIVE: Is Intelligent Data Analysis-score (IDA-score) a useful tool in daily routine IVF laboratory practice to select embryos?  

MATERIALS AND METHODS: This retrospective mono-centric study was performed in our reproductive medicine unit from September to December 2021. A total of 167 embryos from 58 couples undergoing ICSI were monitored on a daily-basis and scored at Day-5 by IDA-score and morphological scoring by a panel of senior embryologists blinded from results of IDA-score. In all, 52 single embryos selected by embryologists were transferred during fresh or frozen cycles. Clinical pregnancy rates were defined by presence of fetal heartbeat on ultrasound. Each embryo was monitored and scored at Day-5 by both morphological scoring and IDA-score. Only the best 3 embryos were ranked and compared. Morphological score was based on Gardner-and-Schoolcraft grading system and classified according to morphological score as top-quality (≥B4BB), good-quality (≥B3BB) and poor-quality (<B3BB; trophectoderm/inner-cell-mass:CC) embryos. IDA-scores were ranked from 1-10. We compared hierarchical classification by IDA-score and embryologists using appropriate statistical tests and IDA-scores of transferred blastocysts with successful implantation and those without.

RESULTS: The level of agreement across all morphokinetic parameters was at least strong (tPNF, t2, t3, t4, t6, t7, t8, t9, tM, tEB), if not very strong (t5, tSB, tB). Across all 3 clinics, the level of agreement for all morphokinetic parameters assessed was at least strong.

<table>
<thead>
<tr>
<th>Event Overall</th>
<th>Agreement with experienced embryologists</th>
<th>Clinic 1</th>
<th>Clinic 2</th>
<th>Clinic 3</th>
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<tbody>
<tr>
<td>tPNF 0.77 Strong</td>
<td>0.92</td>
<td>0.69</td>
<td>0.91</td>
<td></td>
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<tr>
<td>t2 0.73 Strong</td>
<td>0.86</td>
<td>0.64</td>
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<tr>
<td>t3 0.79 Strong</td>
<td>0.81</td>
<td>0.76</td>
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<td>t4 0.65 Strong</td>
<td>0.7</td>
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<td>0.78</td>
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<tr>
<td>t5 Very Strong</td>
<td>0.82</td>
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<td>t6 0.79 Strong</td>
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<td>t7 0.69 Strong</td>
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<td>t8 0.68 Strong</td>
<td>0.67</td>
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<tr>
<td>t9 0.69 Strong</td>
<td>0.71</td>
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<tr>
<td>tM 0.78 Strong</td>
<td>0.77</td>
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<td>0.78</td>
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<tr>
<td>tSB 0.92 Very Strong</td>
<td>0.9</td>
<td>0.93</td>
<td>0.91</td>
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<tr>
<td>tB 0.91 Very Strong</td>
<td>0.88</td>
<td>0.93</td>
<td>0.92</td>
<td></td>
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<tr>
<td>tEB 0.79 Strong</td>
<td>0.82</td>
<td>0.48</td>
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</tbody>
</table>

RESULTS: The mean of women was 33.96±0.66 years. Morphological scoring led to 68.8% (115/167) top quality embryos, 80.2% (134/167) good quality embryos and 19.8% (33/167) poor quality embryos. Mean IDA-scores of embryos were respectively 9.06 ± 0.48 for top-quality, 8.72 ± 0.5 for good-quality and 7.42 ± 0.34 for poor-quality. We failed to observe any statistically significant difference between embryos transferred that implanted (8.92 ± 0.79) and embryos that did not implant (8.69 ± 0.93; p=0.37) according to IDA-scores. However, IDA-scores tended to be higher in case of clinical pregnancy. In order for the observed difference of 0.2 in IDA-scores to reach the level of significance, at least 674 embryos should be transferred.

CONCLUSIONS: We present preliminary results of an external independent series to confirm the efficiency of IDA-score in daily routine practice. Since IDA-score is not consistent with human scoring concerning hierarchical classification, its performance has to be further assessed to clearly establish the input of artificial intelligence in IVF laboratory practice.

IMPACT STATEMENT: If artificial intelligence is proved to be efficient to select the most competent embryo, it will replace the skilled embryologists for it.

P-14 6:30 AM Monday, October 24, 2022

DOES ADMINISTRATION OF PREDNISOLONE TO ANTI-CENTROMERE ANTIBODY-POSITIVE PATIENTS IMPROVE OOCYTE MATURATION AND FERTILIZATION RATES AFTER OVM PICKUP AND INTRACYTOPLASMIC SPERM INJECTION? Masashi Shioya, M.Sc.,1 Miki Okabe-Kinosita, M.Sc.,2 Maki Fujita, M.D., Ph.D.,3 Keiichi Takahashi, M.D.2 Takahashi Women’s Clinic, Chuo-Ku, Japan;3 Takahashi Women’s Clinic, Chiba, Japan.

OBJECTIVE: It has been reported that anti-nuclear antibody (ANA)-positive patients have a lower oocyte maturation rate after ovum pickup (OPU). In particular, patients with positive anti-centromere antibodies (ACA), a member of the ANA family, are more likely to have a low oocyte maturation rate and abnormal fertilization rate. Previous reports showed that administration of prednisolone in ANA-positive patients improved intracytoplasmic sperm injection (ICSI) outcomes. However, its effects in ACA-positive patients are unknown. Therefore, this study aimed at investigating whether prednisolone administration before OPU improves oocyte maturation and ICSI outcomes in ACA-positive patients.

MATERIALS AND METHODS: In this study, we included oocytes obtained from ACA-positive patients between January 2012 and December 2021. The ACA were detected on human epithelial (HeP-2) cells using the indirect immunofluorescence method. ACA positivity was defined as the presence of a distinct speckled fluorescent pattern. The patients were divided into a prednisolone group and a control group. The prednisolone group was given 5 to 20 mg of prednisolone daily for up to 90 days before the OPU. Cumulus-oocyte complexes were collected from follicular fluid, and the oocytes were denuded from the surrounding cumulus cells using hyaluronidase (CooperSurgical, Trumbull, CT, USA). The Oocytes with the first polar body were used for ICSI. Oocyte maturation rate and fertilization rates after ICSI were compared between those who took prednisolone and those who did not (control group).

RESULTS: This study analyzed 106 oocytes from the prednisolone group and 541 oocytes from the control group. No significant difference in patients’ ages was observed between the observed oocytes group and the control group (36.6±2.6 vs. 36.9±2.5, p = 0.256). There were also no significant differences in the oocyte maturation rate (MII: 49.1% vs. 48.5%, p = 0.626, GV: 16.0% vs. 13.1%, p = 0.37) after OPU. In addition, fertilization rates were not significantly different between the two groups (2PN: 36.5% vs. 35.1%, p = 0.846, 1 PN: 5.8% vs. 6.9%, p = 1.000, 0 PN: 15.4% vs. 12.6%, p = 0.586, 3 PN: 36.5% vs. 35.1%, p = 0.846, and degeneration rates: 5.8% vs. 10.3%, p = 0.440).

CONCLUSIONS: Administration of prednisolone before OPU in patients with positive ACA did not improve oocyte maturation and ICSI outcomes.
***IMPACT STATEMENT:*** In a previous report, the administration of prednisolone effectively improved ICSI outcomes in patients with ANA. However, the results of this study suggest that prednisolone is not effective in patients with ACA.

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**P-16 6:30 AM Monday, October 24, 2022**

**DEEP LEARNING-ENABLED PREDICTION OF PREGNANCY BASED ON THE CHARACTERISTICS OF PATIENTS IN IVF-ET CYCLES.** Sangho Lee, MS,1 Sohyun Hwang, Ph.D,2 Gaecheon Jo, BS candidate,3 Hwang Kwon, MD,1 Jihyang Kim, MD,4 So Yeon Shin, MD,1 Hyekyung Yoon, MD,1 Jieun Ko, MD,1 Sang Woo Shim, Ph.D,1 Hee-Jun Chi, Ph.D1 1Fertility Center, CHA Bundang Medical Center, CHA University, Seongnam-si, Gyeonggi-do, Korea, Republic of (South); 2Department of Biomedical Science, College of Life Science, CHA University, Seongnam, Korea, Republic of (South).

**OBJECTIVE:** To develop a deep learning algorithm based on multi-layer perceptron (MLP) trained by the clinical data of patients. This deep learning model predicts possibility of pregnancy in IVF-ET cycle.

**MATERIALS AND METHODS:** Base on 9,769 cases in IVF-ET cycles with known clinical pregnancy outcome following embryo transfer, we trained to train a multi layer perceptron (MLP) model using scikit-learn. A success of clinical pregnancy means ultrasound confirmation of a gestational sac. Data sets were from January 2010 to January 2022. Among 9,769 IVF-ET cycles, 3,855 cases (39.46%) resulted in success of clinical pregnancy. Data has seven explanatory variables such as age, E2 hormones level (before OPUS), AMH hormone level, the number of eggs collected, endometrial thickness, ET days, hCG injection days, and the number of previous IVF. The annotation for learning was the outcome of clinical pregnancy. Data sets were randomly allocated into three parts: training set (72%, n=7033), validation set (18%, n=1759) and test set (10%, n=977).

**RESULTS:** We labelled a success of clinical pregnancy as positive. Following training and validation, the area under a ROC curve in test set reached 0.69 with 64.18% accuracy. The Confusion matrix showed true positive reached 0.69 with 64.18% accuracy. The Confusion matrix showed true positive = 140, true negative = 487, false positive =104, and false negative =246. Additionally, We confirmed that the data sets for deep learning was not biased by principal component analysis and unsupervised clustering analysis.

**CONCLUSIONS:** This is the first time to predict the possibility of pregnancy in IVF ET cycle based on deep learning as a retrospective single-center large cohort study. This study showed deep learning-enabled prediction of pregnancy without the feature of embryo grade critically influenced on IVF-ET.

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**IMPACT STATEMENT:** Our classification model based on deep learning could be a useful tool to select an effective strategy in assisted reproductive technology.

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**P-17 6:30 AM Monday, October 24, 2022**

**ANTAGONIST OR PROTAGONIST: ASSESSING STMULATION PROTOCOLS THROUGH THE LENS OF ARTIFICIAL INTELLIGENCE.** Victoria S. Jiang, MD,1 Panagiotis Chereouveim, MD,1 Mackenzie N. Naert, B.A.,1 M.D.,1 M.S.C.,1 Manoj Kanakasabapathy, M.S.C.,1 Prudhvi Thiramalaraju, BS,1 Irene Dimitriadis, MD,1 Irene Souter, MD,1 Hadi Shafiee, PhD,1 Charles L. Borrmann, PhD2 MGH Fertility Center, Harvard Medical School, Boston, MA; 2Brookline, MA; Division of Engineering in Medicine, Department of Medicine, Brigham and Women’s Hospital, Cambridge, MA; 3Massachusetts General Hospital Fertility Center, Massachusetts General Hospital and Harvard Medical School, Boston, MA.

**OBJECTIVE:** To determine if there are differences in oocyte/embryo quality and clinical pregnancy outcomes among patients who undergo either GnRH antagonist or low-dose luteal GnRH agonist (Lupron) stimulation (LDLL) protocols by using deep machine learning algorithms.

**MATERIALS AND METHODS:** Retrospective review was performed for 446 IVF cycles between January 2016 – December 2021 at a single academic fertility center in Boston, Massachusetts. Cycle characteristics were reviewed for patients undergoing IVF cycles with fresh or frozen-thawed single embryo transfer. Time-lapse imaging was obtained using the EmbryoScope (Vitrolife), and an artificial intelligence (AI) algorithm was generated using convolutional neural networks to evaluate multiple morphologic markers such as oocyte fertilization rate, Day 3 cleavage to blastocyst stage conversion rate, Day 5 blastocyst conversion rate, and implantation potential. Two-tailed t-tests were used to compare differences, with p-value less than 0.05 set for statistical significance.

**RESULTS:** Among 446 single embryo transfers, 223 cycles were antagonist cycles and 223 were LDLL cycles. When comparing antagonist versus LDLL protocols, there was no difference in AI-predicted oocyte fertilization rate (antagonist 77.08% vs LDLL 78.91%), Day 3 cleavage to blastocyst stage conversion rate (antagonist 53.04% vs LDLL 52.69%), AI-predicted implantation rate (antagonist 58.69% vs LDLL 61.67%), or implantation potential (antagonist 46.85% vs LDLL 44.52%). Following fresh and frozen-thawed single embryo transfers, there was no significant difference in clinical pregnancy rate (antagonist 62.33% vs LDLL 61.43%, p=0.85). These results suggest that there is no difference in oocyte or embryo development amongst antagonist versus LDLL stimulation protocols, subsequently resulting in similar pregnancy rates.

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**IMPACT STATEMENT:** Given the subjectivity of image evaluation and processing among clinicians and embryologists, this AI system allows for objective review of embryo morphology to assess for oocyte and embryo quality amongst these cycles. Future directions include prospective use of AI algorithms to assess patient outcomes between protocols and regimens, not only focusing on protocol type but also degree of gonadotropin stimulation such as conventional IVF, minimal stimulation IVF, and natural cycle IVF.

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**P-19 6:30 AM Monday, October 24, 2022**

**COMPREHENSIVE COMPARISON OF NUMBER OF EMBRYOLOGY HOURS PER CYCLE AND RISK BEFORE AND AFTER INTRODUCTION OF CHLOE EQ™ (FAIRTILITY) INTO A 100% TIME-LAPSE IVF CLINIC.** Cristina Hickman, PhD1 Michelle Tran, BS1 Noam Bergelson, B.Sc.,3 Assaf Ben-Meir, MD,1 Iris Har-Vardi, PhD,1 Yael Klir, MBA,7 Adriana Brualla Mora, MSc4 FAIRTILITY, United Kingdom; 2FAIRTILITY, London, United Kingdom; 3FAIRTILITY, Israel; 4FAIRTILITY, Beer-Sheva, Israel; 5FAIRTILITY, Sant Cugat Del Valles, Barcelona, Spain.

**OBJECTIVE:** To consider how staffing requirements & risk in an IVF lab change with the introduction of CHLOE EQ™ (FAIRTILITY).

**MATERIALS AND METHODS:** Systematic analysis of embryology process steps & associated time & risks before & after introduction of CHLOE into a lab operating 100% time-lapse incubation. Risk quantification using Failure Mode Effects Analysis (FMEA) and embryology hours per cycle calculated based on the summation of average time required per process step. Main outcome is the number of cycles capacity per embryologist.

**RESULTS:** Prior to CHLOE there were four steps for every embryo evaluation: (i) viewing the embryo development in the viewer & annotating each embryo; (ii) writing down daily embryo grade onto the treatment form; (iii) typing the daily observation into the electronic medical record (EMR); & (iv) post embryo transfer, emailing grade and results to the Embryologist (REI) to update on embryo development. These steps carry the risk of operator variation, transcription errors, embryo anomalies being missed & embryos being incorrectly graded, leading to the most viable embryo not being prioritised for transfer, viable embryos being discarded, or non-viable embryos being selected for treatment, leading to reduced pregnancy chances, increased time to pregnancy, & unnecessary additional emotional burden & funds.

Post CHLOE, these four steps are replaced by a single step where the embryologist verifies CHLOE’s automatic annotations, which are automatically integrated from the time lapse incubator (TLI), through CHLOE and directly into the EMR. Patient communication is performed as part of the verification process, with the patient receiving daily verified email reports from a single click from the CHLOE software. CHLOE removes 17 of the 24 steps, reducing time per cycle from 9.76 to 6.43 hours: a 33% reduction in time/cycle spent vs TLI and 15% increase in cycle capacity. Additionally, a 50% increase in annual cycle capacity. In a 10,000 cycle per annum program, this represents an increase in cycle capacity per embryologist from 196 to 294 cycles/embryologist. At 1000 cycles per annum, the increase is from 167 to 250 cycles per embryologist.

According to FMEA, introduction of CHLOE leads to the elimination of 50 failure modes and a further reduction in risk in 22 failure modes. The highest risk number is reduced from 36 (High) to 16 (Moderate risk).

**CONCLUSIONS:** Introduction of CHLOE, an AI-based embryology assistant tool that is directly integrated with TLI and with the EMR, replaces manual with automatic data capture, eliminates redundancies and reduces risk, thus leading to 50% more cycles per embryologist with less stress.

**IMPACT STATEMENT:** With increasing demand for IVF treatments & subsequent shortage of embryologists, embryologists worldwide are...
experiencing increased burnout, human error, stress and mental health issues associated with overworking. Supportive tools, such as CHLOE, can relieve this burden by increasing workflow efficiencies,embryology retention and even attraction by making embryology less administrative, safer, more effective & more enjoyable.

**P-20** 6:30 AM Monday, October 24, 2022

**A HIGH KIDSCORE EMBRYO THAT RESULTED IN MONOZYGOTIC DICHRIONIC DIAMNIOTIC PREGNANCY AFTER SINGLE EUPOILD EMBRYO TRANSFER.** Rafael Trinchant, MSc, 1 Catalina Maria Roig Juliá, MD, 1 Neus Moranta Perelló, MSc, 1 Ana Calderon, MSc, 1 Javier Marqueta Sobrino, MD, 1 Margarita Torres, M.D., 1 Amaia Mugica, MSc, 1 Clara Colome, MD 1 IVI Mallorca, Palma, Spain; 2IVIRMA Mallorca, Palma, Spain.

**OBJECTIVE:** To report a case of a monozygotic dichorionic diamniotic pregnancy after single euploid embryo transfer with high KIDScore.

**MATERIALS AND METHODS:** Case report of a 40-year-old female who presented to a fertility center with secondary infertility. She underwent an ivf cycle with pre-implantation genetic testing for aneuploidy (PGTA-Seq) based on Next Generation Sequencing, with subsequent frozen embryo transfer (FET). Ovarian stimulation was performed using gonadotrophins and progesterone as GnRH analogue for 12 days. Ovulation was triggered using GnRH analogues. Embryos obtained were cultured in Embryocope+ Time-Lapse system and graded using both Gardner criteria and artificial intelligence KIDScore v5 algorithm.

**RESULTS:** A total of 11 eggs were retrieved at the day of oocyte pick-up and 7 of them were in metaphase II stage. Three blastocysts were obtained and bio-pseed on day 5 stage development: embryos #1, #6 and #7, graded as 5AA, 5BB, 5AA with respective KIDscores of 9.4, 3.7, 7.9 and subsequently frozen. After PGTA]Seq analysis, only embryo #1 was determined as euploid. A FET was performed and a dichorionic diamniotic pregnancy was assessed on week 6+6. First trimester screening concluded a high risk for trisomy 21 in both fetuses, 1/56 and 1/58 respectively, however non-invasive prenatal testing in cell free DNA confirmed the euploidy of the twins.

**CONCLUSIONS:** Despite a single embryo transfer in blastocyst stage was performed, this case report highlights the possibility of a dichorionic diamniotic pregnancy, particularly after the transfer of a good quality euploid embryo assessed via Gardner and KIDScore.

**IMPACT STATEMENT:** To our knowledge, a single blastocyst transfer resulting in multiple pregnancy with two different placentas is a rare event. The underlying mechanism behind these phenomenon remains yet to be explained by the scientific community. Here we present evidence of the first monozygotic dichorionic diamniotic pregnancy achieved after the transfer of a highly-rated KIDScore euploid embryo.

**SUPPORT:** None

**E-PAPER ABSTRACT SESSION: 3**

**P-21** 6:30 AM Monday, October 24, 2022

**LIPID SUPPLEMENTATION IN WARMING MEDIA IMPROVES DEVELOPMENTAL POTENTIAL OF MOUSE OOCYTES AND ZYGOTES.** Rebecca Kile, MS, Heather Rogers, MSc, Kalyen Trowbridge, BS, William B. Schoolcraft, MD, Ye Yuan, PhD Colorado Center for Reproductive Medicine, Lone Tree, CO.

**OBJECTIVE:** Oocyte and embryo vitrification has been widely used in human assisted reproductive technology (ART) as the preferred approach for fertility preservation. However, vitrified oocytes had compromised developmental potential compared to the fresh oocytes. The objective of this study is to examine whether additional of exogenous lipid during warming would improve developmental potential of mouse oocyte and zygotes. We also tested the longevity of the lipid-supplemented media by examining lipid peroxidation and the performance of the media after extended period of storage.

**MATERIALS AND METHODS:** In the first experiment, in vivo matured oocytes were collected from CF-1 mice following FMSG and hCG stimulation and vitrified using Cryotop® Kit (Kitazato BioPharma) after cumulus cell removal. At the time of warming, oocytes were warmed in warming solutions with (0% lipid) or without 1% (1% lipid) chemically defined lipid supplementation. Fresh in vivo matured oocytes were collected and used as the positive control. Oocytes were in vitro fertilized and in vitro cultured for four days, and oocyte survival, percent of fertilization and percent of blastocyst formation were examined to assess the developmental potential. In the second experiment, oocytes from Swiss Webster mice were in vitro matured and in vitro fertilized, and zygotes with two pronuclei were vitrified and used to test the warming solution with 0% or 1% lipid supplementation that were prepared and stored for three months. Warmed zygotes were cultured for five days, the percent of survival after warming, percent of cleavage, blastocyst formation on day 4, and blastocyst hatching on day 5 were recorded.

**RESULTS:** In the first experiment, the percent of survival and percent of fertilization remained similar between oocytes warmed with 0% or 1% lipid supplementation. However, the blastocyst development in the 1% lipid group was significantly increased compared to the 0% lipid group (69.5% versus 52.5%, p < 0.05), but still lower than the fresh oocytes (78.2%). This experiment was replicated three times with a total of 258 oocytes. In the second experiment, percent of survival (100% in 0% lipid group versus 98.97% in 1% lipid group) and blastocyst development on day 4 (41.3% in 0% lipid group versus 46.9% in 1% lipid group) were similar, but increased cleavage (79.4% in 0% lipid group versus 92.7% in 1% lipid group) and blastocyst hatching on day 5 (47.8% in 0% lipid group and 69.8% in 1% lipid group) were observed in the 1% lipid group. This experiment was replicated three times with a total of 189 zygotes.

**CONCLUSIONS:** In conclusion, lipid supplementation in warming solutions improved developmental potential of vitrified-warmed oocytes and zygotes. The stability of the warming solution supplemented with the lipid remained unchanged.

**IMPACT STATEMENT:** This study demonstrated the benefit of utilizing lipid-enriched warming solution to improve vitrified oocyte quality in an animal study and provided a potential opportunity to improve clinical outcome in human ART.

**P-22** 6:30 AM Monday, October 24, 2022

**IMPACT OF FRESH-EMBRYO PARAMETERS ON ONGOING PREGNANCY IN VITRIFIED/WARMED EUPOILD BASTOCYST CYCLES.** Aila Coello, PhD,1 María del Mar NOHALES Cóceles, PhD,2 Marco P. Meseguer, Ph.D,3 Jose Remohi Giner, MD PhD,4 Begoña Valllejo, embryologist,1 Ana Cobo, PhD,5 Valencia, Spain; 2IVIRMA VALENCIA, Valencia, Spain; 3IVIRMA Global, Valencia, Spain; 4IVI-RMA Valencia, Valencia, Spain; 5IVIRMA, Valencia, Spain.

**OBJECTIVE:** To evaluate the independent effect of the morphological parameters on predicting ongoing pregnancy after vitrified/warmed euploid blastocyst transfer.

**MATERIALS AND METHODS:** A total of 1543 vitrified/warmed single euploid blastocyst transfer cycles were included. Pre-vitrification morphological parameters analyzed for all blastocysts were as follows: i) blastocyst expansion degree: expanded (BE), hatching out of zona (BHI) and hatched (BHH); ii) trophectoderm (TE) quality (A, B and C); iii) inner cell mass (ICM) quality (A, B and C); and iv) day of vitrification (5 and 6). Ongoing pregnancy was analyzed using logistic regression analysis. Odds ratios and 95% confidence intervals (CI) were calculated. P<0.05 was considered statistically significant. All odds ratios were adjusted for patient age, oocyte origin, endometrial preparation and body mass index.

**RESULTS:** The ongoing pregnancy is significantly higher for blastocysts with ICM A (56.8%; OR 2.41; 95% CI 1.55 to 3.78) or B (46.8%; OR 1.72; 95% CI 1.17 to 2.53) compared with those with ICM C (31.1%). Blastocysts with TE C (37.0%) yielded a decreased in ongoing pregnancy than those with TE A (61.5%, OR 0.54, 95% CI 0.31 – 0.96) or B (48.5%, OR 0.77, 95% CI 0.56 – 1.06). Although cycles in which day 5 blastocysts were transferred yielded significantly higher ongoing pregnancy that those with day 6 blastocysts (48.7% vs. 41.8%, P=0.03), these differences did not remain significant after controlling for all confounders. The degree of blastocyst expansion had no apparent effect on the ongoing pregnancy.

**CONCLUSIONS:** Higher ICM and TE grades are shown to associate with higher ongoing pregnancy when a warmed euploid embryo is transferred. Therefore, these parameters should be used to select the best blastocyst in patients with multiple euploid embryos.

**IMPACT STATEMENT:** Embryo euploidy is not enough to guarantee reproductive success. Morphological classification is predictive of pregnancy in euploid blastocysts.
ADDITIONAL PROTEIN SUPPLEMENTATION IS NOT REQUIRED FOR SUPERIOR OUTCOMES OF POST WARMING CULTURE OF VITRIFIED BLASTOCYSTS. Wei-Hua Wang, PhD,1 Lindsay Watson, MS,2 Craig Witz, MD,3 Daniel Williams, MD,4 Ghasan Haddad, M.D.,5 1Aspirehi-Houston Laboratory, Houston, TX; 2FUJIFILM Irvine Scientific, Santa Ana, CA; 3Houston Fertility Institute, Houston, TX; 4Houston Fertility Institute, Houston, TX; 5Houston Fertility Institute, Tomball, TX.

OBJECTIVE: To ascertain whether additional protein supplementation is indeed required for the successful survival and warm recovery of blastocyst stage embryos when using a pre-supplemented commercial embryo culture medium for recovery.

MATERIALS AND METHODS: There are many studies citing the reasons for, and required use of, additional protein supplementation and its need in the successful survival and recovery of embryos, post thaw. However, much of this work is performed on early iterations of slow freeze-thaw medium. This is very little discussed related to the current need for extraneous protein supplementation now that vitrification and warming are the most widely used form of cryopreservation.

Retrospective analysis was performed on all calendar year 2021 frozen embryo transfer cycles. All patients that presented at the laboratory for a blastocyst transfer cycle were included. This resulted in a total of 2591 patient cycles and 2976 blastocysts warmed. Of the 2976 blastocysts warmed, 2944 were vitrified in FUJIFILM Irvine Scientific Vitr Kit – Freeze NX. The remaining 32 were vitrified elsewhere and the media is not recorded. All of the blastocysts were warmed in Vit Kit – Warm NX. 1270 blastocysts were recovered immediately in global total medium and 1706 blastocysts were recovered immediately in Continuous Single Culture Medium NX. The minimum blastocyst recovery time for both media was 30 minutes, up to 4 hours.

RESULTS: 1270 blastocysts were warmed and then recovered with global total medium, containing 4.4 mg/mL HSA and 0.6 mg/mL α- and β-globulins. Of these, 98.6% survival, 53.9% implantation, and a 57.6% clinical pregnancy rate, as defined by fetal cardiac activity, was achieved. 1706 blastocysts were warmed and then recovered in FUJIFILM Irvine Scientific Continuous Single Culture Medium NX containing only 5 mg/mL HSA. From this recovery medium, a survival rate of 98.3%, implantation rate of 53.1% and a 56.9% clinical pregnancy rate was realized. As evidenced, both recovery mediums had near identical rates for all parameters explored and none had significance over the other. There was no statistical difference in the average patient age between the recovery mediums.

CONCLUSIONS: The data concluded that vitrified blastocysts can be successfully warmed through the vitrification warm medium and then recovered prior to frozen embryo transfer in a pre-supplemented medium containing 5 mg/mL HSA, without the need for any additional protein supplementation.

IMPACT STATEMENT: The findings that standard, commercially available pre-supplemented and ready-to-use culture media containing 5 mg/mL HSA strongly supports recovery of warmed blastocysts could remove the need for additional protein supplementation for blastocyst warming. The absence of this additional labour step could reduce errors and workload as well as media ordering.

SUPPORT: No

P-24 6:30 AM Monday, October 24, 2022

INNOVATIVE METHOD FOR VITRIFICATION IN LESS TIME. Lexie Clark, B.Sc.,1 Elisabetta Kasa, B.A.,2 Anthony R. Anderson, D.SC., M.S., M.SC.3 1EmbryoDirector IVF Academy, San Antonio, TX; 2Reproductive Medicine Associates of Texas, PA; 3Spring Branch, TX.

OBJECTIVE: To demonstrate the efficacy of a short exposure to equilibration vitrification solutions and a single 1-minute thaw in to the one molar sucrose thaw solution without compromising viability of the embryo post thaw.

MATERIALS AND METHODS: Phase I of the study was a single embryos vitrified in a one minute exposure to equilibration solution (ES), 7.5% ethylene glycol (EG) and 7.5% dimethyl sulfoxide (DMSO) solution followed by a one minute exposure to vitrification solution (VS) 15% EG/15% DMSO solution with 0.5M Sucrose. Phase II warming was to thaw the embryo in a single step of 1 molar sucrose solution, thaw solution (TS), and move to a washing solution (WS). The embryo was vitrified and thawed following the described method 1 minute ES, 1 minute VS for freezing. Warming was 1 minute TS and 3 minutes WS before performing the freeze again.

RESULTS: Single embryo was frozen and warmed over 10 complete cycles while maintaining viability over the multiple freeze warming cycles. Each time the integrity of the membrane was observed by 2 other embryologists to determine viability. If the embryo was determined viable it was re-frozen and warmed.

CONCLUSIONS: A typical vitrification procedure takes up to 20 to 30 minutes. The typical warming protocol takes 20 to 30 minutes each. With this shortened protocol the time saved over 1000 freeze and 1000 warming procedures per year is over 600 hours of time saved in the laboratory time over the year.

IMPACT STATEMENT: We are in a time when we need to think again about how we perform our laboratory procedures and determine if we can shorten the times and the observations in the laboratory to increase the time to perform more procedures safely with less stress on the laboratory staff.

SUPPORT: none

P-25 6:30 AM Monday, October 24, 2022

DEGREE OF BLASTOCYST EXPANSION PREDICTS SURVIVAL IN EUPLIOD VITRIFIED/WARMED EMBRYOS. Aila Coello, PhD,1 María DEL MAR NO-HALES Córcoles, PhD,2 Marcos Meseguer, Ph.D.,3 Pilar Campos, Embryologist,1 Jose Remohi Gimenez, MD Ph.D.4,5 Ana Cobo, PhD,6 Valencia, Spain; 2IVIRMA VALENCIA, Valencia, Spain; 3IVIRMA Global, Valencia, Spain; 4IVIRMA VALENCIA, VALENCIA, Spain; 5IVI-RMA Valencia, Valencia, Spain;

OBJECTIVE: To identify blastocyst features predictive of survival in vitrified/warmed euploid blastocysts.

MATERIALS AND METHODS: This is a retrospective study included 1627 euploid blastocysts. Assisted hatching was performed on day 3 of embryo culture. Vitrification and warming procedures were performed on day 5 or 6 using Cryotop method. Blastocyst parameters analyzed were as follows: i) blastocyst expansion degree: completely inside of zona pellucida (EB), hatch out of zona pellucida (HIB) and hatch out of zona pellucida (HB); ii) trofoectoderm (TE) grade (A, B and C); iii) inner cell mass (ICM) grade (A, B and C) and iv) day of vitrification (5 and 6). Survival was compared between groups using chi-square test. P<0.05 was considered statistically significant. Multivariate logistic regression was performed to analyze the relationships between survival and the morphological parameters. Odds ratios and 95% confident intervals (CI) were calculated.

RESULTS: The survival rates for blastocysts classified as EB, HIB and HB were 98.7%, 96.6%, and 93.3%, respectively, showing significant differences (P=0.005). The ICM and TE grades had no apparent effect on survival rate. Day 5 blastocysts yielded comparable survival than day 6 embryos (96.8% vs 96.6%, P=0.05). The degree of blastocoele expansion was the only blastocyst morphology parameter that exhibited a significant ability to predict survival by multivariate logistic regression. The odds of survival decreased in blastocysts classified as HB compared with those classified as HIB (OR 0.49; 95% CI 0.25 to 0.95; P=0.03), and as HB (OR 0.18; 95% CI 0.06 to 0.6; P=0.003).

CONCLUSIONS: This study confirms that degree of expansion is the best predictor of survival of euploid blastocysts. Blastocysts totally within the zona pellucida show the higher survival rates.

IMPACT STATEMENT: The lower cryosurvival shown in HB could be related to the fact that these embryos are more exposed because they do not have the zona pellucida and therefore can be more easily damaged. In addition, the processes of dehydration and permeation of cryoprotectants can be altered.

P-26 6:30 AM Monday, October 24, 2022

WHAT IS THE OPTIMAL ENDOMETRIAL PREPARATION PROTOCOLS IN EUPLIOD FROZEN EMBRYO TRANSFER (FET)? Junghyun Lee, MS,1 Eun A. Park, MS,2 Juyoung Lee, M.S.,3 Gayun Song, MS,1 Hyunsoo Kim, MS,1 Hyejin Jeong, MS,1 Yun Jung Hur, M.D.,4 Eun Jeong Yu, M.D.,5 Myung Joo Kim, M.D.,6 You Shin Kim, M.D.7 1CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South); 2CHA Seoul Fertility Center, Seoul, Korea, Republic of (South); 3CHA Fertility Center-Seoul Station, Seoul; 4CHA Fertility Center Seoul Station; 5CHA Fertility Center, Seoul, Korea, Republic of (South); 6CHA
OBJECTIVE: Various factors, including treatment protocols, can influence the outcomes of frozen embryo transfers (FETs). In order to prepare the endometrium, several protocols have been suggested: natural cycles, where detecting the luteinising hormone (LH) surge, and, therefore, the ovulation, defines the timing of the transfer; modified natural cycles, where ovulation is triggered by the administration of human chorionic gonadotropin (hCG); hormone replacement therapy (HRT) or artificial cycle with estradiol (E2) and progesterone (P4), with or without using gonadotropin-releasing hormone (GNRH) analogs; and, finally, stimulated cycles with low doses of gonadotropins. However, there is still some controversy as to the ideal endometrial preparation protocol. Also, the efficacy and the safety of these FET protocols have been examined by multiple studies, but there is a lack of consensus on how the endometrium should be prepared and synchronized. Is the pregnancy outcomes in euploid frozen embryo transfer (FET) cycles affected by the endometrial preparation protocols?

MATERIALS AND METHODS: A retrospective study was conducted at a CHA fertility center Seoul station between January 2019 and October 2021 in patients undergoing PGT for aneuploidies. A total of 1005 euploid FET cycles were divided into the three study groups according to endometrial preparation protocols: Group 1 (n=699 cycles), hormone replacement therapy cycle (HRT); group 2 (n=89 cycles), natural cycle triggered by hCG; group 3 (n=217 cycles), natural cycle triggered with spontaneous LH surge.

RESULTS: The mean (±SD) ages across group 1, 2 and 3 were 37.4 (±3.6), 37.3 (±3.0) and 37.1 (±3.4) years, respectively. Interestingly, the number of embryos transferred was also similar in the comparison of group 1 (1.24 ± 0.43), group 2 (1.22 ± 0.42) and group 3 (1.21 ± 0.41). A significant difference higher pregnancy (77.4% versus 61.8% versus 66.8%, P<0.05), clinical pregnancy (67.7% versus 57.3% versus 59.0%, P<0.05) ongoing pregnancy rates (61.2% versus 56.2% versus 53.9%, P<0.05) was observed in group 1 when compared to group 2 or group 3. However, no significant differences were found in pregnancy, clinical pregnancy and ongoing pregnancy rates between group 2 and 3.

CONCLUSIONS: In the present study, the data indicate that an hormone replacement therapy (HRT) protocol is the optimal endometrial preparation protocols in euploid frozen embryo transfer (FET).

P-28 6:30 AM Monday, October 24, 2022

TRANSMFERING SINGLE THAWED CLEAVE STAGE EMBRYO AT BLASTOCYST STAGE IS AT LEAST SUCCESSFUL AS TRANSFERRING SINGLE THAWED BLASTOCYST IN TERMS OF ART CYCLE OUTCOME

Ahmet Zeki Isik, M.D., 1 Eser Colak, M.D., 2 Funda Gode, M.D., 3 Burcu Tamer, biologist, 1 Merve Isik, student, 7 Volkan Emirdar, M.D. 2 Izmır Su Hospital Private IVF Center, 3 Izmır, Turkey, 4 Kent Hospital, Izmir, Turkey, 5 Koç University Faculty of Molecular Biology and Genetics, 6 Izmır Economy University School of Medicine, Karsiyaka-Izmir, Turkey.

OBJECTIVE: To study and compare the effects of thawed cleavage-stage embryo transfer at the blastocyst stage, and thawed blastocyst-stage embryo transfer in terms of ART cycle outcome.

MATERIALS AND METHODS: A retrospective analysis was conducted on frozen-thawed cycles of patients, who had single blastocyst transfer. The data of 240 frozen-thawed cycles were collected between January 2017 and March 2020 at a private IVF Center in Izmir, Turkey. Patients who were older than 39 years of age and who had preimplantation genetic testing performed on their embryos were excluded. Also cycles without TE (Testicular sperm extraction) sperm were included.Only the data of the first frozen-thawed embryo transfer cycles in all freeze groups were evaluated. Two groups were formed. Group 1 included 184 patients with thawed cleavage-stage embryos which were transferred at the blastocyst stage. In this group of patients there were less than four high quality embryos at day 3 of which at least two of them were frozen as center policy. Also in this group of patients at least one high quality blastocyst embryo were frozen. In Group 2, 121 patients with thawed blastocyst-stage embryo transfer were included. All of the embryos were frozen at blastocyst stage. The standard practice in this private IVF Center includes artificial preparation of all cycles. Pregnancy was defined as a human chorionic gonadotropin (hCG) level higher than 5 IU/L on day 12 of embryo transfer. Clinical pregnancy or implantation was defined as the gestational sac seen in the uterus at the 6th week of pregnancy.

RESULTS: The demographic variables are described in table 1. There were no significant differences in terms of age (41.0 vs. 43.7 years, p=0.15) among the study groups. The duration of infertility was longer in the 5-5 groups, and the difference was statistically significant (p=0.03). Overall positive pregnancy and clinical pregnancy rate were comparable between the day 3–5 and day 5–5 groups (69.7% vs. 61.2%, p<0.05 and 58.8% vs. 52%, p<0.05, respectively). Although the rates were higher in the 3-5 group than in the 5-5 group, the difference was not statistically significant.

CONCLUSIONS: In recent years, the indications to freeze all embryos have increased. A few studies in recent years have shown that embryos that are frozen at the cleavage stage and transferred as blastocysts after culturing for 2 days have better pregnancy rates. Freezing embryos at the cleavage stage and culturing them to blastocyst stage may be a good option.
DOES TIME OF BLASTOCYST CULTURE POST WARMING HAVE ANY IMPACT ON PREGNANCY OUTCOMES IN FROZEN THAWED CYCLES. V. Mishra, MD, PhD; V. V. Naithani, MD, MRCOG; Bhrahmbhatt, MSc; Molecular biology and biochemistry; Kunar Shah, MRCOG, FACOG; Hardik Jyoti Sheth, MSc, Microbiology; G.M.A. Hospital, Management; Kajal Kundan Patel, B.Sc, Biotechnology, MLT; Kushali Patel, Bsc Microbiology, MLT; Anika Anil Suther, B.Sc, Microbiology, MLT; Dr. Priyanka Repswal, BDS, MSc CE; Director IKDRC, Ahmedabad, India; Chief embryologist, Ahmedabad, India; Associate Professor, Ahmedabad, India; Embryologist and Scientific Officer, Ahmedabad, India; Perinatal biologist, Ahmedabad, India; Junior Andrologist, Ahmedabad, India; Embryologist (INTERN), DENTIST, Ahmedabad, India.

OBJECTIVE: To determine the impact of culture time of blastocyst post warming on pregnancy outcome in frozen thawed embryo transfers.

MATERIALS AND METHODS: A total number of 326 patients from January 2020 to January 2022 having 559 blastocyst undergoing frozen thawed embryo transfer cycles were involved in the study. And were divided into three groups, in Group A (n = 58) where transfer was done after 1 hour of culture post warming (<1 hour), Group B (n = 200) blastocyst transfer within (2-4 hours) of culture, post warming and Group C (n = 104) (4-6 hours) of culture post warming. Patients with age >36 years were excluded from the study. Primary outcome of the study was to detect implantation rate and clinical pregnancy rate.

RESULTS: In group B where Blastocyst were transferred within 2 to 4 hours after warming and further culture, the implantation rate was (52.5%) and clinical pregnancy rate was (88.5%) which was higher than in group A where the implantation rate was (18.9%) and clinical pregnancy rate was (72.7%) versus in group C which have (44.3%) implantation rate and (65.2%) clinical pregnancy rate. Significant difference was found in the implantation rate (p = 0.0000) and clinical pregnancy rates (p = 0.002) of group B versus group A and group C.

CONCLUSIONS: Timing of blastocyst culture post warming plays a very important role in observing the re-expansion and assessing the degree of expansion post warming. Our study concludes that blastocyst transferred 2 to 4 hours after warming and further culture has better implantation rate and clinical pregnancy rates as compared to Immediate transfer (within 1 hour) and late transfer (4-6 hours).

IMPACT STATEMENT: Larger studies are needed to strengthen these results but our study concludes that there should be a minimum culture time of 2 to 4 hours post warming procedure this time window between warming and transfer provide us better outcomes with reference to implantation rate and clinical pregnancy rates.

E-PSTER ABSTRACT SESSION: 4

P-30 6:30 AM Monday, October 24, 2022

REPRODUCTIVE OUTCOMES OF POOR GRADE BLASTOCYSTS. Krishna Mantravadi Dr., MBBS, PGIDHOM, Master in clinical embryology; Rakhi R, POST GRADUATE IN MICROBIOLOGY; Durga Gedela Rao Dr., MRCOG; Spoorthy Rao, MBBS; Oasis fertility, Hyderabad, India; Oasis Fertility, Hyderabad, India.

OBJECTIVE: To analyze whether poor grade blastocysts offer acceptable reproductive outcomes?

MATERIALS AND METHODS: This is a retrospective observational cohort study conducted from 2017 to 2021. Couples undergoing Frozen Embryo transfer (FET) cycles with two poor grade blastocysts (n = 234) were considered in the study group. Couples undergoing FET with two good grade blastocysts (n = 143) were considered in the control group. Only FET cycles with women aged <37yrs, self gamete cycles with no PGT (Pre-Implantation genetic Screening), and embryos showing 100% survival post vitrification were included in this study.

Blastocysts on Day 5 or Day 6 were graded based on the ALPHA CONSENSUS GRADING system. Embryos with Trophoectoderm and Inner Cell Mass with Grade 3 were considered poor quality and the rest were considered as good grade blastocysts. All embryos were vitrified and warmed based on the protocol described by the KITAZATO method. Embryo survival of poor Vs good grade blastocysts was evaluated. Only embryos with a 100% survival rate were transferred in a FET cycle. All cycles had two blastocysts transferred (institute policy). Implantation Rate (IR), Miscarriage Rate (MR), Multiple Pregnancy Rate (MPR), and Live Birth Rate (LBR) were compared between the groups.

RESULTS: Reproductive outcomes between Poor and Good Grade embryo groups were as follows: IR – 34% Vs 36% (p = 0.67), MRR – 11% Vs 5% (p = 0.045), MPR – 12% Vs 30% (p = 0.0001), LBR – 35% Vs 63% (p = 0.0001). 100% embryo survival post warming – 94% vs 98% (p = 0.0689). Data from this study shows that Vitrification-Warming seems to offer good embryo survival irrespective of the embryo grade.

CONCLUSIONS: The low grade Blastocysts seem to offer reasonable reproductive outcomes. Adequate care has to be exercised before discarding the poor grade blastocysts.

IMPACT STATEMENT: Poor grade Blastocysts seem to offer reasonable reproductive outcomes. Couples with poor grade blastocysts during their IVF cycles should be counseled accordingly before considering discard of poor grade blastocysts.

THE CLINICAL IMPACT OF THE MORPHOLOGICAL PARAMETERS AFTER THAWING OF EUPLOID EMBRYOS IN FROZEN EMBRYO TRANSFER CYCLES. Gulcin Ozkara, PhD; Hakan Kadir Yelke, M.S.C.; Mehmet ALL Tüfekçi, PhD; Semra Yildiz, B.Sc.; Yesim Kuntupe Colakolu, M.Sc.; Semra Kahraman, M.D., Prof1, Istanbul Memorial Sisli Hospital, Istanbul, Turkey; 2Istanbul Memorial Hospital, Istanbul, Turkey.

OBJECTIVE: To analyze the parameters that are affecting the clinical outcomes of single Embryo transfer cycles in a single ART center.

MATERIALS AND METHODS: Clinical outcomes of 3124 PGT-A cases who applied for ART treatment to Istanbul Memorial ART and Genetics Center between 2017-2021 were retrospectively assessed. Students’ t-test was performed to compare clinical parameters between study groups (positive pregnancy (n = 2327) vs negative pregnancies (n = 797) and ongoing pregnancies (n = 1849) vs aborted cases (n = 478). Stepwise backward logistic regression model was used to find out risk factors related to negative and aborted pregnancies. Depended variable was chosen as pregnancy results and independent variables were selected from embryological parameters after thawing (vitality (≥ 90% vs <90%), reexpansion at 0,2 and 4 h after thawing, necrotic foci at ICM and TE, presence of seperated blastomer on Day5/6, embryo transfer day (Day 5 vs 6), embryo quality (TQ, GQ and MQ+PQ), age (< 37yrs, 38-39, 40+), R< 90%, reexpansion at 2h after thawing (p = 0.006, OR: 1.44, CI 95%(1.200-1.737)), absence of re-expansion at 2h after thawing (p = 0.035, OR: 1.46, CI 95%(1.028-2.089)). Additionally, the risk factors in aborted embryo group were found as age ≥ 43 vs 35 (p = 0.001, OR: 3.24, CI 95%(1.657-5.667)), absence of re-expansion at 2h after thawing (p = 0.032, OR: 1.83, CI 95%(1.053-3.182)), presence of granulation in blastocysts (p = 0.001, OR: 1.86, CI 95%(1.354-2.554)). Presence of necrotic foci at ICM or TE were not found as risk factors for neither negative nor ongoing pregnancy in euploid embryo transfer cycles.

CONCLUSIONS: According to our data, vitality, embryo transfer day and embryo quality seem to affect the implantation of euploid embryos. Moreover, advanced maternal age, embryo quality, granulation and separated blastomer existence in the blastocysts are the factors that have an impact on miscarriage of euploid embryos.
IMPACT STATEMENT: It is still a matter of debate finding out the factors affecting the ART outcomes negatively in euploid embryo transfers. Morphological parameters such as granulation, reexpansion, separated blastomeres etc. of thawed euploid embryos should be evaluated in detail after thawing procedure. Advanced maternal age should also be taken into consideration as a negative factor on ongoing pregnancies.

P-32 6:30 AM Monday, October 24, 2022

WORKING WITH FATIGUE: ASSESSMENT OF CYROPEBIOSORIES, Michael G. Collins, M.D., Ph.D.,1 William Venier, M.Sc.,2 Abeer Salhia, R.N., Ph.D.,3 Angelina Beltsos, M.D.,4 Joseph A. Lee, B.A.,5 Alan B. Copperman, M.D.,6 Jessica Bailey, M.S.,6 Denny Sakkas, Ph.D.,3 Aline Broussard, Ph.D.1
1TRMW Life Sciences, Inc., New Orleans, LA; 2San Diego Fertility Center, San Diego, CA; 3Vios Fertility Institute, Chicago, IL; 4Kindbody/Vios Fertility Institute, Chicago, IL; 5Reproductive Medicine Associates of New York, New York, NY; 6Boston IVF - The Eugin Group, Waltham, MA; 7Generation Next Fertility/Tmwr Life Sciences, Reading, MA.

OBJECTIVE: To observe the amount of time spent in fatiguing work (bending, lifting and usage of stools and ladders) in the management of in vi tro fertilization (IVF) biorepositories.

MATERIALS AND METHODS: Level checking and filling LN2 in Dewars was observed at 4 United States (US) IVF centers. In addition, a sampling of the annual Dewar inventory was conducted at each site (~1 Dewar per site). As well as, observing specimen retrievals from storage and moving specimens into storage (at least 12 each per site). Data were captured from 12 subjects (range: 1-5 per site) via 2 digital video cameras (Sony FDR AX33) with 256 GB microSD card media. Time data points were determined using Movies & TV app (Microsoft, v10.2).

Fatiguing time, defined as: 1) time spent bending over (typically looking into Dewars), 2) time lifting heavy objects (typically 2L liquid nitrogen containers or heavier), 3) time standing on a stool (either working with large format tanks or pulling objects from shelves) was determined. Data is presented as the percentage, calculated by time in fatiguing work out of the total time working with equipment to perform the laboratory tasks.

RESULTS: Among the 4 US IVF sites, embryologist were observed directly working with cryopreservation biorepository equipment (Dewars) for a total of 07:46:56 (HH:MM:SS). Of the total time, 31.5% (02:26:53) was spent bent over and often at an angle. Embryologist spent 10.8% (00:50:39) of the total time lifting heavy objects while 4.9% (00:23:05) of the total time the use of a stool was necessary to complete a task. The total fatiguing time for an embryologist was 47.25% (03:40:37).

CONCLUSIONS: The data demonstrated that current manual cryostorage equipment relies heavily on fatiguing manual work conditions. Of the work tasks observed in this study, specimen retrieval and storage are required daily, while Dewar level checking and filling of LN2 are performed at least once per week. Similarly, the annual inventory is not a daily process, but involves a large amount of time spent in fatiguing work. Taken as a whole, the data support that daily working conditions for IVF biorepository cryomangement are fatiguing, with this stemming directly from the manual nature of the current cryostorage systems.

IMPACT STATEMENT: The application of automation, with software guided specimen retrieval and storage, along with automated tank filling, coupled with constant telemetry of environmental conditions including LN2 level checking, while providing for an upright working condition should improve the fatiguing conditions experienced in IVF biorepository cryomangement.

P-33 6:30 AM Monday, October 24, 2022

IMPACT OF EQUILIBRATION DURATION ON THE OUTCOME OF OOCYTE VITRIFICATION/THAWING CYCLES: RESULTS OF AN OBSERVATIONAL PROSPECTIVE SIBLING-OOCYTE STUDY. Yasmine Boumerdassi, M.D.,1 Solmaz Sarandi, M.D.,2 Vincent Puy, M.D.,1 Florence Eustache, M.D., Ph.D., Julie Labrosse, M.D., Violes Claire, M.D.,1 Maeïss Peigné, M.D., Ph.D., Michael Gryningberg, M.D., Ph.D., Christophe Sifer, M.D.1 Paris, France; France; 2Bonidy Clinics, France; 1Assistance Publique Des Hôpitaux De Paris, France; 3Jean Verdier Hospital, Bondy, France; 4Jean Verdier Hospital, Paris.

OBJECTIVE: Over the last decade, oocyte vitrification has become daily practice in centers for reproductive medicine. Regarding technical aspects, the instructions provided by manufacturers indicate various durations of the equilibration step (ranging from 10 to 14 minutes). The present investigation aimed to evaluate the potential impact of the equilibration step duration in the course of the vitrification protocol on oocyte outcome after thawing.

MATERIALS AND METHODS: Single-center observational prospective study, between 2013 and 2021, including all the oocyte vitrification/thawing cycles. Oocyte vitrification/warming was performed using the Cryotop method, following the manufacturer’s protocol (Kitazato, Japan). One to nine oocytes were firstly exposed to progressively increasing concentration of cryoprotectants (6 minutes), and then deposited by one to three in drops of equilibration solution (ES), depending on the number of mature oocytes retrieved. After 12 minutes, the vitrification step was initiated for the first three oocytes (1 minute), and the following oocytes in the other drops were vitrified thereafter, respectively after 13 and 14 minutes of equilibration. Main study outcomes were fertilization, cleavage rates, and day-2 embryo quality. Top-quality and good-quality embryos were defined at day-2 respectively as 4 and 3-5 adequate-sized blastomeres, without multinuclea-

CONCLUSIONS: Our findings indicate that the shortest equilibration duration (12 min ES) during oocyte vitrification leads to better fertilization and cleavage rates. Further prospective studies focusing on clinical outcomes are needed to confirm our results.

IMPACT STATEMENT: Reduction of equilibration duration might reduce the toxicity of cryoprotectants and therefore improve the oocyte outcome. Moreover, this strategy could allow the optimization of IVF centers workflow in view of the increasing activity of oocyte vitrification.

SUPPORT: Non

P-34 6:30 AM Monday, October 24, 2022

PROTECTIVE EFFECT OF L-PROLINE ON HUMAN SPERM CHARACTERISTICS DURING CRYOPRESERVATION. Motjaba Moradi, DVM,1 Bahareh Moradi, MSc.,2 Azita Faramarzi, Ph.D.2 1Department of Clinical Sciences, Faculty of Veterinary Medicine, Razi University, Ker-
manshah, Iran, Iran (Islamic Republic of); 2Fertility and Infertility Research Center, Health Technology Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran.

OBJECTIVE: To explore the effectiveness of L-proline inclusion in freezing medium on sperm parameters, sperm DNA and chromatin quality, as well as the nitro-oxidative status of sperm culture medium in normozoospermic men who received antioxidant supplements during the freezing-thawing pro-
cess.

MATERIALS AND METHODS: The study included forty healthy, nor-
mozoospermic, non-smoker males who received antioxidant supplements (zinc + vitamin C) between the ages of 28 and 39. Each prepared semen sam-
pal was aliquoted into four portions. Aliquots 1 as the control group were not supplemented with L-proline. Aliquots 2 to 4 were supplemented with different concentrations of L-proline (1, 2, and 4 mmol/L) into the cryopres-
ervational medium. Sperm parameters, including total and progressive motility, viability, and morphology, were analyzed for each aliquot. Further, sperm chromatin and DNA integrity were assessed using Toluidine blue (TB) staining, Chromomycin A3 (CMA3) staining, and sperm chromatin dispersion (SCD) testing. Finally, the levels of nitric oxide (NO), reactive oxygen...
species (ROS), and total antioxidant capacity (TAC) were measured in the sperm freezing medium. All evaluations were performed pre and post-freezing-thawing for each aliquot.

RESULTS: According to our results, 2 and 4 mmol/L of L-proline maintained sperm motility and viability higher than in the control groups. In terms of normal morphology percentage, however, we observed a non-significant improvement in the L-Proline-treated groups. The oxidative status analysis indicated that NO and ROS levels were markedly lower in the 2 and 4 mmol/L of L-proline group compared to the control group. Similiarly, supplementing sperm medium with 2 and 4 mmol/L of L-proline improved the maintenance of TAC levels in comparison to the control group. Moreover, the presence of 4 mmol/L of L-proline during the freezing-thawing process of human sperm had a beneficial effect on the chromatin quality-related parameters compared to the control group. After supplementation with 4 mmol/L of L-proline, we observed significant reductions in TB and CMA3 tests compared to the control group. A notable reduction in SCD levels was also observed in 2 and 4 mmol/L of L-proline groups as compared to the control group.

CONCLUSIONS: L-Proline inclusion in the sperm freezing medium improves sperm quality and preserves sperm chromatin and DNA integrity, possibly through the reduction of oxidative stress and the enhancement of antioxidant levels.

IMPACT STATEMENT: The study highlights the potential role of L-proline as a novel additive and antioxidant in order to refine the human sperm cryopreservation medium.

P-35 6:30 AM Monday, October 24, 2022
PRELIMINARY DEVELOPMENT RESULTS OF A NEW VITRIFICATION DEVICE FOR OOCYTES AND EMBRYOS: VITRI CARRIER FROM ZURE®, Iván Anduaga Marchetti, BSc,1 Marcela Cullere, PhD,1 Maximiliano Beltramo, Sr., Bsc,1 Juan Manuel Paturlanne, Bsc,2 Valeria Soledad Martínez, Bsc,2 Lucia Saggori, Bsc,2 Cesar Sanchez Sarmiento, PhD1 NASCENTIS, ESPECIALISTAS EN FERTILIDAD Y GENETICA REPRODUCTIVA, Argentina; 2NASCENTIS, ESPECIALISTAS EN FERTILIDAD Y GENETICA REPRODUCTIVA.

OBJECTIVE: The development of new devices to vitrify oocytes and embryos requires implementation of accurate regulations, technology, design and functionality. To consider these aspects during the design stage, is important to provide greater safety to the biological material being preserved and to the operating embryologist. The ZURE® Vitr Carrier appears as an alternative of Argentine origin, in which the comfort experience of the user was considered among the embryologists who tested it. We aimed to obtain preliminary data on recovery and survival rates of vitrified and devitrified oocytes and embryos. The ZURE® Vitr Carrier was designed in accordance with the ASTM and ISO 1137-1/2/3/4 standards. All devices were divided into 3 sterilization groups with different radiation doses (J: 15 KGy, M: 20 KGy, P: 25 KGy) according to IAEA guidelines. 190 freezing and thawing tests of immature oocytes (P1 or MI) were performed to determine recovery and survival rates, user perception of cell adherence to the device, and media behavior during loading and unloading of oocytes. These data were recorded to make future changes to the carrier design and to achieve definitive validation prior to use it with patient oocytes and embryos.

RESULTS: Recovery rates for all oocytes (98.7%) and for each of the sterilization groups were determined: J: 100% (n=38), M: 97.2% (n=57) and P: 99.16% (n=93). In addition, post-thaw survival rates were 96.3% for the total group, 97.9% for J, 94.5% for M, and 96.6% for P. On the other hand, the operators observed during vitrification good adhesion and dispersion of the medium on the device, while during devitrification the oocytes generally detached quickly and were visualized without inconvenience.

CONCLUSIONS: Oocyte recovery and survival rates were always higher than 94% in the first step for the validation of ZURE® supports. Likewise, acceptable interactions between cells and media with the device were observed, regardless of the radiation levels to which they were exposed. These preliminary results are comparable to those obtained in the tests of other commercial carriers and allowed us to adjust details to continue with the process of definitive validation. Next steps are aimed to use this device for vitrification of patients gametes and embryos.

IMPACT STATEMENT: The development of local technologies that include embryologists in the production process leads to excellent results in the vitrification and devitrification of oocytes.

P-36 6:30 AM Monday, October 24, 2022
ANTIOXIDANTS IN THE EMBRYO CULTURE MEDIA. A SIBLING OOCYTE STUDY. Oscar Perez, Ph.D.,1 Jessica Kozlowski, B.S.,1 Hannalie H. Adriaanse, B.S.,1 Linda Lay, B.S.,1 Ravi Gada, M.D.,2 Samuel J. Chantilis, M.D.,1 Gabriella Navarrete, B.S.,1 Breanna Tilley, MSc1 Dallas Fertility Center, Dallas, TX; 2Dallas Fort Worth Fertility Associates, Dallas, TX; 3Dallas-Fort Worth Fertility Associates, Dallas, TX; 4Dallas Fertility Center, Dallas.

OBJECTIVE: Initial studies in humans have indicated a beneficial effect of adding antioxidants in the embryo culture media. The objective of this study was to evaluate the use of antioxidants in the culture media in two different IVF centers with two different culture media systems in a prospective randomized sibling oocyte study.

MATERIALS AND METHODS: Oocytes were collected from two IVF centers from fifty-three non-donor IVF patients aged 29-44 years old. A total of one thousand fifteen sibling MII oocytes were randomly assigned to the experimental groups. The culture media treatment groups consisted of a single-step culture system (Global, Life Global), Sequential Culture System (Quin’s Advantage Sequential Media, Origio), and the commercial antioxidant culture system (GX media, Vitrolife). The variables to evaluate were fertilization rate, Day-3 embryo quality, the total number of blastocysts, and the cryopreservation blastocyst rate. For outcome purposes, the patient population in this study was divided into two age groups; Group one with patients aged 35 years old and group two with patients aged 36-44 years old. Statistical differences between culture systems were analyzed using the Chi-square test. A P-value of P<0.05 was considered significant.

RESULTS

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>IVF Center 1</th>
<th>≤35 Years Old</th>
<th>Antioxidant Media</th>
<th>Global</th>
<th>Single Step</th>
<th>36-44 Years Old</th>
<th>Antioxidant Media</th>
<th>Global</th>
<th>Single Step</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI Oocytes (n)</td>
<td>200</td>
<td>205</td>
<td>103</td>
<td>110</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fertilization (n/%)</td>
<td>131 (66%)</td>
<td>139 (68%)</td>
<td>71 (69%)</td>
<td>63 (75%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day-3 (%)</td>
<td>73 (56%)</td>
<td>82 (59%)</td>
<td>31 (44%)</td>
<td>47 (57%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥8 cell-stage</td>
<td>92 (70%)</td>
<td>100 (72%)</td>
<td>35 (49%)</td>
<td>45 (54%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Blastocysts</td>
<td>52 (63%)</td>
<td>70 (77%)</td>
<td>35 (67%)</td>
<td>38 (63%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cryopreserved</td>
<td>40 (49%)</td>
<td>56 (62%)</td>
<td>17 (33%)</td>
<td>31 (52%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blastocysts (AA-AB)</td>
<td>77 (59%)</td>
<td>85 (61%)</td>
<td>29 (41%)</td>
<td>38 (46%)</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

a,b Superscripts showed statistical significance (P<0.05).
CONCLUSIONS: Even though no statistical differences were detected in almost all of the evaluated endpoints, there was a slight increment in fertilization, day-3 embryo quality, total blastocysts, and blastocyst cryopreservation without the use of antioxidants in the culture media. More studies, including clinical pregnancies and implantation rates, will provide more information on the positive use of antioxidants in the IVF culture media.

IMPACT STATEMENT: In this prospective randomized sibling oocyte study, the use of antioxidants in the culture media did not improve the laboratory outcomes.

P-37 6:30 AM Monday, October 24, 2022

THE EFFECT OF DIFFERENT CULTURE VOLUME OF SIBLING HUMAN EMBRYOS ON CLINICAL OUTCOMES. SU Hee Seok, M.Sc.; So- Yeon Ahn, M.Sc., Jae Kyun Park, Ph.D., Jin Hee Eum, Ph.D., Ji Eun Park, M.D., Haengjun Jeon, M.D., Ji Won Kim, M.D., M.SC., Woo Sik Lee, M.D., Ph.D.1 CHA Gangnam Medical Center, CHA University, Seoul, Korea, Republic of (South); CHA Gangnam Medical Center, CHA University, Seoul; CHA Fertility Center Gangnam, CHA University, Seoul, Korea, Republic of (South).

OBJECTIVE: In order to select viable human embryos for transfer, single embryo culture has been adapted. Many efforts have been made to complement the drawbacks of individual culture. Previous studies demonstrated that culturing embryos in small volume improves embryonic development by enhancing autocrine factor. However, embryo-toxic factor may impair the embryo development. Since most studies were done by mouse, little work has been done in human. Earlier study showed that there is no correlation between reduced culture volume and human blastocyst formation. But two recent studies demonstrated contrasting results in human blastocyst development. The optimal culture volume is still under debate. Our study aims to evaluate the effect of different culture volume on embryo developmental competence.

MATERIALS AND METHODS: This is a retrospective cohort study performed from November 2018 to November 2019 at CHA Fertility Center Gangnam. A total of 6173 sibling embryos from 799 patients were individually cultured in either 30 µl (n=3271) or 10 µl (n=2902) drops of culture medium. Only normal responder women undergoing IVF/ICSI were included in the study. Sibling embryos were cultured in either 30 µl or 10 µl droplets of Sydney IVF cleavage medium under paraffin oil at 37°C, 6% CO2, 5% O2 and 99% humidity. On day 3, embryos were transferred to corresponding volume of Sydney IVF blastocyst medium. Embryo quality on day 2, 3 and 5 and utilization rate on day 5 were evaluated.

RESULTS: No statistically significant difference was found in embryo utilization rate (25.62% vs 26.22%; p=0.59) with regard to embryos cultured either in large (30 µl) or small (10 µl) drops of culture medium. Similarly, no significant differences were observed in embryo quality on day 2 (45.36% vs. 42.66%; p=0.18), day 3 (44.88% vs. 43.31%; p=0.22) and day 5 (38.00% vs. 18.00%; p=0.82) and clinical pregnancy rates of day 3, 4 and 5 embryo transfers between two different culture drops (36.36% vs. 50.00%; p=0.90, 48.00% vs. 38.30%; p=0.29, 43.30% vs. 45.65%; p=0.32).

CONCLUSIONS: Culture drop size does not have an effect on embryo quality and embryo utilization rate nor on clinical pregnancy rates. Other culture condition, such as oxygen, incubation system, microwell culture system and embryo-conditioned media need to be further considered.

IMPACT STATEMENT: Our results strengthen the finding from the earlier study that smaller culture volumes have no significant effect on human blastocyst development. This may provide a baseline data that can flexibly adjust study that smaller culture volumes have no significant effect on human blastocyst formation. But two recent studies demonstrated contrasting results in human blastocyst development. This may provide a baseline data that can flexibly adjust study that smaller culture volumes have no significant effect on human blastocyst formation. But two recent studies demonstrated contrasting results in human blastocyst development. This may provide a baseline data that can flexibly adjust

P-38 6:30 AM Monday, October 24, 2022

CHARACTERISTICS OF OILS USED FOR ASSISTED REPRODUCTIVE TECHNOLOGY PROCEDURES. Elizabeth White, BS,1 Melissa M. Wittman, BA, in English Composition and Rhetoric,2 Amanda Cinquin, B.SC, PH.D.,1 Robert Newman, PhD3 Irvine Scientific, Santa Ana, CA;4 Fujifilm Irvine Scientific, Santa Ana, CA; 5 Santa Ana, CA; 6 Fujifilm Irvine Scientific, Santa Ana, CA.

OBJECTIVE: Some publications have evaluated mineral oils (MO) and paraffin oils based on labeling as light or heavy, terms which have been used to describe either density or viscosity, and as MO or liquid paraffin (LP). Such studies tested mouse embryo development, pH, osmolality, temperature, viscosity, density, and peroxide value. MO and light mineral oil (LMO), defined in the United States Pharmacopeia, and LP and light liquid paraffin (LLP), defined in the European Pharmacopoeia have requirements for viscosity and density but the defined ranges don't align exactly. All four are defined as mixtures of hydrocarbons. This work characterizes the hydrocarbon molecule sizes in the samples to evaluate similarities between MO, LMO, LP, and LLP with their overlapping definitions.

MATERIALS AND METHODS: The oils for assisted reproductive technology (ART) evaluated include Fujifilm Irvine Scientific Oil for Embryo Culture and Heavy Oil for Embryo Culture, Vitrolife Oovol and Oovil Heavy, LifeGlobal Paraffin Oil P.G., LifeGuard, and LiteOil, and Medicliq Liquid Paraffin. Due to limited volumes, not every sample was used for every test. Viscosity was determined at room temperature, at 2-8°C, and at 37°C with an Ubbelohde viscometer. Density was determined at room temperature using a graduated cylinder and a laboratory balance. MEA was performed in a humidified CO2 box incubator using 1-cell B6C3F1 x B6D2F1 mouse embryos cultured for 96 hours. Carbon numbers were determined based on the ASTM D2887 Standard Test Method for Boiling Range Distribution of Petroleum Fractions by Gas Chromatography.

RESULTS: Viscosity centistoke (cSt) ranges were 55-622 (cold), 25-163 (room temperature), and 16-89 (37°C). Density ranged from 0.82 to 0.87 g/mL. All samples passed MEA. One of the more viscous oils had a wider spread of carbon numbers with percentages over 1%, with a peak of 8% at C25-C26, and skewed towards higher carbon numbers. A second oil tested was multimodal, with peaks of 17% at C27-C28, 19% at C34-C35, and 7% at C41-C42. Three lower viscosity oils had more similar carbon number profiles, with nearly normal distributions of carbon numbers for those with percentages over 1%, with peaks at 11-15% around carbon numbers C22 – C24.

CONCLUSIONS: Correlation between blastocyst rate and density or viscosity was weak, but there was a positive correlation between increased blastocyst rate and larger molecular size. There was no correlation between molecular size and labeling as either MO LM0 or LP/LP, but labeling as light or heavy did correlate with smaller and larger sizes, respectively. Labeling as MO, LMO, LP, or LLP may not sufficiently convey the oil properties, such as density, viscosity, and potentially molecular size. Future studies could examine the makeup as paraffinic, naphthenic, or aromatic in ART oils, to further evaluate whether differences in molecular structures, performance or outcomes can be determined between products labeled as either mineral or paraffin oils.

IMPACT STATEMENT: Further work remains to be done to continue characterizing oils for ART and to correlate differences in chemical properties to changes in performance.

P-39 6:30 AM Monday, October 24, 2022

PATIENCE IS A VIRTUE: THE CLINICAL VIABILITY OF EMBRYOS DERIVED FROM LATE MATURING OOCYTES. Carlos Hernandez–Nieto, MD,1 Tamar Alkon-Meadows, MD,1 Joseph A. Lee, BA,1 Richard E. Slikin, B.A., T(ABB), CLT(NYS),1 Chelsea M. Canon, MD,1 Christine Britton-Jones, PhD,1 Tammy Mulkerjee, MD,2 Benjamin Sandler, MD,1 Alan B. Coppperman, MD1 Reproductive Medicine Associates of New York, New York, NY;2 Tcahn School of Medicine at Mount Sinai, New York, NY.
OBJECTIVE: During egg freezing cycles, patients who suffer from compromised ovarian reserve or low metaphase II (MII) oocyte counts at retrieval after stimulation may benefit from culturing immature oocytes. Yet, limited data has been published about developmentally delayed oocytes that have been matured in culture prior to ICSI. This study assessed the clinical utility of blastocysts derived from late maturing oocytes.

MATERIALS AND METHODS: The study included all patients who underwent an elective oocyte vitrification cycle(s) with subsequent thawing and fertilization from 2016 to 2022. After retrieval, immature oocytes (Germinal Vesicle and Metaphase I) underwent maturation in culture for 24 hours or until reaching the MII stage of oocyte development. All late-MII and normally developed MII oocytes were vitrified and then thawed prior to ICSI. All frozen oocytes that reached the blastocyst stage of embryo development underwent preimplantation genetic testing for aneuploidy (PGT-A). A paired analysis with sibling Late-MII and MII oocyte(s) was performed in the same patient cycle(s). Fertilization rate, blastulation rate, and euploidy rates were evaluated. Descriptive analysis and paired t-test also, a multivariate regression analysis fitted with a GEE model were performed for statistical analysis.

RESULTS: A total of 128 patients underwent an oocyte thaw cycle. Patients had a mean age of 36.6 SD 3.4, BMI of 24.2 SD 4.4, AMH 3.3 SD 2.6, and an average of 16 SD 9.1 frozen oocytes during their retrieval cycle. 261 Late-MII oocytes were compared with 1370 MII oocytes. Oocyte thaw survival were comparable among Late-MII and MII oocytes (74.3% vs. 78.2%, p<0.17). Fertilization rates (55.5% vs 77.2%, p<0.0001) and blastulation rates (85.9% vs 88.7%, p=0.01) were comparable in Late-MII compared with MII oocytes. An adjusted multivariate analysis confirmed a significant association between Late-MII oocytes and lower fertilization rate (aOR 0.26 CI95% 0.20-0.33), and lower blastulation rate (aOR 0.32 CI95% 0.22-0.43). No differences in the percent of euploid, aneuploidy and mosaic embryos were found between Late-MII and MII oocytes. Finally, an adjusted analysis showed no association between Late-MII oocytes and high odds of embryo aneuploidy. (aOR 0.61 CI95% 0.37-0.80).

CONCLUSIONS: Blastocysts derived from cryopreserved/thawed late maturing-MII oocytes have reproductive utility, albeit reduced in comparison to normally developing MII oocytes. Yet, we suggest egg freezing patients with compromised ovarian reserve or low metaphase II (MII) oocyte counts at retrieval achieve pregnancy with blastocysts derived from delayed oocytes. Although these blastocysts have a decreased blastulation rate, viability and euploidy rates are comparable to MII oocytes. These results suggest that egg freezing oocytes with delayed maturation may still be beneficial for patients.

IMPACT STATEMENT: Why some top quality blastocysts fail whereas some poor grade blastocysts successfully implant: the corresponding d3 morphology evaluation may be the key that should not be bypassed.

E-POSTER ABSTRACT SESSION: 5

P-41 6:30 AM Monday, October 24, 2022

DIFFERENTIAL PROTEIN EXCHANGE BETWEEN SINGLE STEP CULTURE MEDIUM AND THE GROWING EMBRYO BETWEEN EUPOID AND ANEPOID EMBRYOS. Sonia Perez-Albala, PhD, Lorena Bori Arnal, PhD, Student; Elena Payo Bosch, Ph.D., Student; Maria de los Angeles Valera, Ph.D., Student; Jose Maria de los Santos, Ph.D., Marcos Meseguer, Ph.D. IVIIRMA Global, Valencia, Spain; IVIIRMA Valencia, Valencia, Spain; IIVIRMA Global, IIVI Foundation, Valencia, Spain; IIVI Valencia. Plaza Policia Local, 340015. Valencia, Spain., Valencia, Spain.

OBJECTIVE: To explore modifications in the protein profile of the spent embryo culture medium in the preimplantation genetic testing program.

MATERIALS AND METHODS: This prospective study included 164 samples of culture medium from treatments of the preimplantation genetic testing for aneuploidies (PGT-A) program. Embryos were cultured until the blastocyst stage in EmbryoScope systems (Vitrolife, Sweden) with single-step medium (Gems, Gena). The spent culture medium was collected on day 5/6 of embryo development (day of trophectoderm biopsy) and chromosone analysis was performed using next-generation sequence technology. The relative concentrations of 92 proteins from 141 samples of spent embry culture medium and 23 control samples (medium in which no embryos had been cultured) were analyzed using Proseek Multiplex Assays (Olink Biosciences, Sweden) based on proximity extension assay (PEA) technology. Proteins were measured using the Proseek Multiplex PEA Panel using 1 ul of each sample. Data were then quality controlled and normalized and the final assay readout was presented as Normalized Protein Expression (NPX) values, which are arbitrary units on a log2 scale, where a high value corresponds to a higher protein expression. Measurements of the 92 proteins were compared between controls and culture media without embryos and also between euploid and aneuploid embryo culture media.

FERTILITY & STERILITY®
RESULTS: Out of the total, 43 were euploid embryos and 98 were aneuploid.

A higher relative concentration of a given protein in the control medium may indicate its consumption by the embryos. For aneuploid embryos, IL-1β and IL-12p40 were significantly higher in control culture media in comparison with embryo culture media. This consumption was also seen for TNSF-14, CCL11 and TNF-beta proteins by euploid embryos. Conversely, fourteen proteins showed higher NPX values in both groups of embryo culture medium compared to control medium, indicating possible secretion by the embryos (IL-8, IL-9, IL-16, uPA, IL-6, IL-17C, MCP-1, CXCL1, TRANCE, 4E-BP1, IL-4, CCL20, STAMPB, ADA). Three proteins showed significantly different concentrations between culture medium samples from euploid and aneuploid embryos: leukemia inhibitory factor receptor (LIF-R), caspase-8 (CASP-8) and Tumor Necrosis Factor beta (TNF-beta). The mean of NPX value for LIF-R was 0.65±0.12 in euploid embryos and 0.73±0.17 in aneuploid embryos. Relative concentration of CASP-8 was also higher in aneuploid embryos (0.98±0.21) than in euploid embryos (0.89±0.22). Culture medium samples from aneuploid embryos also had higher values of TNF-beta compared to media from euploid embryos (0.58±0.24 vs 0.48±0.20).

CONCLUSIONS: This preliminary study demonstrated that a high-performance immunomassay is able to find differences between the protein secretion profile of euploid and aneuploid embryos with only 1 μl of spent culture medium.

IMPACT STATEMENT: Detailed study of protein consumption and secretion by embryos cultured in single step medium could uncover new non-invasive markers of ploidy.

SUPPORT: Supported by Spanish Ministry of Science and competitiveness (Instituto de Salud Carlos III) project: P12I00283.

P-42 6:30 AM Monday, October 24, 2022

EXTERNAL VALIDATION STUDY OF THE ULTRA-FAST BLASTOCYST WARMING TECHNIQUE – OPTIMIZING EFFICIENCY WITHOUT COMPROMISING OUTCOMES. Mackenzie N. Naert, B.A., M.D., M.S.C., Victoria S. Jiang, MD, Irene Dimitriadis, MD, Irene Souter, MD, Charles L. Bornmann, PhD Massachusetts General Hospital Fertility Center, Massachusetts General Hospital and Harvard Medical School, Boston, MA.

OBJECTIVE: To evaluate blastocyst survival and re-expansion rates for biopsied and non-biopsied blastocyst stage embryos following warming with ultrafast warming (UFW) protocol compared to standard warming (SW) protocol.

MATERIALS AND METHODS: Two hundred vitrified blastocysts were warmed using a SW protocol (100 embryos total; 50 biopsied, 50 non-biopsied) and a UFW protocol (100 embryos total; 50 biopsied, 50 non-biopsied). SW protocol involved warming blastocysts for 1 minute in thaw solution (TS) at 37°C, then at room temperature, rinsing for 4 minutes in dilution solution (DS), and two rinses in wash solution (WS) for 8 minutes. UFW protocol involved warming blastocysts for 1 minute in TS followed by four washes in culture medium, all at 37°C. Results were stratified by Gardner’s blastocyst stage. Initial blastocyst survival rate and full blastocyst re-expansion rates at 2- and 4-hours post-warming were evaluated among all cohorts. Two-tailed t tests were performed to compare groups, with statistical significance set at p < 0.05.

RESULTS: There was a 100% initial survival rate for blastocysts in both warming protocol groups (n = 200), regardless of blastocyst stage or biopsy status. There were no differences in the rate of blastocell re-expansion at 2 hours (84.0% vs 82.0%, p > 0.99; SW vs UFW, resp.) and 4 hours (94.0% vs 93.6%, SW vs UFW, resp.) post-warming for blastocysts of all stages, with and without biopsy. Embryos were then divided into early blastocysts (Stage 3), expanded blastocysts (Stage 4), and hatching blastocysts (Stage 5 and 6) with and without biopsy. Among non-biopsied embryos (n = 100), there was no difference in rates of full blastocyst re-expansion for early blastocysts (2 hours: 80.0% vs 83.3%, p = 0.55; 4 hours: 80.0% vs 88.9%, p = 0.74; SW vs UFW protocol, resp.), expanded blastocysts (2 hours: 82.5% vs 80.8%, p = 0.86; 4 hours: 95.0% vs 96.2%, p = 0.83; SW vs UFW protocol, resp.), or hatching blastocysts (2 hours: 100.0% vs 83.3%, p = 0.39; 4 hours: 100.0% vs 100.0%, SW vs UFW protocol, resp.). Among biopsied embryos (n = 100), there was no difference in rates of blastocyst re-expansion for early blastocysts (2 hours: 62.5% vs 75.0%, p = 0.70; 4 hours: 87.5% vs 100%, p = 0.51; SW vs UFW protocol, resp.), expanded blastocysts (2 hours: 71.4% vs 88.9%, p = 0.41; 4 hours: 100.0% vs 100.0%, SW vs UFW protocol, resp.), or hatching blastocysts (2 hours: 88.6% vs 83.8%, p = 0.56; 4 hours: 94.3% vs 91.9%, p = 0.09; SW vs UFW protocol, resp.).

CONCLUSIONS: Our study found similar rates of blastocyst survival and re-expansion at 2 and 4 hours between standard and ultra-fast warming protocols. This is the first external validation study assessing the ultra-fast protocol. In addition, we found that neither the blastocyst stage at the time of vitrification (ranging from stages 3-6) nor the biopsy status of the embryo affected these results.

IMPACT STATEMENT: This study demonstrates that ultrafast blastocyst warming is a potential method of decreasing thaw time without compromising blastocyst survival and re-expansion. Further studies should investigate embryo implantation and live birth rates following the ultra-fast warm protocol.

P-44 6:30 AM Monday, October 24, 2022

SIMPLE AND LOW-COST FABRICATION OF WELL-OF-THE-WELL (WOW) DISHES WITH ARBITRARY SHAPES FOR EMBRYO CULTURE. Yunjin Zhao, M.S., Audrey Bowden, Ph.D. Vanderbilt University, Nashville, TN.

OBJECTIVE: To demonstrate the use of 3d printing as a simple, cost-effective strategy to produce novel well-of-the-well (WOW) dishes with arbitrary shapes/dimensions for future explorations of optimal culture conditions.

MATERIALS AND METHODS: We first designed a negative mold in SolidWorks (Dassault Systèmes) to template WOW dishes comprising four cylindrical wells (6 mm diameter, 3 mm high), each capable of holding up to 81 μl of culture media. Each well was filled with identical microwells in one of the following four different microwell designs, each 200-μm deep: 1) large truncated cones (top diameter 400 μm, base diameter 200 μm); 2) small truncated cones (top diameter 300 μm, base diameter 100 μm); 3) hemispheres (diameter 400 μm) and 4) pyramids (side length 400 μm). Thus, a single dish comprised 36 microwells. The negative mold was 3d-printed (Core 530, B9Creations) using high-detail resin. To verify the printing quality, we assessed the microstructures in the mold using Optical Coherence Tomography (OCT, Thorlabs). To fabricate the dish, the 3d printed mold was then treated with trichloro(1H, 1H, 2H, 2H-perfluorooc- toxyl)trichlorosilane (PFDOCTS, Sigma) overnight to facilitate removal. Polydimethylsiloxane (PDMS, Sylgard 184, DOW) was prepared following the manufacturer manual, degassed for 30 minutes, and then poured directly on the mold. Subsequently, a second 20-minute degassing step was performed to remove any trapped air bubbles. Then, we covered the PDMS-filled mold with a methacrylate-treated glass slide to form a flat WOW bottom and cured it at 75 °C in an oven for at least three hours. After that, we removed the glass slide and retrieved the cured WOW from the mold. Finally, the WOW structure was glued to an IVF Petri dish (NUNC, Thermo Fisher) by a droplet of PDMS and cured for at least 48 hours at room temperature, allowing the final WOW dish to hold mineral oil to eliminate evaporation and to possess a vented lid to facilitate air exchange.

RESULTS: The microstructures in the 3d printed mold showed consistency in their shape and dimensions during the printing quality assessment using OCT. Fabricated WOWs as inspected by micro-CT, indicated that all microstructures were reliably transferred from the mold and met design requirements. The cost of each WOW dish, including the cost for the 3d-printed mold, mold surface treatment chemicals, PDMS, glass slide and Petri dish, is about $3.80. Each mold can be reused to make at least 25 WOWs.

CONCLUSIONS: We proposed a simple and low-cost method that can fabricate WOWs of arbitrary shape.

IMPACT STATEMENT: Embryo culture is an essential and critical step in the IVF procedure. WOWs are known to yield better culture quality, but the optimal WOW design remains unknown. Pyramidal microwells have been shown to yield better culture outcomes for stem cells, but such shapes have not been tested for embryo culture. Our simple and low-cost fabrication strategy, which combines 3d printing with one-step PDMS molding, provides a new handle to tune embryo culture conditions by exploring the effect of WOW shapes / dimensions on enhanced culture outcomes.

OBJECTIVE: Comparison of the rates of recovery mature oocytes, fertilization, cleavage, expanded embryos, blastocysts formation and clinical pregnancy, between cycles using hydrotropiosine and cycles with flexible GnRH antagonist analogues to block the LH surge.

MATERIALS AND METHODS: 100 cycles of patients enrolled in IVF-ICSI treatment comprised from June 2018 to July 2019 were analyzed. Of these cycles, 50 were performed using 20mg of daily Dydrogesterone (Duaphaston®, Abbott) as an alternative protocol to suppress the premature LH surge during follicular phase (Group 1); and for the other 50 cycles, 0.25mg of daily flexible GnRH antagonist (Ganirelix acetate, Orgalutran®, MSD) protocol was chosen (Group 2). For all patients, 225 U of Alifalutropine + 150 U of Alifalutropine (Pergoveris®, Merck) were administered daily, subcutaneously, starting day 02 of menstrual cycle and lasting for at least 09 days. Trigger parameter consisted of at least 02 dominant follicles larger than 17mm, when 2.5mg of Leuprolrelone Acetate were administered subcutaneously for all patients. Oocyte retrieval were performed 35 hours after trigger. All embryos were cultured and frozen in blastocyst stage. The laboratory and clinical parameters analyzed were: total number of mature oocytes recovered (MII); fertilization rate, cleavage rate; blastocyst formation; clinical pregnancy rate. Patients were also matched by age, as a bias variable. To compare the variables according to the two induction protocols, the Mann-Whitney test and the Chi-square test were used. For all analyses, the significance level was p<0.05. The statistical program used was Minitab version 18.1.

RESULTS: No statistically significant results were found regarding the number of oocytes obtained and the oocyte maturation rate between groups 1 and 2 (338/345 p=0.86, 76.92%/78.84% p=0.55) respectively. ICSI was performed in 260 oocytes of group 1 and 272 of group 2. There was no difference in fertilization rates (79.62%/77.94% p=0.64), cleavage embryos and top quality embryos rate (98.55%/96.23% p=0.14, 71.57%/69.12% p=0.59), as well as blastulation rates and top quality blastocysts (48.78%/58.72% p=0.17, 32.50%/43.75% p=0.25). Regarding clinical pregnancy rate, the results were similar, with no significant differences between groups 1 and 2, respectively (38.78%/42.00%, p=0.74). When separated by age (≤ 37 years and ≥ 38 years), the groups also did not present statistically significant differences in any of the variables analyzed.

CONCLUSIONS: The use of dydrogesterone in ovarian stimulation protocols to suppress LH surge in IVF cycles can produce similar laboratory and clinical results compared to the use of GnRH antagonist analogues. The necessity of cryopreservation and its cost benefits represents an issue to be better evaluated.

IMPACT STATEMENT: Considering patient driven awareness strategies, the novel oral protocol using dydrogesterone appears to be an excellent option to conventional antagonist LH suppression surge protocol. Further studies are necessary.
The embryos with the least chromosome imbalance (#4 and #7) reached more advanced stages of development. The patient subsequently underwent treatment with donated eggs and had a successful live birth following the first ET.

CONCLUSIONS: Despite normal early cleavage, 6/7 2PN embryos arrested prior to reaching the expanded blastocyst stage. The impact of other environmental factors on embryonic arrest or implantation failure was unlikely considering the patient’s successful treatment with donor eggs. This illustrates how extensive embryo aneuploidy from aberrant maternal meiosis may impede embryo development beyond the time of the morula-blastocyst transition. The severity of genomic imbalance in embryos may also dictate the stage of embryo arrest in vitro, or following ET. This is supported by the continued development of the 3PN and the embryo containing the least meiotic aneuploidy developing furthest.

IMPACT STATEMENT: This is the first evidence to suggest that maternal meiotic aneuploidy may play a part in pre-implantation embryonic arrest. The full impact of meiotic aneuploidy on blastocyst development remains unknown.

P-48 6:30 AM Monday, October 24, 2022
ARTIFICIAL REMOVAL OF ZONA PELLUCIDA AT THE PRONUCLEAR STAGE (ZP-FREE CULTURE) DECREASES THE INCIDENCE OF ABERRANT DIVISION AT THE FIRST CLEAVAGE. Keitaro Yumoto, B.S., Toko Shimura, B.S., Minako Sugishima, B.S., Minori Nakaoka, M.S., Yasuyuki Mio, MD, PHD Mio Fertility Clinic, Yonago, Japan.

OBJECTIVE: Aberrant division, also known as the direct cleavage (DC), often occurs in human zygotes and is known to adversely affect the implantation rate. To date published data show that the incidence of DC at the first cleavage is approximately 14%. Moreover, studies from our clinic have previously demonstrated that the incidence of DC at the first cleavage is 18.6% (952/5,121). Recently, the ZP-free culture has been conducted in our clinical settings, and the rate of good quality embryos and the blastocyst development are improved by this new culture method. However, how this new culture method affects the subsequent embryo development has not yet been fully clarified. This study aims to determine if the ZP-free culture method affects the incidence of aberrant division at the early cleavage.

MATERIALS AND METHODS: The present study included 532 normally fertilized ZP-free cultured zygotes from 214 cycles of IVF or ICSI in 141 cases with a recurrent ART failure due to severe fragmentation. Zygotes were observed by time-lapse imaging, and the incidence of aberrant division at the first and second cleavage was examined and compared with the previously obtained results by ZP-intact zygotes. For ZP-free culture, the ZP was completely removed by laser irradiation and “medium-blowing” method using biopsy pipettes while being placed in hypersonic solution at the pronuclear stage was performed. Based on their cleavage patterns, the resultant ZP-free zygotes were classified into four groups: Group 1 (Normal cleavage, NC); Group 2 (from 1-cell to ≤3-cell, DC1-3); Group 3 (from 2-cell to ≥5-cell in 5 hours after the first cleavage, DC2-3); and Group 4 (from 2-cell to ≥5-cell, DC2-5).

RESULTS: The proportion of zygotes classified in Groups 1 to 4 was 88.3% (n=482), 4.0% (n=22), 2.9% (n=16), and 4.8% (n=26), respectively. The incidence of aberrant division at the first cleavage (the sum of Group 2 and 3) in ZP-free cultured zygotes was 6.9% (n=38). On the other hand, in our previous study for ZP-intact zygotes, the classification proportion of Groups 1 to 4 was 83.8% (n=4289), 8.9% (n=456), 9.7% (n=496), and 6.6% (n=336), respectively. So, the incidence of aberrant division at the first cleavage in ZP-intact zygotes was 18.6% (n=952). As a result, ZP-free cultured zygotes showed the significantly lower incidence of aberrant division compared to ZP-intact (P<0.01). Furthermore, the blastocyst development rate (BDR) was significantly lower in ZP-free cultured zygotes with the aberrant division at the first cleavage (Group 2 and 3: 7.9%, n=9) than in zygotes with normal division (Group 1: 62.7%, n=302) (P<0.01).

The embryos with the least chromosome imbalance (#4 and #7) reached more advanced stages of development. The patient subsequently underwent treatment with donated eggs and had a successful live birth following the first ET.

CONCLUSIONS: Despite normal early cleavage, 6/7 2PN embryos arrested prior to reaching the expanded blastocyst stage. The impact of other environmental factors on embryonic arrest or implantation failure was unlikely considering the patient’s successful treatment with donor eggs. This illustrates how extensive embryo aneuploidy from aberrant maternal meiosis may impede embryo development beyond the time of the morula-blastocyst transition. The severity of genomic imbalance in embryos may also dictate the stage of embryo arrest in vitro, or following ET. This is supported by the continued development of the 3PN and the embryo containing the least meiotic aneuploidy developing furthest.

IMPACT STATEMENT: This is the first evidence to suggest that maternal meiotic aneuploidy may play a part in pre-implantation embryonic arrest. The full impact of meiotic aneuploidy on blastocyst development remains unknown.

P-47 6:30 AM Monday, October 24, 2022
MOSAICISM INCIDENCE IS INDEPENDENT OF THE TYPE OF CULTURE MEDIUM – A COMPARISON BETWEEN CONTINUOUS CULTURE MEDIUM (CCM) AND SEQUENTIAL CULTURE MEDIUM (SCM). Andrea Abdala, M.Sc.,1 Ibrahim Elkhatib, M.Sc.,1 Asina Bayram, M.Sc.,1 Ahmed El-Damen, M.Sc.,1 Daniela Nogueira, PhD,3 Laura Melado, M.D, PhD,2 Raquel Del Gallego, PhD,1 Lawrenz Barbara, M.D., PhD,1 Human M. M. Fatemi, M.D., PhD,1 Human M. M. Fatemi, M.D., PhD,1 Yuki Yamada, M.D., PhD,112 Colette Cogné, PhD,212 Enrique de la Maza, PhD,212 University of Zaragoza, Zaragoza, Spain.

OBJECTIVE: To evaluate whether the type of culture medium affects mosaicism rates when sibling oocytes were cultured using CCM or SCM.

MATERIALS AND METHODS: A single center observational study was performed between January 2019 and December 2021, including 4802 sibling oocytes inseminated and cultured in CCM and SCM (74.3% vs 72.2%, p=0.127). Although blastulation rates on D5 and usable blastocyst rates (biopsied blastocysts/2PN) were significantly higher in CCM than SCM (70.5% vs 61.1%, p=0.001 and 60.5% vs 54.6%, p=0.001), euploidy rates did not differ significantly (44.6% vs 45.1%, p=0.823 for CCM and SCM, respectively). Mosaicism rates were comparable regardless of whether blastocysts were cultured in CCM or SCM (4.2% vs 4.8%, p=0.483, respectively), without a difference in the proportion of low or high mosaic rates (3.1% vs 4.3%, p=0.170 and 1.0% vs 0.6%, p=0.222 for CCM and SCM, respectively).

CONCLUSIONS: Mosaicism rates are not affected by CCM or SCM, with a prevalence of 9% mosaic blastocytes regardless of the type of culture medium.

IMPACT STATEMENT: Biological mosaicism is caused by mitotic errors during the post-zygotic stage. Hence, culture conditions including the type of culture medium can influence mosaicism incidence. The current study clearly demonstrated that the risk of mosaicism is comparable between CCM and SCM, proving the safety of choosing one type of culture over another.

SUPPORT: None.

P-130 10:00 AM Monday, October 24, 2022

OBJECTIVE: To perform a comprehensive analysis of the complete genome of all embryos following preimplantation genetic screening using a next-generation sequencing-based approach.

METHODS: The study was performed by ReproSeq Mosaic PGS w1.1 workflow on Ion Reporter using Ion ChefTM-Ion GeneStudioTM S5 Prime System (ThermoFisher Scientific). Aneuploidy analysis of each embryo was performed by ReproSeq Mosaic PGS w1.1 workflow on Ion Reporter using standard parameters. Mosaicism was classified as low (30-50%) and high (50-70%) based on the level of the abnormal chromosomal constitution detected in the TE samples. Assay’s sensitivity and specificity were 98.2% and 95%, respectively. Chi-square test was used for statistical analysis, considering p<0.05 statistically significant.

RESULTS: Women mean age was 33.3 ± 6.4 years old. Total fertilization rate was not significantly different between oocytes inseminated and cultured in CCM and SCM (74.3% vs 72.2%, p=0.127). Although blastulation rates on D5 and usable blastocyst rates (biopsied blastocysts/2PN) were significantly higher in CCM than SCM (70.5% vs 61.1%, p=0.001 and 60.5% vs 54.6%, p=0.001), euploidy rates did not differ significantly (44.6% vs 45.1%, p=0.823 for CCM and SCM, respectively). Mosaicism rates were comparable regardless of whether blastocysts were cultured in CCM or SCM (4.2% vs 4.8%, p=0.483, respectively), without a difference in the proportion of low or high mosaic rates (3.1% vs 4.3%, p=0.170 and 1.0% vs 0.6%, p=0.222 for CCM and SCM, respectively).

CONCLUSIONS: Mosaicism rates are not affected by CCM or SCM, with a prevalence of 9% mosaic blastocytes regardless of the type of culture medium.

IMPACT STATEMENT: Biological mosaicism is caused by mitotic errors during the post-zygotic stage. Hence, culture conditions including the type of culture medium can influence mosaicism incidence. The current study clearly demonstrated that the risk of mosaicism is comparable between CCM and SCM, proving the safety of choosing one type of culture over another.

SUPPORT: None.
CONCLUSIONS: Our present data reveal that the ZP-free culture significantly decreases the incidence of aberrant division. Furthermore, since the BDR of DC1-3 and DC2-3 zygotes was significantly lower than NC zygotes, ZP-free culture is likely to improve the pregnancy rate by decreasing the incidence of aberrant division at the early cleavage.

IMPACT STATEMENT: The incidence of aberrant division at the first cleavage can be decreased by the artificial ZP removal at the pronuclear stage (ZP-free culture).

SUPPORT: non

P-49 6:30 AM Monday, October 24, 2022

ASSESSMENT OF THE OXIDATIVE STATUS OF SPENT GROUPED EMBRYO CULTURE MEDIA AS A POTENTIAL BIOMARKER OF QUALITY OF BLASTOCYST COHORTS IN ASSISTED REPRODUCTION TREATMENTS. María de los Ángeles Valera, PhD Student,1 Akhil Garg, PhD Student,2 Lorena Bori Arnal, PhD Student,2 Fernando Meseguer, PhD Student,2 Marcos Meseguer, Ph.D.1 1IVIRMA Global, IVI Foundation, Valencia, Spain; 2IVIRMA Global, Valencia, Spain.

OBJECTIVE: To assess the oxidative profile of spent culture media of grouped time-lapse embryo culture system and its relationship with the quality of embryo cohorts.

MATERIALS AND METHODS: The study was performed over 287 ICSI treatments (153 autologous (AT), 134 ovum donation (ODT)), performed in a single IVF clinic over 3 consecutive years, in which embryo cohorts were cultured in an EmbryoScope Plus incubator (VitroLife), with Gems single-step culture media (Genea Biomedx). The EmbryoSlide+ has two separate pools of 180µL, with capacity for 8 embryos each. All pools with at least two fertilized oocytes were collected, (406 samples in total, 213 autologous, 193 ovum donation). The oxidative status of the spent media was analyzed in the Fertissimo Thermochemiluminiscence (TCL) Analyzer13 (Carmel Diagnostics), which quantifies the total oxidation capacity of the media by counting photon emission per second after heating. TCL results were normalized and summarized in the H2 parameter, expressing TCL amplitude at 155s of reaction. Distribution of H2 was compared between spent media from autologous and ovum donation treatments through non-parametric Kruskal-Wallis test (K-W). Blastocyst rate (BR), good quality blastocyst rate (GQBR; proportion of blastocysts classified as A or B by ASAPERI morphological criteria) and euploidy rate (ER) in PGT-A treatments (n=70) were calculated per each embryo pool separately. The correlation of the calculated developmental rates, as well as the oocyte age of the cohorts, with standardized H2 values was assessed through the Spearman’s ρ correlation coefficient.

RESULTS: H2 parameter resulted significantly higher in media samples from ODT compared to AT: KW=4.876; P=0.027, indicating higher oxidation in the media. A significant inverse correlation was found between H2 and oocyte age (Rho=-0.116; P=0.019). No significant correlation was found between H2 and the BR (Rho=0.044; P=0.372), but it resulted positively correlated with the GQBR (Rho=0.128; P=0.027). When stratifying by oocyte source, in AT no correlation was found between H2 and oocyte age (Rho=-0.022; P=0.744) or BR (Rho=0.027; P=0.693), but a direct correlation was found with GQBR (Rho=0.200; P=0.004). In media samples from ODT, no significant correlation was found between H2 and any of the studied rates (Rho (oocyte age)=-0.125, P=0.083; Rho(BR)=0.03, P=0.683; Rho(GQBR)=-0.007, P=0.918). These variables were significantly different between the two types of treatment: oocyte age=35.10±3.97 AT vs 25.22±4.70 years ODT, P<0.001; BR=68.62±28.28 AT vs 77.22±21.70 ODT, P<0.001; GQBR=48.18±34.91 AT vs 62.22±29.43 ODT, P<0.001. In PGT-A treatments, a direct correlation was found between H2 and the ER (Rho=0.247; P=0.040).

CONCLUSIONS: Results suggest that blastocyst morphology and euploidy are related to their oxidative metabolic competence, which is reflected in the oxidation of the spent culture media.

IMPACT STATEMENT: Measurement of the oxidative status of the embryo spent culture media might be a valid biomarker of the environment of the growing embryo and reflect the overall quality of blastocyst cohorts.

SUPPORT: The authors’ research is supported by the Generalitat Valenciana (Conselleria de Educacion, Investigacion, Cultura y Deporte) and European Social Fund (ACIF/2019/264).

P-50 6:30 AM Monday, October 24, 2022

HOW MANY EGGS DO I NEED? NUMBER OF OOCYTES REQUIRED TO CREATE ONE EUPLOID BLASTOCYST USING FRESH RETRIEVALS OR FROZEN OOCYTES. David H. McCulloh, PhD.1 Caroline McCaffrey, H.C.L.D, PH.D,2 Brooke Hodes-Wertz, M.D., M.P.H.,3 James A. Grifo, MD, PhD.4 1NYU Langone Health, New York, NY; 2New York Langone Health, NYU Fertility Center, New York, NY; 3NYU Langone Prelude Fertility Center, New York, NJ; 4NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: A recent trend in ART is to perform preimplantation genetic testing for aneuploidy (PGT-A) to select single euploid embryos for transfer. This results in higher live birth rates per transfer, per transferred embryo and lower miscarriage rates. It is not yet clear how many oocytes are required to generate sufficient euploid embryos to achieve patient’s goals for family building.

MATERIALS AND METHODS: The experience at our large academic practice that is heavily reliant upon the use of PGT-A was summarized to determine how many euploid embryos (using PGT-AI2, Cooper Genomics) resulted from the numbers of oocytes utilized in ART procedures. The inverse quantity (oocytes/euploid embryo) was used to estimate the mean number of oocytes necessary to obtain one euploid blastocyst. The 95% confidence limits (CL) of euploid embryos per oocyte were inverted to estimate the 95% CLs of the mean number of oocytes.

RESULTS: Table 1 shows the mean number of oocytes required and the means’ 95% confidence limits. Note that the numbers of fresh or frozen oocytes are similar for donors and patients up to age 31. At ages 41-46, the 95% confidence limits include large values exceeding 100 oocytes. Between 32 and 40 years, roughly 3-10 (30-90%) more frozen oocytes than fresh oocytes were needed to obtain one euploid blastocyst.

Table 1. Fresh or Frozen Oocytes Needed (means and 95% Confidence Limits (CLs) to Obtain 1 Euploid Blastocyst

<table>
<thead>
<tr>
<th>Age</th>
<th>Fresh Oocytes Retrieved</th>
<th>Frozen Oocytes Thawed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean 95% CLs</td>
<td>mean 95% CLs</td>
</tr>
<tr>
<td>donor</td>
<td>5.1 4.5 - 5.9</td>
<td>6.2 5.2 - 7.7</td>
</tr>
<tr>
<td>&lt;30</td>
<td>6.1 5.7 - 7.5</td>
<td>6.1 4.5 - 9.5</td>
</tr>
<tr>
<td>30</td>
<td>4.9 4.2 - 5.8</td>
<td>6.9 4.4 - 16</td>
</tr>
<tr>
<td>31</td>
<td>5.2 4.6 - 6.6</td>
<td>7.4 4.3 - 24.2</td>
</tr>
<tr>
<td>32</td>
<td>5.4 4.9 - 6.1</td>
<td>10.1 6.8 - 19.7</td>
</tr>
<tr>
<td>33</td>
<td>5.3 4.8 - 5.8</td>
<td>8.4 6.6 - 11.8</td>
</tr>
<tr>
<td>34</td>
<td>5.2 4.7 - 5.7</td>
<td>8.4 6.6 - 11.5</td>
</tr>
<tr>
<td>35</td>
<td>6.0 5.5 - 6.6</td>
<td>9.0 7.2 - 12</td>
</tr>
<tr>
<td>36</td>
<td>6.0 5.4 - 6.6</td>
<td>10.1 8.2 - 13.2</td>
</tr>
<tr>
<td>37</td>
<td>6.4 5.8 - 7.1</td>
<td>12.3 10 - 15.9</td>
</tr>
<tr>
<td>38</td>
<td>7.1 6.3 - 8.1</td>
<td>12.1 9.8 - 15.6</td>
</tr>
<tr>
<td>39</td>
<td>8.6 7.5 - 9.9</td>
<td>13.9 11.1 - 18.5</td>
</tr>
<tr>
<td>40</td>
<td>12.3 10.8 - 14.2</td>
<td>22.2 14.2 - 49.9</td>
</tr>
<tr>
<td>41</td>
<td>15.4 12.9 - 19</td>
<td>48.9 22.9 - &gt;200</td>
</tr>
<tr>
<td>42</td>
<td>28.2 23.4 - 35.6</td>
<td>45.0 25.4 - 198.4</td>
</tr>
<tr>
<td>43</td>
<td>45.0 31.8 - 77.2</td>
<td>42.8 18 - &gt;200</td>
</tr>
<tr>
<td>44</td>
<td>50.6 21.8 - &gt;200</td>
<td>ND ND ND ND</td>
</tr>
<tr>
<td>45</td>
<td>105.5 49.4 - &gt;200</td>
<td>ND ND ND ND</td>
</tr>
<tr>
<td>46</td>
<td>180.0 60.8 - &gt;200</td>
<td>ND ND ND ND</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The number of oocytes necessary to obtain 1 euploid blastocyst increases with patient age. It is well known that the number of oocytes retrieved per cycle decreases with increasing patient age. Therefore, as patient age increases, it is increasingly unlikely that a patient will achieve the required number of oocytes within one retrieval to achieve a euploid blastocyst. More frozen oocytes than fresh oocytes are needed to achieve one euploid blastocyst. Both fresh and frozen oocyte groups may need more oocytes to achieve a live birth.
OBJECTIVE: The present study aimed to evaluate the potential of deep models in the process of machine learning-based prediction of clinical pregnancy and live birth based on clinical data and single static-morphology blastocyst images.

MATERIALS AND METHODS: This is a retrospective single-center cohort study analyzing blastocyst images (acquired at 116 hours post ICSI) collected over a 4-year period (2018-2021). A total of 2,270 images was gathered from 837 patients. These patients were selected using the Sivbase architecture test set of 100 images. To assess the potential of the Sivbase architecture to mimic Gardner score annotation with respect to clinical pregnancy and live birth prediction, the experiment was repeated while replacing the human annotated Gardner criteria by the Sivbase predictions. RESULTS: Live birth rate was associated with blastocyst expansion and ranged from 31% (early blastocysts) to 42% (hatching blastocyst). Inner cell mass quality was less predictive of live birth as compared to trophectoderm quality. Swin base architecture prediction scores were comparable to human annotated Gardner scores in the accuracy to predict pregnancy (0.68 vs. 0.70), clinical pregnancy (0.67 vs. 0.69), and live birth (0.75 vs. 0.74). CONCLUSIONS: The present study demonstrates the potential of artificial intelligence in a process of selecting and ranking blastocysts based on a single static-morphology blastocyst image. There is particular great potential to deselect blastocysts with limited chance of implantation on the basis of static morphology images. Inclusion of more clinical data and hybrid deep learning models will further help to improve prediction potential.

P-53 6:30 AM Monday, October 24, 2022
ARE THE MORPHOKINETIC PARAMETERS OF EUPOID EMBRYOS DIFFERENT FROM THAT OF ANEUPLOID EMBRYOS? Gulcin Ozkara, PhD,1 Beril Yuksel, M.D., Assoc., Prof.,1 Hakan Kadir Yelke, M.SC.,2 Mehmet Ali, Tufekci, PhD,3 Semra Kahraman, M.D., Prof.,4 Yesim Kutunep Celakoglu, M.Sc3 Sisli Memorial Hospital, Istanbul, Turkey;2 Senior Embryologist, Istanbul, Turkey;2 Istanbul Memorial Sisli Hospital, Istanbul, Turkey;2 Memorial Sisli Hospital, Istanbul, Turkey;2 Istanbul Memorial Hospital, Istanbul, Turkey;2 Senior embryologist, Esenler, Turkey.

OBJECTIVE: To compare the morphokinetic parameters (MPs) of euploid and aneuploid embryos cultured in a time-lapse imaging system (TLI).

MATERIALS AND METHODS: This retrospective cohort study was conducted using the database of Sisli Memorial Hospital, ART and Reproductive Genetics Center between January 2017 and December 2020. A total of 1,840 euploid and 1,408 aneuploid embryos cultured in incubators with a TLI (EmbryoScope Plus®, Vitrolife) were reviewed retrospectively. All MPs of the embryos, from fertilization up to blastocyst expansion, were evaluated. Trophoderm biopsy (TB) was performed on embryos that reached the blastocyst stage (at least 2AB) on day 5 or 6. Embryos were diagnosed as euploid or aneuploid by Next Generation Sequencing (NGS). Morphokinetic parameters (time to pronuclei appearance (PNAP), time to pronuclei fading (PNAP)), time to cleavage into the cells of 2 (t2) - 9 (t9), time to morula (tM), time to start blastulation (tSB), time to blastulation (tB), time to expanded blastulation (tEB), and interval t2-tB, tM(tB), t9-tB) were analyzed to compare euploid and aneuploid embryos. Statistical analysis was done with Student’s t-test (Table).

RESULTS: The mean of t2, t7, t18 (p < 0.005), tSB, tB, tEB (p < 0.0001) of aneuploid embryos were statistically significantly longer than euploid embryos. In addition, the mean interval of tM-tB and t9-tB were in aneuploid embryos statistically significantly longer in euploid embryos, (p < 0.001).

CONCLUSIONS: MPs in time-lapse imaging may be useful for non invasive finding the embryos for transfer because the MPs of euploid and aneuploid embryos are different.

IMPACT STATEMENT: Aneuploidy is one of the most important causes of implantation failure and miscarriage. The final diagnosis of aneuploidy is established by PGT-A. In cases where PGT-A cannot be performed for social or financial reasons, TLI may be used as an embryo selection method to predict euploid embryos.
Table. Comparison of morphokinetic parameters between euploid and aneuploid embryos by TLI

<table>
<thead>
<tr>
<th>Stage</th>
<th>Euploid n=864 (Mean duration (hours) ± SD)</th>
<th>Aneuploid n=1408 (Mean duration (hours) ± SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>tPNa</td>
<td>8.43 ± 4.43</td>
<td>8.46 ± 3.09</td>
<td>.883</td>
</tr>
<tr>
<td>tPNI</td>
<td>23.47 ± 4.27</td>
<td>23.68 ± 3.68</td>
<td>.205</td>
</tr>
<tr>
<td>t2</td>
<td>25.99 ± 3.14</td>
<td>26.28 ± 3.73</td>
<td>.051</td>
</tr>
<tr>
<td>t3</td>
<td>36.86 ± 4.36</td>
<td>37.15 ± 5.02</td>
<td>.140</td>
</tr>
<tr>
<td>t4</td>
<td>38.65 ± 4.57</td>
<td>39.13 ± 5.60</td>
<td>.028</td>
</tr>
<tr>
<td>t5</td>
<td>49.38 ± 6.71</td>
<td>50.09 ± 7.57</td>
<td>.021</td>
</tr>
<tr>
<td>t6</td>
<td>52.11 ± 6.17</td>
<td>52.99 ± 7.11</td>
<td>.002</td>
</tr>
<tr>
<td>t7</td>
<td>54.83 ± 7.03</td>
<td>55.70 ± 8.24</td>
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<tr>
<td>t8</td>
<td>58.47 ± 8.81</td>
<td>59.67 ± 9.93</td>
<td>.003</td>
</tr>
<tr>
<td>t9</td>
<td>69.42 ± 8.70</td>
<td>70.41 ± 9.64</td>
<td>.012</td>
</tr>
<tr>
<td>tSC</td>
<td>81.04 ± 8.83</td>
<td>81.87 ± 9.25</td>
<td>.162</td>
</tr>
<tr>
<td>tM</td>
<td>86.16 ± 8.88</td>
<td>86.24 ± 9.45</td>
<td>.846</td>
</tr>
<tr>
<td>tSB</td>
<td>97.67 ± 7.49</td>
<td>99.36 ± 7.82</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>tB</td>
<td>105.03 ± 7.29</td>
<td>107.29 ± 7.89</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>tEB</td>
<td>111.07 ± 6.46</td>
<td>113.51 ± 6.46</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>t2±8</td>
<td>32.57± 7.94</td>
<td>33.46± 8.48</td>
<td>.012</td>
</tr>
<tr>
<td>t9±M</td>
<td>16.83± 9.83</td>
<td>16.06± 10.54</td>
<td>.086</td>
</tr>
<tr>
<td>tM±tSB</td>
<td>11.69± 8.26</td>
<td>13.29± 6.71</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>t9±tB</td>
<td>35.92± 6.87</td>
<td>37.93± 9.88</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Transferring euploid Day 5 embryos resulted in higher IR versus Day 6, and no difference in P-Rt was observed between the two groups.

IMPACT STATEMENT: The present study provides useful information for embryo selection according to the day of biopsy and vitrification in clinics that utilize a high percentage of PGT and subsequent FET. Previous studies utilized varied parameters that were difficult for comparison. Recommendations to transfer Day 5 over Day 6 may have resulted in disposition of viable embryos with the ability to result in live birth. The inclusion of a larger dataset could strengthen the recommendation of the superior day of transfer. Embryo selection is a multifactorial process encompassing a range of parameters and further investigation is warranted.

P-55 6:30 AM Monday, October 24, 2022

DEVELOPMENTAL POTENTIAL OF OOCYTES THAT ARE IMMATURE (MI) AT THE TIME OF INTRACYTOPLASMIC SPERM INJECTION. Theodore Saydah, BS, Alicia Broussard, PhD, Edward J. Nejat, MD, FACOG, Janelle Luk, M.D., Jesse J. Hade, M.D. Generation Next Fertility, New York, NY.

OBJECTIVE: Oocyte nuclear maturation resumes following ovulation and the complex events of cytoplasmic maturation. Patients with low ovarian reserves and advanced maternal age often yield very few oocytes during oocyte retrieval. In vitro fertilization (IVF) can be a long and expensive process that requires a great emotional toll on the patient. The patient also may have little opportunity to obtain their own oocytes due to age and ovarian factors. Utilizing every oocyte possible gives the patient an increased chance of success with their own oocytes. At the time of oocyte retrieval and stripping, patients often have a population of mature and immature oocytes. Immature oocytes (MI) have a substantially lower developmental potential than mature oocytes (MII) and are typically discarded at most centers. The use of them in IVF is still unclear. Here we explore the developmental potential of MI oocytes and their potential to result in viable pregnancies.

MATERIALS AND METHODS: This was a retrospective study to evaluate clinical practices in our laboratory. In patients with MII and MI oocytes retrieved, MI oocytes with adequate morphology were injected. In 391 cycles between January 2021 and March 2022 (n=506 cycles) either ICSI (intracytoplasmic sperm injection) or PICSI (prior to ICSI) was performed on 1032 MI oocytes. Development of the oocytes was tracked through determination of fertilization by the presence of two pronuclei, blastocyst development and pregnancy following either a fresh or frozen embryo transfer. Embryos were cultured only following the display of 2 pronuclei on day 1 and were cultured separately from embryos derived from MII oocytes.

RESULTS: A total of 1032 MI injected oocytes were observed with a 49.6% (512) rate of fertilization, 22.1% (113) developed into blastocyst and six embryo transfers resulted in viable clinically confirmed pregnancies. In 82 valid transfers compared to day 3 cycles, 38 MI derived blastocysts transferred resulted in pregnancies and live births. Of that 38 MI derived blastocysts were biopsied, with a euploid rate of 34.2% (13), aneuploidy rate of 63.2% (24) and 2.4% mosaic rate (1).

CONCLUSIONS: MI oocytes yield a relatively low rate of development where 6.6% develop to blast and 0.76% result in pregnancy. MI rates of euploidy at 34.2% demonstrate there is a significant pool of M1 derived blastocysts available for transplantation that are frequently unused. The patients in this study also had MII oocytes injected at the time of ICSI. However, in the case of patients with low ovarian reserves and advanced maternal age, utilizing these oocytes gives the patient an additional opportunity for a biological child.

IMPACT STATEMENT: The embryonic developmental potential and pregnancy rates are substantially lower when oocytes undergo ICSI during the MI stage of maturity compared to MII oocytes. However, they may offer additional opportunities for a successful outcome for patients with diminished ovarian reserve.
A NEW MORPHOLOGICAL TIMING OF DIVISION IN HUMAN EMBRYOS BASED ON THE FORMATION AND QUALITY OF BLASTOCYST

OBJECTIVE: The objective of this retrospective study is to check the existing time intervals of division reported in previous studies and to establish new intervals for selecting good quality of blastocysts.

MATERIALS AND METHODS: In order to compare large number of embryos with minimal variation in cultivating conditions, we have used time-lapse system (GERI;Genea Biomedx, NSW, Sydney). Digital images of developing embryos were captured every 5 mins by the time-lapse system. In this study, 1010 embryos were randomly analyzed from 167 IVF patients in our center from January to December 2021. The embryo development was analyzed in the following variables of time intervals (VTI): two-cell (t2 after ICSI), three-cells (t3), four-cell (t4), five-cell (t5), eight-cell (t8) and morula (tM). Additionally, the duration of the second cell cycle (cc2), t3-t2 and complete synchronous cell division (s2; t3-t2) were analyzed. Using these VTI, the difference between blastocysts (BL) and Non blastocysts (NBL) were comparatively analyzed. Among the embryos developed to BL, grades were subdivided into Good, Fair and Poor through Society of Assisted Reproductive Technology (SART) Grading. We investigated the statistical significance between the Good, Fair and the Poor groups, and developed a new VTI based on the mathematical statistical analysis for the good quality BL.

RESULTS: The randomly selected 1010 zygotes from 167 participants, 569(56%) developed to BL and 441 (44%) failed to reach BL. In the BL formation, tM and t2 showed the greatest difference in all VTIs (t2-tcc2). The average division time in each VTI showed a significant difference between BL and NBL. 569 BL were classified into Good (81), Fair (239), and Poor (269) quality BL. There was no significance in VTI between Good and Fair, but between Good and Poor. Therefore, the difference in VTI between Good-Fair (320) vs. Poor (269) was analyzed, and the largest differences were observed in t3 and s2. Based on the results, a new VTI was developed suitable for Good+Fair BL. To do this, we checked the distribution of Good+Fair BL in each section, and made a histogram and a variance table. And the area of the section with the highest distribution was analyzed using mathematical statistical techniques to divide the VTI. As a result of analysis by applying this formula, the overall ratios of selected good morphology BL in the new VTI was higher than in the previous VTI. In the new VTI, t3 and tM showed the greatest difference in all variables.

CONCLUSIONS: Although the existing timing of division was based on the BL formation, we improved the efficiency in predicting and selecting high quality BL through the new VTI based on the Good+Fair quality BL. Additionally, the distribution of the second cell cycle (cc2; t3-t2) and complete synchronous cell division (s2; t3-t2) were analyzed. Using these VTI, the difference between blastocysts (BL) and Non blastocysts (NBL) were comparatively analyzed. Among the embryos developed to BL, grades were subdivided into Good, Fair and Poor through Society of Assisted Reproductive Technology (SART) Grading. We investigated the statistical significance between the Good, Fair and the Poor groups, and developed a new VTI based on the mathematical statistical analysis for the good quality BL.

REFERENCES: none


difference in number of oocytes retrieved, oocyte maturity, OSI, fertilization, usable blastocyst development or pregnancy rates between cohorts.

CONCLUSIONS: In this study LPS and FPS resulted in similar number of usable blastocysts per patient. Earlier blastulation of euploid embryos was observed for patients <35yo after LPS. Prospective evaluation is needed to confirm these findings.

IMPACT STATEMENT: This retrospective is reassuring that for patients planning IVF-freeze all cycles, LPS seems to have at least equivalent embryology outcomes and FPS.

SUPPORT: None

P-59 6:30 AM Monday, October 24, 2022

PERFECT MAY NOT BE THE BEST: AN ANALYSIS OF EMBRYO QUALITY ON PREGNANCY OUTCOMES IN ELECTIVE SINGLE EMBRYO TRANSFER. Crystal Dupont, M.D., M.S.,1 Jason L. St Pierre, Ph.D.,1 Anthony Leonard, Ph.D.,1 Suruchi Thakore, MD1 University of Cincinnati College of Medicine, Cincinnati, OH; 1University of Cincinnati Medical Center, West Chester, OH.

OBJECTIVE: To analyze the association of embryo quality on pregnancy rates of patients undergoing elective single embryo transfer (sSET).

MATERIALS AND METHODS: A retrospective cohort study of all fresh day 5 sSET cycles completed at the UCHealth Center for Reproductive Health from 2017 to 2021 was performed. The modified Lucinda Veeck grading system was used to assign a quality rating to each embryo based on blastocyst expansion (numbered 1-6), inner cell mass (A-D), and trophoderm (A-D). The grades were organized into 22 hierarchical categories and collapsed into 17 subcategories. An analysis was conducted to determine the association with pregnancy outcomes including positive hCG and clinical pregnancy using chi-square analysis and logistic regression. All p-values were two-tailed and p < 0.05 was considered significant.

RESULTS: 170 embryos met inclusion criteria with grades ranging from morula to 5AA. Expansion grades of 4 and 3 were the most frequently encountered (48.23% and 29.41% respectively). 4BB had the highest hCG pregnancy rates (83.33%). 2BA had the highest clinical pregnancy rates (80%). Starting at morula grade, logistic regression analysis of the 22 and 17 categories revealed that hCG and clinical pregnancy rate decreased as embryo grade increased. However, this was not found to be significant (hCG p = 0.08 and p = 0.11; clinical pregnancy p = 0.21 and p = 0.29 respectively).

When analyzing the grade parameters independently, embryos with an inner cell mass with grade B demonstrated the highest hCG and clinical pregnancy rates (p = 0.0009 and p = 0.03 respectively). Embryos with BA grades had higher clinical pregnancy rates than AB grades (P = 0.04). Embryos with a BA grade had the highest positive hCG and clinical pregnancy rates (p = 0.03 and p = 0.02 respectively).

CONCLUSIONS: Embryos with an inner cell mass with grade B is associated with significantly increased positive hCG and clinical pregnancy rates. Specifically, BA grades demonstrated the highest hCG and clinical pregnancy rates. A linear relationship between expansion grade and pregnancy rate does not seem to exist, indicating that the level of expansion may not be a significant predictor of success as previously described.

IMPACT STATEMENT: Embryos with an inner cell mass with larger and looser cells (grade B) demonstrate a higher overall pregnancy rate. This answers a critical question regarding embryo selection when there are multiple embryos with the same level of expansion available for transfer. This information will be beneficial when counseling patients undergoing sSET regarding embryo selection and probability of a successful outcome.

SUPPORT: None

P-60 6:30 AM Monday, October 24, 2022

USE OF A MODIFIED SPECIFIC GRAVITY DEVICE TO DETERMINE VIABILITY AND QUALITY OF HUMAN CRYOPRESERVED EMBRYOS: A PILOT TRIAL. Samuel D. Prien, Ph.D.;1 Audrey Brown, B.S.;2 Abiodun Okimi, B.S.;3 Khalil Ahmad, Ph.D.;1 Lindsay L. Penrose, Ph.D1 1Texas Tech University Health Sciences Center, Lubbock, TX; 2Texas Tech University, Amarillo, TX.

OBJECTIVE: Cryopreservation is currently the only effective means of long-term embryo storage, transport, and genetic testing of human and animal embryos. It also provides for significant flexibility in ART practices. However, cryopreservation can also lead to embryo damage, affecting embryo viability and post-thaw development. Previous research from this lab has demonstrated that a Modified Specific Gravity Device (MSGD) can be used to determine the viability status and future development potential of embryos in various animal species. The current pilot trial describes the use of the MSGD to predict post-thaw survival of donated cryopreserved human blastocysts.

MATERIALS AND METHODS: A series of 192 vitrified human blastocysts (both non-biopsied and biopsied) from 44 patients have been donated for research. Only non-biopsied embryos were passed through the MSGD to determine their buoyancy and drop time. Embryos were first thawed using standard laboratory techniques. Once thawed, the diameter of zona pellucida was measured using the optical micrometer, the re-expansion status of the embryos was also noted. The embryo was then dropped through the MSGD, and cultured at 37°C for 3 hrs in an incubator. After 3 hrs, each step was repeated and then embryos were returned to culture for an additional 24 hrs to determine hatching. Statistical analyses compared embryos that expanded by 3 hrs and hatched by 24 hrs to their descent time through the MSGD.

RESULTS: To date, we have completed data collection for 33 embryos. It was observed that most embryos at the initial time point did not demonstrate any expansion, and no differences were seen in their initial drop times (P = 0.754). However, after 3 hrs in culture, re-expanded embryos dropped slower than those that did not expand (P < 0.04). Hatched embryos had the faster drop rates at both the initial and 3 hr measurement (P < 0.001 and P < 0.05), most likely due to concentration differences between cellular constituents and the media environment.

CONCLUSIONS: Differences seen in descent time through MSGD continue to suggest that a simple test of buoyancy may allow the determination of post-thaw embryo viability. Further studies are needed with a much larger embryo population to confirm these observations.

IMPACT STATEMENT: As in animal studies, the MSGD appears to allow the detection of viable human embryos and predict their future development.

SUPPORT: None
P-61 6:30 AM Monday, October 24, 2022

**BLASTOCYST WITH MORPHOKINETIC ABNORMALITIES CAN BE A VAILABLE OPTION FOR EMBRYO TRANSFER.**

**OBJECTIVE:** To determine whether selection of blastocyst with morphokinetic abnormalities during embryonic development is a viable option for Embryo Transfer (ET) or freezing.

**MATERIALS AND METHODS:** This was a retrospective cohort study that determined the pregnancy and miscarriage rate of total of 701 embryos from 194 patients who underwent both Time-Lapse (TL) incubator (Embryo Scope) and pre-implantation genetic testing (PGT) in our laboratory between 2014-2021. Fertilized oocytes were cultured in TL recording various morphokinetic abnormalities until day 5 or 6 and were graded into Excellent, Good, Fair before undergoing biopsy for PGT. Partial trophoderm (TE) cells of blastocyst were removed and chromosomal aneuploidy was confirmed by PGT using either NGS or array-CGH. Correlations were studied between normally cleaved (group NC) and irregularly cleaved (group IC) embryos. A p-value of < 0.05 was considered statistically significant.

**RESULTS:** Among embryos that underwent PGT, the percentage of group NC and group IC embryos was 91% (638/701) vs 9% (63/701), blastocyst formation was 56.6% vs 49.4% and of those that were suitable for ET/IVF ET was 45.1% vs 35.2%, respectively. Euploid percentage was 31.2% (156/553) in group NC and 35.1% (52/148) in group IC embryos. Group IC embryos resulted slightly higher euploid percentage however was not statistically significant.

**CONCLUSIONS:** It has been reported that embryo with morphokinetic abnormalities undergoes self-correction process and able to become euploid blastocyst. Similarly, our results have demonstrated that whilst group NC embryos resulted to have higher percentage in both blastocyst formation and quality, both group NC and group IC embryos developing into blastocyst showed comparable percentage in euploid rate and rather slightly higher in IC embryos. It is assumed that when morphokinetic abnormality appears; these embryos are selected based on more stringent criteria; if it is considered for ET. Furthermore, pregnancy and miscarriage rates were performed in a fresh cycle. The day of transfer was considered as the independent variable, grouping the patients in Group A (D2-3) and Group B (D5). The main outcome was defined as pregnancy rate (BHCIG+). The following confounding variables were considered in the analysis: male factor (MF), percentage of good quality embryos (GQE), percentage of difficult transfers (DT), age of the patient, number of usable oocytes (MII), and the use of clomiphene citrate (CC) for ovarian stimulation.

The Chi square test was used to compare the non-parametric variables, and the T-Student test (unpaired) for the parametric variables. A p<0.05 was considered as statistical significance.

**RESULTS:** The results obtained are shown in the following tables:

**Table 1** shows the results when comparing the variables between Groups A and B.

<table>
<thead>
<tr>
<th>Age</th>
<th>Group A</th>
<th>Group B</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>37.8 ± 3.6</td>
<td>38.1 ± 3.5</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>MII</td>
<td>1.76 ± 0.79</td>
<td>2.18 ± 0.81</td>
<td>0.01</td>
</tr>
<tr>
<td>MF</td>
<td>32.5 %</td>
<td>33 %</td>
<td>0.99</td>
</tr>
<tr>
<td>CC</td>
<td>11.3 %</td>
<td>14.5%</td>
<td>0.59</td>
</tr>
<tr>
<td>DT</td>
<td>11.3 %</td>
<td>10.4%</td>
<td>0.99</td>
</tr>
<tr>
<td>GQE transferred</td>
<td>66.4%</td>
<td>56.3%</td>
<td>0.18</td>
</tr>
<tr>
<td>Pregnancy rate</td>
<td>24%</td>
<td>46%</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**Table 2** shows the results when comparing the variables between Groups A and B within the patients who achieved pregnancy.

<table>
<thead>
<tr>
<th>Age</th>
<th>Group A</th>
<th>Group B</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.7 ± 2.6</td>
<td>37.4 ± 4.1</td>
<td>0.82</td>
<td></td>
</tr>
<tr>
<td>MII</td>
<td>1.95 ± 0.76</td>
<td>2.17 ± 0.76</td>
<td>0.35</td>
</tr>
<tr>
<td>MF</td>
<td>24%</td>
<td>36.4%</td>
<td>0.22</td>
</tr>
<tr>
<td>CC</td>
<td>15.8%</td>
<td>9.5%</td>
<td>0.46</td>
</tr>
<tr>
<td>DT</td>
<td>9%</td>
<td>9.1%</td>
<td>0.53</td>
</tr>
<tr>
<td>GQE transferred</td>
<td>84.4%</td>
<td>64.4%</td>
<td>0.07</td>
</tr>
<tr>
<td>GQE transferred</td>
<td>84.4%</td>
<td>72.5%</td>
<td>0.2</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** The pregnancy rate in patients with poor ovarian response was higher in group B compared to group A. In this group of patients, despite having a smaller number of oocytes, the transfer in stage D5 is related to an improvement in reproductive results. Regarding the pregnancy rate, the prognostic value of embryo quality assessment in D2-3 is lower compared to D5. It is important to recognize that one of the weaknesses of this study was the impossibility of calculating the transfer cancellation rate.

**IMPACT STATEMENT:** aAlthough we were not able to evaluate the cancellation rate, we believe that the culture expanded to day 5 provides greater biological definition to the embryos and allows a better selection of them.

**SUPPORT:** None

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**P-62 6:30 AM Monday, October 24, 2022**

**SUCCESS RATE OF CLEAVAGE STAGE VS BLASTOCYST TRANSFERS IN POOR OVARIAN RESPONSE PATIENTS.**

**OBJECTIVE:** To compare the pregnancy rate of patients with poor ovarian response who transfer embryos on day 2 or 3 (D2-3) vs. day 5 (D5) in a single assisted reproduction center.

**MATERIALS AND METHODS:** For this study, 201 patients were re-recruited (August 2017–December 2021). Women who obtained 3 or fewer mature oocytes (metaphase II/MII) were included. All embryo transfers were performed in a fresh cycle. The day of transfer was considered as the independent variable, grouping the patients in Group A (D2-3) and Group B (D5). The main outcome was defined as pregnancy rate (BHCIG+). The following confounding variables were considered in the analysis: male factor (MF), percentage of good quality embryos (GQE), percentage of difficult transfers (DT), age of the patient, number of usable oocytes (MII), and the use of clomiphene citrate (CC) for ovarian stimulation.

**RESULTS:** The results obtained are shown in the following tables:

**Table N’1** shows the results when comparing the variables between Groups A and B.

<table>
<thead>
<tr>
<th>Table N’1 shows the results when comparing the variables between Groups A and B.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group A</strong></td>
</tr>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td><strong>MII</strong></td>
</tr>
<tr>
<td><strong>MF</strong></td>
</tr>
<tr>
<td><strong>CC</strong></td>
</tr>
<tr>
<td><strong>DT</strong></td>
</tr>
<tr>
<td><strong>GQE transferred</strong></td>
</tr>
<tr>
<td><strong>Pregnancy rate</strong></td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** The pregnancy rate in patients with poor ovarian response was higher in group B compared to group A. In this group of patients, despite having a smaller number of oocytes, the transfer in stage D5 is related to an improvement in reproductive results. Regarding the pregnancy rate, the prognostic value of embryo quality assessment in D2-3 is lower compared to D5. It is important to recognize that one of the weaknesses of this study was the impossibility of calculating the transfer cancellation rate.

**IMPACT STATEMENT:** Although we were not able to evaluate the cancellation rate, we believe that the culture expanded to day 5 provides greater biological definition to the embryos and allows a better selection of them.

**SUPPORT:** None
OBJECTIVE: Because of rapidly increasing utilization of preimplantation genetic testing for aneuploidy (PGT-A) in the U.S., despite not being recommended for routine use by the ASRM, we determined live birth outcomes per intended retrieval according to the degrees of utilization of PGT-A by individual in vitro fertilization (IVF) centers.

MATERIALS AND METHODS: This is a retrospective cohort study mining the National Summary and Clinic Table Dataset of the Center for Disease Control and Prevention (CDC) for 2018. The reporting clinics were divided into 2 groups, low PGT utilization rate (0-19.9%) and high PGT utilization rate (80-100%) by percentages of transfers in which at least one embryo, in all age groups, had undergone PGT-A, and then compared total live birth rates with reference point intended retrieval for PGT-A percentages, stratified by patient age. Live birth rates (LBRs) were compared using the chi-square test and 95% confidence intervals were established using the Wilson test for binomial proportions. Since CDC data do not allow differentiation between PGT-A and PGT-M or SR, the latter group of patients are included but historically do not exceed 5% of all PGT cases and, therefore, only unlikely affect here reported outcomes.

RESULTS: A total of 43,841 IVF cycles were compared between the low and high PGT-A utilization groups. Of these, 15,599 were in women <35 years with low 0-19.9% PGT-A cycles and 3,399 with high 80-100% PGT-A utilization. The live birth rates significantly declined with the higher utilization (45.6% high utilization vs 50.6% low utilization, p < 0.0001, CI 44.0-47.4% and CI 49.8-51.4%, respectively). At older ages, 35-37; 38-40; 41-42 and ≥43 years, no differences in LBRs rates were observed between low and high PGT-A utilization. For all ages combined, the live birth rates significantly declined with the higher PGT-A utilization (29.8% high utilization vs 36.8% low utilization, p < 0.0001, CI 28.9-30.7% and 36.3-37.3% respectively).

CONCLUSIONS: These data offer further evidence that high utilization of PGT-A at no age improves live birth rates. Moreover, centers that utilize PGT-A indiscriminately in 80-100% of IVF cycles in their youngest patients <35 years, will affect their live birth chances adversely.

IMPACT STATEMENT: At a time when, likely, already over half of all U.S. IVF cycles utilize PGT-A, this study adds further evidence that routine high use of PGT-A, while adding significant effort as well as cost to IVF, does not offer any outcome improvement and in certain patient populations actually impair precision and live birth chances. The routine offering of PGT-A in IVF, therefore, should be discouraged.

SUPPORT: Intramural funds from The Center for Human Reproduction and Foundation for Reproductive Medicine.

P-64 6:30 AM Monday, October 24, 2022
A NOVEL Bластомер пRÓРPHIJO MРЯORPHIJO MAKERP RНH FЕLСIЕV SТАG Е EΜРРYBOРS STRONGLY PЕDIСT BлАСТОСТРΥС DEVELOPMENT AND PЕNСANCY OUTCOME. Biswanath Ghoshdastidar, M.B.B.S., M.S. 1 Sudarsan Ghosh Dastidar, M.D. 2,3 IIPGMER & SSKM Hospital, Kolkata, West Bengal, India; 2 GD Institute for Fertility Research Pvt. Ltd., Kolkata, India; 3 G D Institute for Fertility Research.

OBJECTIVE: In our IVF practice we have observed that a novel morphological feature of cleavage stage embryos seems to correlate well with blastocyst formation and clinical pregnancy. We performed this retrospective cohort study to examine whether our observed blastomere marker in cleaving embryos has any impact on blastocyst development and clinical pregnancy rates following single blastocyst transfers.

MATERIALS AND METHODS: Morphological assessment of cleaving embryos based on established parameters has long been the standard of practice for embryo selection in IVF-ICSI cycles. In addition, we have observed that maximum expansion of blastomeres to result in optimal spatial orientation leading to flattening of the blastomere margin in contact with the zona pellucida (contact flattening) seems to be indicative of embryo quality. We have been documenting the above features as ‘blastomere sign’ (BS). We undertook the present retrospective cohort study to examine whether BS positive embryos resulted in higher blastocyst development and clinical pregnancy rates compared to BS negative embryos.

The study was carried out at a tertiary fertility center after institutional review board (IRB) clearance. Data from IVF-ICSI frozen embryo transfer (FET) cycles performed between July 2021 to December 2021 was initially analyzed. Number of blastocysts generated following warming of vitrified embryos and culture to day 5; number of top quality blastocysts generated (4AA or above, Gardner and Schoolcraft classification); and clinical pregnancy rates were compared between blastocysts generated from cleaving embryos with blastomere positive sign versus absent blastomere sign. Final data analysis included only elective single blastocyst transfers. Only first FET cycle data was included in data analysis.

Data was analyzed using a statistical package for social sciences (SPSS) Version v16.0. Data was presented as mean and standard deviation (S.D) and compared using student’s t test (2 tailed). Results were deemed to be statistically significant at 5% level of significance (p < 0.05).

RESULTS: Mean age was comparable between BS positive and BS negative transfers (33.2±5.8 vs 34.4±5.47). Mean AMH level in the BS positive group was 1.91±1.56 ng/ml vs 2.67±2.38 ng/ml in the BS negative group. Blastocyst formation rate (78.2% vs 52.4%, p = 0.0001), top quality (4AA or above) blastocyst formation rate (45.5% vs 26.2%, p = 0.0007) and ongoing clinical pregnancy rate (68.9% vs 25%, p = 0.0001) were found to be significantly higher in the blastomere sign positive group.

CONCLUSIONS: Presence of blastomere sign in cleaving embryos was positively correlated with blastocyst development and pregnancy rates in single blastocyst FET cycles.

IMPACT STATEMENT: This novel parameter could be a simple, efficient and cost-effective non-invasive tool for assessment of cleavage stage embryo quality and better selection of the most viable blastocyst for elective single embryo transfer (eSET).

SUPPORT: none
PREDICTION OF BLASTULATION, EMBRYO UTILISATION AND LIVE BIRTH FROM SINGLE MORPHOLOGICAL OR MORPHOKINETIC VARIABLES: ANALYSIS OF 31,323 EMBRYOS GIVES INSIGHTS FOR SELECTION AND ALGORITHM DEVELOPMENT. Alison J. Campbell, PhD,1 Bjorn M. Petersen Dr, PhD,2 Rachel Smith, BSc,3 Amy Barrie, PhD3 1CARE Fertility, Nottingham, United Kingdom; 2BMP Analytics; 3CARE Fertility Group.

OBJECTIVE: Analyses of the power of time-lapse imaging (TLI) to predict IVF outcomes are mostly based on data from transferred embryos, creating selection bias as data do not represent the whole embryo cohort. This study aimed to reveal the most predictive variables for blastulation, utilisation (frozen and transferred) and live birth.

MATERIALS AND METHODS: A total of 31,323 embryos, from 8 clinics, were imaged, cultured and comprehensively, prospectively annotated, using EmbryoScope (Vitrolife, Sweden), until blastulation. Fate of the embryos was recorded as vitrified, transferred or discarded. For live birth analysis, only single embryo transfers were included (n=4805). Receiver operating characteristic analyses were utilised to determine the predictive ability of singular variables in terms of Area Under the Curve (AUC).

RESULTS: When considering the transferred embryos, the later morphokinetic variables were most predictive of live birth, especially time of starting blastulation (tSB; AUC = 0.59). Considering the entire cohort, prediction of utilisation was high, with AUC values up to 0.80 (expanded blastocyst; tEB). Whether an embryo will reach the full blastocyst stage (tB), can be predicted early, using time of pronuclear fading and time to two-cells (AUC = 0.63 and 0.65 respectively). Subjective trophectoderm (TE) and inner cell mass (ICM) morphologies are less predictive of live birth than morphokinetics (AUC 0.55 and 0.53 respectively).

CONCLUSIONS: Most morphokinetic selection models are built exclusively on transferred embryos with known outcomes. To maximise predictive power of algorithms, timepoint of insemination (rather than pronuclear fading) should be included. Even single morphokinetic variables can have profound predictive values. Early variables are predictive of subsequent blastulation, but less predictive of live birth. Later variables are predictive of embryo utilisation and live birth.

IMPACT STATEMENT: This study highlights the relative predictive power of morphokinetics over blastocyst morphology and the potential pitfalls of focusing on a preselected population of embryos for anything other than live birth prediction.

REFERENCES:


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<table>
<thead>
<tr>
<th>Using time from insemination AUC values</th>
<th>Using time from pronuclear fading AUC values</th>
</tr>
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P-67: USE OF A MOBILE APP TO COMPARE THE CLASSIFICATION OF HUMAN BLASTOCYSTS IN 11 IVF LABORATORIES. Scarlett E. Salter Dr, PhD,1 Craig Doyle, BSc,2 Colin Duncan Prof, PhD,3 Alison J. Campbell, PhD,3 Amy Barrie, PhD,1 Colin M. Howles, PhD,2 Carol Lynn Curchoe, PhD, HCLD5 1CARE Fertility Group; 2University of Edinburgh, Edinburgh, United Kingdom; 3CARE Fertility, Nottingham, United Kingdom; 5ART Compass App.

OBJECTIVE: The objective of this study was to compare the standardization of human blastocyst classification in 11 IVF laboratories, all working to the same protocols, using a mobile app as a quality assessment tool.

MATERIALS AND METHODS: A specialized mobile app was employed to compare blastocyst classification across 11 IVF laboratories within the same organization. Fifty-seven experienced embryologists completed ‘surveys’ in which they were shown the same images of 240 blastocysts, for an unlimited time frame in a single focal plane, and asked whether they would choose to cryopreserve or dispose the blastocyst pictured. In support of the app results, data collected routinely within these laboratories from 1st January to 31st December 2021, were analyzed to determine the differences in embryo grading, utilization and resulting clinical pregnancy rates. Furthermore, blastocysts will be classified morphologically by up to five expert assessors using the Gardner grading scheme. This will then be used to inform whether the subjectivity is consistent across all blastocysts or whether it is more pronounced in certain quality categories.

RESULTS: The app identified significant differences in blastocyst classification between individual embryologists. The embryologists unanimously agreed on the fate of the embryos in only 38.8% of cases. Of these, 16.7% was agreement to cryopreserve and 22.1% was agreement on which to dispose. This means that embryologists disagreed in over half of cases with some choosing to cryopreserve and others choosing to dispose the pictured blastocyst.

CONCLUSIONS: This study highlights the subjectivity in blastocyst classification within the field of IVF. The decision about which embryos to select for utilisation has a direct impact on clinical pregnancy rates, it is therefore vital that subjectivity is minimised as far as possible through regular quality assurance and the use of objective methods for embryo classification such as artificial intelligence. The analysis of clinical outcome data and whether the subjectivity exists across all embryo grades will support the use of technology such as this mobile app to improve standardisation.

IMPACT STATEMENT: The use of a mobile app allowed for quick and widespread assessment of agreement in blastocyst classification and could be used for evaluating performance on an individual and clinic-wide level. Current blastocyst classification is heavily subjective and the use of technology such as this mobile app could assist in the standardization of clinical decision making such as embryo utilization.
THE EFFECT OF DELAYED MATURATION IN OOCYTES AFTER RETRIEVAL ON EMBRYO POTENTIAL AND PLOIDY STATUS. Jennifer L. Matucha, M.S.,1 Bradford Bopp, M.D.,2 Matthew Will, M.D.,2 Erica Ansanch Will, MD,2 Kathleen M. O’Leary, M.D., M.S.,2 Glen Adaniya, PhD1 Ovation Fertility, Carmel, IN; *Midwest Fertility Specialists, Carmel, IN.

OBJECTIVE: The objective was to determine if the delayed maturation of oocytes affected subsequent embryo development, as well as the impact of these oocytes within in vitro fertilization (IVF) cycles with preimplantation genetic testing for aneuploidy (PGT-A).

MATERIALS AND METHODS: This exempt retrospective chart review was approved by the University of South Florida Institutional Review Ethics Committee. Cycle data was collected from January 2021 to January 2022. Cycles were designated as 422 IFV with PGT-A cycles, as normo- or aneuploidic sperm injection (ICSI) as the method of insemination, between January 2021 and January 2022. Retrievals were performed 36 hours post-trigger. Maturity was initially assessed after cumulus cell removal, and oocytes reassessed at the time of ICSI were labeled Metaphase I with delayed maturation to Metaphase II (MI; N = 189), or mature Metaphase II oocytes at the time of denuding (MII; N = 1,512). Cycles had at least one oocyte with delayed oocyte nuclear maturation (Delayed; N = 130) or no delay in maturation (No Delay: N = 292). There were 1,953 embryos biopsied, and samples were sent to a single testing facility for PGT-A. Delayed cycles were examined to compare fertilization and embryo development between MI and MII sibling oocytes. Primary outcomes reviewed were fertilization and embryo development, as well as rates of euploidy, aneuploidy and mosaicism. Independent t-tests were used to compare data such as age, anti-mullerian hormone (AMH), body mass index (BMI), and number of oocytes retrieved. Aggregate data was analyzed by proportional z-tests, and a p-value < 0.05 was defined as statistically significant, with a 95% confidence interval.

RESULTS: The time between retrieval and initial maturation assessment, time between initial assessment and ICSI, average age, and BMI were not significant between Delayed and No Delay cycles. A significant difference was seen between AMH (3.4 ± 2.9 vs. 2.5 ± 2.3; p = 0.018) and the average number of oocytes retrieved (16.1 ± 9.0 vs. 13.2 ± 9.0; p = 0.002). Within the Delayed cycles, matured MI oocytes had significantly lower fertilization (59% vs. 77%; p < 0.001), day 3 progression (67% vs. 83%; p < 0.001), and blastocyst development (21% vs 55%; p < 0.001) compared to their sibling MII oocytes. Delayed cycles had a significantly lower fertilization rate compared to No Delay cycles (75% vs. 82%; p < 0.001). Significantly higher post-ICSI atretic rates (6% vs 4%; p = 0.027) were also found in Delayed cycles, but total maturation; blastocyst development; and rates of euploidy, aneuploidy and mosaicism did not differ between the two groups.

CONCLUSIONS: Oocytes with delayed maturation have significantly lower fertilization and blastocyst development compared to their sibling oocytes. The cycles with these oocytes were affected by having increased post-ICSI atretic rates and lower fertilization, but both groups resulted in similar blastocyst development and euploidy.

IMPACT STATEMENT: Although oocytes with delayed maturation have decreased embryo potential, some of these oocytes go on to create euploid blastocysts. Ultimately, it is beneficial to the patient to reevaluate oocyte maturation at ICSI to increase the number of embryos for transfer.

ROLE OF TRIM71 IN MOUSE OO CYTE MATURATION AND EMBRYO DEVELOPMENT IN VITRO. Sook Young Yoon, Ph.D., SU Hee Seok, M.Sc., Miseon Park, MS, Jungah Yoon, M.S., Jin Hee Eum, Ph.D., Woo Sik Lee, M.D. Ph.D., CHA, Gangnam Medical Center, CHA University, Seoul, Korea, Republic of (South).

OBJECTIVE: Tripartite Motif Containing 71 (TRIM71) belongs to the TRIM-NHL family. The RNA-binding protein and E3 ubiquitin ligase TRIM71 is important for embryogenesis, and its expression has been reported in germ cell tumors and adult mouse testes. TRIM71 has a conserved role in stem cell proliferation, differentiation, and embryonic development. Studies in C. elegans reported that complete loss of TRIM71 homolog, Lin41 displayed a defect of oogenesis, resulting in sterility. In recent study in mouse, germ line specific conditional Trim71 knockout mouse are infertile both male and female. In male mouse, cKO mouse displayed a Sertoli cell only phenotype which in humans. We investigated the role of TRIM71 protein in mouse oocyte maturation.

MATERIALS AND METHODS: Using RT-PCR, qRT PCR, and mRNA expression of TRIM71 was analyzed in mouse tissues. GV and mature oocytes were collected from a 5-week-old female by superovulation. TRIM71 knockdown was induced by chemically synthesized siRNA for TRIM71.

RESULTS: TRIM71 is highly expressed in mouse testis and ovary, but low or undetectable levels of expression were observed in other tissues. During oocyte maturation and preimplantation development, the expression level of TRIM71 increased from GV to MII and reduced in 2 cell embryos and blastocysts. There is no difference in GVBD in control and TRIM71 knockdown. The first polar body formation for oocyte maturation was inhibited by TRIM71 knockdown compared to control and negative control of siRNA injected oocytes (P = 0.005). Mature oocytes underwent in vitro fertilization and showed lower blastocyst formation in TRIM71 knockdown oocytes compared to control oocytes. Also, those TRIM71 knockdown oocytes showed abnormal blastocyst formation.

CONCLUSIONS: TRIM71 might be involved in oogenesis in mouse. TRIM71 is not an essential for the GVBD during oocyte maturation, but it might be involved in cytoplasmatic modification including polar body extrusion. Further studies are needed to understand molecular mechanism involved in cytoplasmatic modification.

IMPACT STATEMENT: Further studies using TRIM71 may enable improvements in oocyte maturation and embryo quality in assisted reproductive technology.

SUPPORT: This research was supported by a grant from Republic of Korea, NRF- 2021R1I1A1A01042374.
P-71 6:30 AM Monday, October 24, 2022

CLINICAL FACTORS ASSOCIATED WITH SUBOPTIMAL BLASTULATION RATE IN ICSI CYCLES: A PARAMETRIC MODELING APPROACH
Erkan Kalafat, M.D. M.Sc., Ipek Keles, Ms, Engin Turkoglu, MD, Sule Yildiz, MD, Gurkan Bozdag, M.D., Baris Ata, M.D. M.Sc Koc University, School of Medicine, Istanbul, Turkey.

OBJECTIVE: Blastulation rate is an important performance marker for assisted reproduction laboratories. Special interest groups suggested competency metrics for blastulation rate and we investigated factors associated with suboptimal blastulation rate in ICSI cycles.

MATERIALS AND METHODS: Couples who underwent ICSI cycles between August 2016 and May 2021 in Koc University Assisted Reproduction Unit and had at least four 2PN embryos were included in the study. The optimal blastulation rate was derived from a subgroup of couples without conditions that may have a detrimental effect on the ‘ideal’ blastulation rate. Advanced age, diminished ovarian reserve, severe teratozoospermia, polycystic ovarian syndrome, endometriosis. Included cycles underwent maximal stimulation with 30 IU of gonadotropin (rFSH or hMG) and all follicles larger than 12mm were aspirated during oocyte retrieval. The distribution of blastulation rate (good quality blastocyst/2PN embryo count) from this group was subjected to parametric modeling assuming a Beta distribution. Using maximum likelihood estimation, the distribution parameters of the ‘ideal’ blastulation rate were determined and the theoretical 10th percentile was chosen as the threshold for suboptimal blastulation. Factors associated with suboptimal blastulation (<10th percentile) were assessed with generalized estimating equations.

RESULTS: During the eligibility period, 895 antagonist ICSI cycles were planned and 493 antagonist cycles had at least four 2PN embryos following oocyte retrieval and ICSI. A subgroup of 126 cycles was identified to estimate the ‘ideal’ blastulation rate. Parametric modeling showed the ‘ideal’ blastulation rate fit to a Beta distribution (α: 1.65; β: 2.4; R²: 0.994) with the theoretical mean of 38.9% and 10th percentile cut-off of ~12.5%. Based on the theoretical 10th percentile cut-off, 90 cycles had suboptimal and 403 cycles had optimal blastulation rates. Female age (mean: 33.3 vs 33.1, P = .830), male age (mean: 38.3 vs 37.6, P = .303), female body-mass index (mean: 25.2 vs 25.4, P = .754), polycystic ovarian syndrome (12.2 vs 13.6%, P = .847), endometriosis (6.7 vs 11.1%, P = .271), male factor subfertility (60.0 vs 54.6%, P = .367), gonadotrophin type (rFSH vs HMG, P = .912), down-regulation method (GnRH antagonist vs. progestin, P = .698), duration of induction (P = .125) or ovulation trigger type (hCG vs. agonist and combined, P = .409 and .724, respectively) did not appreciably affect suboptimal blastulation.

CONCLUSIONS: Suboptimal blastulation rate, as determined via parametric modeling, is not associated with most clinical factors. The lack of robust association with most clinical factors suggests the pathology may be due to clinical factors (non-parametric).

IMPACT STATEMENT: Theoretical estimation of a suboptimal blastulation rate is feasible and the condition does not seem to be explained by clinical factors.

P-72 6:30 AM Monday, October 24, 2022

PREGNANCY OUTCOMES BY DEGREE OF EXPANSION IN THAWED HIGH QUALITY EMBRYOS.
Robert Rydzew, MD,1 Shuning Wang, PhD,2 Shiring-Wern Tsaih, ScD,1 Stephanie Gunderson, M.D.,1 Jayme S. Bosler, MD,3 Kate D. Schoyer, MD,1 Medical College of Wisconsin, Milwaukee, WI; 2Medical College of Wisconsin, Menomonee Falls, WI.

OBJECTIVE: Identifying factors predictive of success in embryo transfer cycles has long been a goal in the field of reproductive medicine. Numerous studies that have identified morphokinetic parameters associated with clinical pregnancy and live birth have highlighted the importance of embryo monitoring. This current study set out to investigate the effect of the degree of embryo expansion post thaw on clinical pregnancy rates as part of a quality improvement project. Clinical pregnancy rates were compared based on the degree of expansion post thaw.

MATERIALS AND METHODS: A retrospective cohort study of patients undergoing a single embryo transfer of a vitrified Day 5 and Day 6 high quality embryo without PGT-A created with autologous oocytes between 2017 and 2022 were included. Embryos were thawed a minimum of 2 hours prior to transfer and grouped into three categories based on the degree of expansion. These categories were no expansion, partial expansion, or full expansion. The outcome of interest was clinical pregnancy rate defined as presence of fetal heart tones on ultrasound. Pregnancy rates were compared using Pearson’s Chi-squared test and one-way ANOVA was used to compare demographic data among the groups. Statistical analysis was performed using R statistical package.

RESULTS: A total of 878 transfers were compared across the 3 groups. Pregnancy rates in the no expansion group (n=25) were 16.0%, in the partial expansion (n=179) were 37.4%, and full expansion (n=674) were 49.9% and were statistically significantly different amongst all 3 conditions (p<0.05). There were no differences in average age at time of freezing, 33.8, 33.5, and 33.2 years respectively. Similarly, there were no differences in average endometrial thickness amongst the 3 groups, 9.81, 9.50, and 9.65mm respectively.

CONCLUSIONS: Full expansion following embryo thaw is associated with statistically significant higher clinical pregnancy rates following warming of high quality previously vitrified blastocysts when compared to both partially re-expanded and embryos with no expansion. This likely serves as a surrogate marker for the metabolic activity and viability of a thawed embryo. More work will need to be done to identify what factors are associated with a higher degree of expansion following thaw.

IMPACT STATEMENT: Taking time to monitor for expansion following embryo thaw can help provide prognostic information regarding success rates, even with high quality blastocysts. This information could alter work flow in the timing of thaw to transfer and clinical decision making regarding whether additional embryo(s) should be thawed and transferred.

P-73 6:30 AM Monday, October 24, 2022

2 PRONUCLEI (2PN) BANKING AS A METHOD TO IMPROVE OUTCOMES FOR PGD/PGS PROGNOSIS PATIENTS DOING MULTIPLE CYCLES WITH PRE-IMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) LEADS TO SIMILAR BLASTOCYST YIELD.
Linnea R. Goodman, MD,1 Abigail L. Bernard, MD,2 Christopher D. Williams, MD,3 Laura P. Smith, MD,4 Scott H. Purcell, PhD,5 1VA Fertility and IVF, Charlottesville, VA; 2University of North Carolina, Chapel Hill, NC.

OBJECTIVE: With lower ovarian reserve and increased rates of aneuploidy, older patients undergoing in-vitro fertilization (IVF) often need to do multiple cycles to obtain an euploid embryo and may want to bank embryos for future use. This can become prohibitively expensive. In addition, multiple biopsy sessions add significant time and resource allocation in the embryology laboratory. Combining multiple stimulation cycles vitrified at the 2 pronuclei (2PN) stage together to thaw, culture to blastocyst and biopsy as one group may offer a more cost-effective approach. Investigation is required to confirm thawing of multiple groups of embryos each created from a distinct cycle and vitrified at 2PN provide similar blastocyst rates compared to growing each fresh embryo cohort to blastocyst before biopsy and vitrification.

MATERIALS AND METHODS: At an academic-affiliated private practice, patients who were anticipated to benefit from multiple cycles due to suspected low euploid embryo yield were offered to participate in a multi-cycle 2PN banking package. These patients underwent standard protocol IVF cycles with the successfully fertilized day one embryos cryopreserved at the 2PN stage. Patients underwent up to three consecutive cycles and then the complete cohort of 2PN embryos were thawed, cultured to blastocyst, biopsied, and again cryopreserved to await results (2PN group). A control group consisting of individual cycles over the same time frame matched for both age of the patient and number of 2PN embryos created were chosen (Control group) with the researcher blinded to number of resultant blastocysts. Primary outcomes were blastocyst rate and number of subsequent euploid embryos. Student’s t-test and Chi-squared test were used as appropriate.

RESULTS: There were a total of 29 patients aged 26-44 years who completed 70 oocyte retrieval cycles in the 2PN group (mean 2.6 +/- 0.9 cycles per patient). These were compared to 70 matched single control cycles. The average age of both groups was 38.8 +/- 3.8 years and 5.1 +/- 4.1 2PN
embryos were created per cycle in each group (p = 0.98). For the 2PN group, at the completion of intended cycles, the average number of 2PN embryos created was 13.3 +/- 10.0 with a resulting 6.1 +/- 5.7 blastocysts per patient. The blastocyst rate was similar between groups (2PN 47.5 +/- 22% vs Control 46.0 +/- 30%; p = 0.46). In the 2PN group there were 177 blastocysts biopsied resulting in 62 euploid and 20 mosaic embryos compared to 163 biopsied embryos resulting in 65 euploid and 19 mosaic embryos in the control group. In the 2PN group, there was an average of 2.1 +/- 2.3 euploid embryos at the completion of their 2PN banking IVF cycles compared to 0.9 +/- 1.2 euploid embryos available to patients who underwent a single cycle in the control group (p = 0.01).

CONCLUSIONS: Banking embryos at the 2PN stage resulted in similar blastocyst yield and euploid embryos available for transfer.

IMPACT STATEMENT: This strategy has implications for substantial patient cost savings and embryology lab resource consolidation for patients that may need multiple cycles to obtain their desired family goals.

P-74 6:30 AM Monday, October 24, 2022

IMPACT OF ARTIFICIAL SHRINKAGE PRIOR TO FRESH BLASTOCYST TRANSFER: A PROSPECTIVE DOUBLE BLIND RANDOMIZED CONTROLLED TRIAL. Anna GALA, MD,1 Alice Ferrière-Hoa, MD,1 Fatima Barry, PhD,1 Sophie Brouillet, PhD,2 Emmanuelle Vintejou, MD,1 Laura Gaspari, MD,1 Tial Anahory, M.D., Ph.D.,1 Samir Hamamah, MD, MDPh,1 Arnaud de Vlieunée Hospital, CHU Montpellier, Montpellier, France;1 Inserm U1203, CHU Montpellier, St-Eloi Hospital, Montpellier, France.

OBJECTIVE: The objective of this study was to assess the impact of artificial shrinkage (AS) of blastocoelic cavity (BC) prior to fresh elective single blastocyst transfer (SBET) on clinical pregnancy rate.

MATERIALS AND METHODS: Prospective, randomized, double blind controlled study. From May 21th 2018 to June 30th 2021, 150 couples elected to fresh elective single blastocyst transfer (SBET) on clinical pregnancy rate.

RESULTS: We induced artificial shrinkage before fresh blastocyst transfer, and “AS-” group (n=50), where fresh blastocyst were transferred without any additional intervention.

OBJECTIVE: Artificial oocyte activation has been used in cases where ICSI did not activate the oocytes, hence resulting in non-fertilization. Artificial oocyte activation has been performed using calcium ionophore, strontium and electroporation (EP), with reports that these treatments improve fertilization rates. However, there have been only a few reports on birth outcomes. Study 1: In mouse test, microinjection of cDNA of PLCZ into zygote stage induced higher blastocyst formation than control eggs significantly (P<0.001). In mouse test, microinjection of cDNA of PLCZ into zygote stage induced higher blastocyst formation than control eggs significantly (P<0.001). Total mRNA from sperm were isolated by Dynabeads® mRNA Purification Kit. Embryo grades were assessed by two embryologists based on embryo morphology. To investigate the effect of microinjection of cDNA of PLCZ on mouse embryo development, we produced artificially activated zygote with 10 mM strontium, and examined microinjection of cDNA PLCZ into zygote stage. Further embryonic developments were observed blastocyst formation for 5 days culture in KSM.

RESULTS: According to the results of qPCR, the expression level of mRNA of PLCZ was independent of the husband’s age. However, in sperm with poor embryonic development, the expression level of mRNA of PLCZ was significantly lower than that of sperm with high-quality embryos (P<0.001). In mouse test, microinjection of cDNA of PLCZ into zygote stage induced higher blastocyst formation than control eggs significantly (P<0.001).

CONCLUSIONS: The mRNA expression level of PLCZ in sperm is thought to affect embryonic development after fertilization. mRNA of PLCZ in sperm might be an indicator of embryonic development.

IMPACT STATEMENT: Further studies using PLCZ may enable improvements in embryo quality in assisted reproductive technology.

SUPPORT: This research was supported by a grant from Republic of Korea, NRF-2018R1D1A1B07043250.

P-76 6:30 AM Monday, October 24, 2022

FOLLOW-UP OF BABIES BORN FROM ICSI OOCYTES THAT UNDERWENT ELECTROPORATION. Hiroya Kitasaka, Ph.D.1 Mami Jose, M.S.2 Noritaka Fukunaga, Ph.D.,2 Yoshimasa Asada, M.D., Ph.D.1 1Nagoya, Japan; 2Asada Ladies Clinic, Nagoya, Japan.

OBJECTIVE: Artificial oocyte activation has been used in cases where ICSI did not activate the oocytes, hence resulting in non-fertilization. Artificial oocyte activation has been performed using calcium ionophore, strontium and electroporation (EP), with reports that these treatments improve fertilization rates. However, there have been only a few reports on birth outcomes and prognosis for calcium ionophore and strontium, but no information on EP. Therefore, in this study, we investigated whether babies born from the transfer of embryos derived after EP have congenital or developmental anomalies.

MATERIALS AND METHODS: There were 11cycles in which EP was transferred between January 2009 and October 2020 and those with a report singleton birth were followed up to 18 months, were included in the study. Excluded were those with a reported singleton birth were followed up to 18 months, were included in the study. Excluded were those with a report singleton birth were followed up to 18 months, were included in the study. Excluded were those with a report singleton birth were followed up to 18 months, were included in the study. Excluded were those with a report singleton birth were followed up to 18 months, were included in the study. Excluded were those with a report singleton birth were followed up to 18 months, were included in the study. Excluded were those with a report singleton birth were followed up to 18 months, were included in the study. Excluded were those with a report singleton birth were followed up to 18 months, were included in the study.

RESULTS: In the 2PN group, there were 177 blastocysts biopsied resulting in 62 euploid and 19 mosaic embryos in the control group. In the 2PN group, there was an average of 2.1 +/- 2.3 euploid embryos at the completion of their 2PN banking IVF cycles compared to 0.9 +/- 1.2 euploid embryos available to patients who underwent a single cycle in the control group (p = 0.01).

CONCLUSIONS: Banking embryos at the 2PN stage resulted in similar blastocyst yield and euploid embryos available for transfer.

IMPACT STATEMENT: This strategy has implications for substantial patient cost savings and embryology lab resource consolidation for patients that may need multiple cycles to obtain their desired family goals.

SUPPORT: None

REFERENCES: None
excellent outcomes even in samples with severe teratozoospermia. The fertilization rates were significantly lower in group 2 than in group 1. [p = 0.31] Respectively, with no significant difference. (Mann-Whitney U test.) Congenital anomalies at birth were observed in 1 case in the EP group and 120 cases in the Control group. Study 2: The percentages of "yes" for survey items (1), (2), and (3) in the EP and Control groups were 100% vs. 0.79%, 81.8% vs. 90.5%, and 100% vs. 99.1%, respectively, with no significant difference. (Fisher’s exact test.)

CONCLUSIONS: Although EP causes extracellular calcium ions to flow into the cells by opening small pores in the oocyte membranes, the results were comparable to those of the Control group from birth to 18 months of age in the items examined. However, since this study was a prospective study up to 18 months of age, it is necessary to examine the effects of EP on development of the babies over a longer period of time.

IMPACT STATEMENT: No effect on the development of babies following EP on oocytes were discerned, suggesting that EP may be an alternative method to initiate artificial oocyte activation.

SUPPORT: None.

REFERENCES: None.

P-77 6:30 AM Monday, October 24, 2022

DOES LOOKS MATTER? EFFECT OF ISOLATED TERAZOOSPERMIA ON FERTILIZATION AND EMBRYO OUTCOME IN ICSI CYCLES.
Charulata Chatterjee, phd.1 C Jyothi Budhi, M.B.B.S.2 1Scienctific Head and Consultant Embryologist, Secunderabad, India; 2Director, Secunderabad, India.

OBJECTIVE: This retrospective study aimed to re-evaluate the clinical value of a 4% cut-off threshold of sperm morphology in Intra Cytoplasmic Sperm Injection - ICSI cycles.

MATERIALS AND METHODS: This study was carried out for a total of 294 ICSI cycles, with sperm samples classified according to WHO classification. Group 1 (Control) included 102 couples with normal sperm morphology (>24% morphology). Group 2 (T; teratozoospermic) included 192 couples, with isolated teratozoospermia in the male partner (morphology <4%).

RESULTS: No statistically significant difference was seen in the two groups regarding age, duration of infertility and embryos transferred. 918 oocytes were retrieved in group 1 where 652 mature oocytes were injected and 613 fertilized [Fertilization rate: 94%] Where as in group 2 a total of 192 ICSI cycles yielded 1728 oocytes and out of 1245 mature oocytes 1109 fertilized [Fertilization rate 89%] The fertilization rates were significantly lower in group 2 than in group 1. [p = 0.004%] But no significant differences were found in embryo quality between groups 1 and 2.

CONCLUSIONS: Sperm morphology assessed by WHO criteria had little prognostic value in ICSI cycle outcomes. Sperm morphology did not appear to influence embryo development or embryo morphology. Microscopic selection of sperm with "normal" morphology during the ICSI procedure allowed excellent outcomes even in samples with severe teratozoospermia.

IMPACT STATEMENT: The classification of morphologically normal sperm has been progressively redefined. Importance of sperm morphology in relation to Assisted Reproductive Technology – ART outcome was studied in detail.

SUPPORT: Not funded by anyone

P-78 6:30 AM Monday, October 24, 2022

MICROFLUIDIC SPERM SORTING COMPARED WITH TRADITIONAL DENSITY GRADIENT CENTRIFUGATION: A COST ANALYSIS.
Chioma Ogbejese, MD.1 Katherine Koniares, MD.2 Prachi N. Godiwala, MD.3 Daniel R. Grow, MD, MHC.M.4 Lawrence Engmann, MD.4 Claudio A. Benadiva, MD, HCLD.1 Alison Bartolucci, PhD5 University of Connecticut, Farmington, CT; 1University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT; 2Center for Advanced Reproductive Services, Farmington, CT; 3Center of Advanced Reproductive Services, Farmington, CT; 4University of Connecticut Health Center, Farmington, CT.

OBJECTIVE: It has been advocated that the use of a microfluidics device may improve blastocyst development and euploidy rates during in vitro fertilization (IVF) cycles. However, the cost of this additional laboratory add-on has not been previously analyzed. We sought to analyze the cost of using the Zymot™ Multi (850 μL) Sperm Separation Device compared with traditional density gradient centrifugation for processing sperm to be used for intracytoplasmic sperm insemination (ICSI).

MATERIALS AND METHODS: The protocols for sperm preparation for traditional density gradient centrifugation and the microfluidics device at a single academic-affiliated infertility clinic were reviewed. The costs of processing sperm to be used for ICSI were calculated. Parameters used to determine the cost of performing each technique included the cost of laboratory supplies/equipment, time to prepare and process the sample, and hourly wage of the laboratory technician utilizing the density gradient. A total of nine samples were analyzed to assess timing of sperm processing: four within the microfluidics group and five within the density gradient group. A comparison for total preparation time and costs of each technique were compared.

RESULTS: It takes laboratory technicians an additional 4.47 minutes to use the microfluidics device. While the total processing time with the microfluidics device was increased by 4.47 minutes, the actual time spent handling the samples was virtually the same. Although these data do not suggest a time saving benefit, the complexity of the handling is lower with the microfluidics device as it involves only one processing container. Therefore, the sample is transferred fewer times to different tubes, reducing the opportunities for error or sample loss.

CONCLUSIONS: Use of microfluidics sperm sorting devices increases total expenditure of laboratory costs compared with standard density gradient centrifugation, but the complexity of the sperm preparation is decreased.

IMPACT STATEMENT: Knowledge of the cost and time expenditure of options available for ICSI and ultimately in IVF may contribute to decreasing overall expenses for patients and fertility centers.

<table>
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<th>Cost Comparison Per Patient Between Groups</th>
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<th>Zymot Multi (850 μL) Microfluidics Sperm Separation Device</th>
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<td>Total time to complete sperm selection procedure</td>
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<tr>
<td>Total cost to prepare one sample</td>
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</table>
ICSI IS ASSOCIATED WITH LOWER BLASTULATION RATES COMPARED TO CONVENTIONAL IVF AMONG COUPLES WITH NON-MALE FACTOR INFERTILITY AND LOW OOCYTE YIELD.

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OBJECTIVE: To determine whether intracytoplasmic sperm injection (ICSI) for non-male factor infertility is associated with higher rates of blastulation compared to conventional in vitro fertilization (IVF) cycles with low oocyte yield.

MATERIALS AND METHODS: We retrieved data from 2371 IVF cycles involving participants presenting to a single clinic setting from January 2017 to February 2022. The following parameters were used as exclusion criteria: 0 or >7 oocytes retrieved, cycles for oocyte cryopreservation, cases of male factor infertility, and cycles involving split fertilization (ICSI and conventional IVF). Cycles were grouped by number of retrieved oocytes (group A: 1-2, B: 3-4, and C: 5-6 oocytes). Blastulation rates were computed as the ratio of total blastocysts to the number of retrieved oocytes. Linear regression was used to examine the association between method of fertilization and total number of blastocysts, after adjusting for the number of oocytes retrieved. P-values < 0.05 were deemed as statistically significant. Prism-GraphPad Version 9.3.1 was used for analyses.

RESULTS: 417 cycles met inclusion criteria. 29.3% (122/417) involved conventional IVF whereas 70.7% (295/417) involved ICSI. There was no statistically significant difference in age, BMI, and AMH between ICSI and conventional IVF for each group (A, B, and C). Higher rates of blastulation were observed among cycles involving conventional IVF compared to ICSI for groups B and C (28.8% [49/170] vs 20.6% [96/467], p = 0.032; 42.7% [114/267] vs 33.3% [196/588], p = 0.009, respectively). There was no significant difference in blastulation rates by fertilization method among group A (p = 0.33), which most likely reflects an attenuation in study power. In regression analyses, ICSI was associated with a significantly lower blastocyst yield after adjusting for the number of oocytes retrieved as a continuous or grouped variable (p = 0.006 and p = 0.007, respectively).

CONCLUSIONS: Our findings suggest that ICSI for non-male factor infertility is associated with poorer rates of blastulation compared to conventional IVF in cycles with low oocyte yield.

IMPACT STATEMENT: ICSI is commonly used in cases of low oocyte yield. This cohort study suggests that conventional IVF is the preferred method of fertilization to achieve the highest rates of blastulation for couples with non-male factor infertility and low oocyte yield. These findings warrant further investigation into whether such differences in blastulation rates correlate with differences in live birth rates.
were cultured directly on day 5/6 and biopsied in the same day (trophectoderm). Embryos were vitrified and according to PGT-A results thawed and transferred. Single euploid frozen embryo transfer outcomes which included implantation rate, miscarriage rates and live birth rates were compared between standard ICSI and PICSI cycles. Also, aneuploidy rates were compared between groups.

RESULTS: Maternal ages and paternal ages were similar and there was no statistical difference according to the sperm parameters in both groups. There were no differences in blastocyst and number of 3BB and above blastocysts between groups. Also, there was no significant difference between the aneuploidy rates in both groups (p = 0.05). Clinical pregnancy (50% vs 52%; p = 0.865) rates, live birth rates (31.3% vs 52%; p = 0.069) and miscarriage rates (12.5% vs 0%, p = 0.064) per blastocyst transferred were found similar in the groups.

CONCLUSIONS: In conclusion, there was no difference in clinical pregnancy and embryo aneuploidy rates in standard ICSI and PICSI cycles. There was a nonsignificant trend of decrement in miscarriage rates and increment in live birth rates in PICSI group. However, large sample sized studies are required to confirm these findings.

IMPACT STATEMENT: Sperm selection strategies and PICSI may be a beneficial option in PGTA cycles to decrease miscarriage rates.

SUPPORT: none

P-82 6:30 AM Monday, October 24, 2022
DOES PHYSIOLOGICAL SELECTION OF SPERMATOZOA FOR ICSI (PICS) IMPROVE IVF OUTCOMES?
Ines Chabchoub, Senior technician,1 Eya Chaeben, techniciain,1 Sonia Minaallah, Embryologist,2 Mohamed Khrouf, Professor Associate,2 Fethi Zhioua, Dr,1 Khaled Mahmoud, Dr,1 Hanen Elloui, Dr5 Fertililla center, Tunis, Tunisia;2 FERTILLIA, Tunisia;3 FERTILLIA center, Tunis, Tunisia;4 clinique La Rose, Centre FERTILLIA, jardin des la cu, Tunis, Tunisia;5 Centre d’aide medicale à la procréation FERTILIA, Tunis, QC, Tunisia.

OBJECTIVE: Sperm DNA fragmentation can lead to implantation failures, lower pregnancy rates, early miscarriages and lower birth rates. It has also shown a negative correlation with embryo quality and fertilization. The use of some techniques, such as PICS (physiologic ICSI) that can identify mature and intact DNA through hyaluronid acid (HA) receptors binding ability has shown inconsistent results. In this study, we aimed to compare PICS and ICSI techniques outcomes in IVF cycles in the same patients.

MATERIALS AND METHODS: This prospective study, was initiated in September 2020, in a private clinic. The PICS technique for sperm selection, performed in the first group (group 1; n = 108) was matched to anterior ICSI cycles (group 2; n = 112) in the same patients.

Our inclusion criteria were previous ICSI attempt in the same AMP center, leading to miscarriage or absence of pregnancy, and at least 2 parameters from the list below:

- Male partner with teratozoospermia < 2% (Kruger Classification)
- Altered nuclear sperm quality (DNA fragmentation index (>15%) by TUNEL assay; Chromatid decondensation (< 20%) by Blue Aniline staining)
- Elevated oxidation reduction potential (> 1.36 mV/106 spermatozoa/ml) by MioxySys system.

We were excluded from this study patients with leukospermia, varicocele, and presence of any endometrial factor that can affect implantation.

The principal outcome of measure was the establishment of clinical pregnancy. The secondary outcomes were the fertilization rate, the embryo development rate, and the blastulation rate.

All statistical analysis was performed using SPSS (Version 23). A p value was considered statistically significant when < 0.05.

RESULTS: One hundred and eight PICS cycles were compared to 112 previous ICSI cycles in the same patients. There were no differences in age, semen analysis parameters of retrieved oocytes, or number of mature oocytes between the PICS and ICSI groups. The fertilization and the blastulation rates were lower in the ICSI group when compared to the PICS group, and the difference was statistically significant (60.91% vs 74.11%; p = 0.014; 29.2% vs 45.54%; p = 0.0003). The comparison of the cleavage rate between the two groups showed no significant difference (99.31% vs 97.5%; p = 0.05). The clinical pregnancy rate for the PICS group was significantly higher than in the ICSI patients (22.58% vs 7.69%; p = 0.0101).

CONCLUSIONS: The use of the PICS technique should be considered for patients with altered nuclear sperm quality undergoing ICSI cycles. These are our preliminary results and sample size will be increased, to confirm these findings.

IMPACT STATEMENT: PICSI is a promising development method improving sperm selection for ICSI procedure. This study identified couples with previous ICSI cycles failure and altered nuclear sperm quality as a category of infertile patients that may benefit from HA sperm selection before ICSI.

P-84 6:30 AM Monday, October 24, 2022
A RETROSPECTIVE ANALYSIS OF CHYMOTRYPSIN USE FOR IVF SPERM PREPARATION AND ITS EFFECTS ON FERTILIZATION, BLASTULATION AND PLOIDY.
David L. Shelley, BA1, Carlos Hernandez-Nieto, MD,2 Dmitry Gounko, B.S., M.A.,3 Joseph A. Lee, BA,2 Natan Bar-Chama, M.D.,4 Rose Marie Roth, MSc, TS(ABB), CLT (NYS),4 Christine Briton-Jones, PhD,2 Alan B. Copperman, MD,2 Richard E. Silfkin, B.A., TS(ABB), CLT(NYS)2 Reproductive Medicine Associates of New York LLP, New York, NY;3 Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE
Previously published research about chymotrypsin treatment has shown no effect on sperm motility or viability, yet, there remains a paucity of data on its association with fertilization, blastulation, and ploidy. This study evaluated whether there is a latent effect on IVF outcomes in patients whom chymotrypsin treatment is used in IVF for sperm preparation.

MATERIALS AND METHODS: The study included patients at a single, academic center who underwent IVF treatment from 2016 to 2022. Preimplantation Genetic Testing for Aneuploidy (PGT-A) with next generation sequencing (NGS) was performed after trophectoderm (TE) biopsy. Inside-nation of fresh oocytes was conducted via intracytoplasmic sperm injection (ICSI). Study patients utilized chymotrypsin treatment due to high seminal viscosity. Control patients did not require use of chymotrypsin. Only patients with fresh ejaculate and a total count of ≥ 30 million total motile were included in the analysis. Patients with recurrent pregnancy loss (RPL), recurrent implantation failure (RIF) and/or chromosomal rearrangements were excluded from the analysis. Baseline demographic characteristics, hormonal profiles, ovarian stimulation parameters, oocyte quality, fertilization rates, blastulation rates, and embryo ploidy rates were compared between cohorts. Comparative statistics and a logistic regression analysis adjusting for potential confounders was performed. A sample size of 329 patients per cohort was calculated to ensure an 80% power to detect a difference of 10% on fertilization rates (α = 0.05). A sub analysis for all cohorts included assessment of pregnancy outcomes after a single euploid embryo transfer on a synthetic endometrial preparation cycle.

RESULTS: 814 IVF/PGT-A cases utilized chymotrypsin while 6610 cases were controls. Significant differences in oocyte age, AMH, male age, total sperm count, and total gonadotropin dosage were found among cohorts. No differences were found in number of stimulation days, peak estradiol during COH, mean oocytes retrieved, and mean M2 oocytes. Oocyte maturity rates, fertilization, blastulation, and euploidy rates were comparable between cohorts. Mosaicism was significantly higher in study group. In a multivariate logistic regression analysis adjusted for oocyte age, AMH, gonadotropin dose, partner’s age, and total sperm count; no association was found between chymotrypsin use and odds of fertilization (aOR 0.9 CI95% 0.8-1.09), blastulation rate (aOR 1.069 CI95% 0.8-1.31), euploidy rate (aOR 0.98 CI95% 0.8-1.1), or rates of mosaicism (aOR 0.85 CI95% 0.5-1.2). Sub-analysis found no differences among controls and patients who utilized chymotrypsin in implantation (73% vs 74% p = 0.83), clinical pregnancy (62% vs 62% p = 0.82), live birth (52% vs 50% p = 0.64), and clinical pregnancy loss rates (11% vs 11% p = 0.68).

CONCLUSIONS: No significant effect was observed on fertilization, blastulation and embryo ploidy rates in patients who utilized chymotrypsin treatment for sperm preparation.

IMPACT STATEMENT: Chymotrypsin appears to be safe and efficient in sperm preparation for IVF cycles.

SUPPORT: None

REFERENCES: N/A

P-85 6:30 AM Monday, October 24, 2022
EFFECT OF STRONTIUM CHLORIDE ON ICSI OUTCOME IN PATIENTS WITH POOR FERTILIZATION AFTER ARTIFICIAL OOCYTE ACTIVATION BY CALCIUM IONOPHORE IS MORE PRONOUNCED IN CASES OF SURGICALLY RETRIEVED SPERM.
BY CALCIUM IONOPHORE IS MORE PRONOUNCED IN CASES OF SURGICALLY RETRIEVED SPERM.
OBJECTIVE: Inadequate oocyte activation is responsible for ICSI fertilization failure and is treated by artificial oocyte activation (AOA). As AOA chemicals, calcium ionophore (Ca-AOA) has been most widely used because of a large volume of clinical data. Although less frequently, oocyte activation by strontium chloride (Sr-AOA) is also utilized. In our center, patients who have had unsatisfied fertilization with Ca-AOA are recommended to undergo another ICSI cycle with Sr-AOA. In this study we assessed whether Sr-AOA improve fertilization and pre-and post-implantation development in patients with a history of poor fertilization even by Ca-AOA. AOA outcome was evaluated also for ICSI oocytes of the same origin.

MATERIALS AND METHODS: This retrospective study was carried out between September 2013 and December 2021 at a fertility center. Efficiency of Sr-AOA was assessed in patients who experienced failed or low fertilization with Ca-AOA in preceding ICSI cycles with ejaculated (Ej-ICSI) or testicular sperm (TESE-ICSI). Total of 202 consenting patients (40.0±4.4 years), 159 Ej-ICSI and 43 TESE-ICSI were involved. Rates of two pronuclei (2PN), blastulation, good-quality blastocyst (3DB and above on day 5), clinical pregnancy (gp), and ongoing pregnancy (OPR) were investigated. For Ca-AOA, oocytes were cultured with 10 mM Calcium ionophore (A23187) for 15 min, while for Sr-AOA, oocytes were cultured with 10 mM Strontium Chloride hydrate for 60 min. In all cases, embryo transfers were carried out with vitrified and warmed embryos.

RESULTS: In Ej-ICSI cases, rates of 2PN, blastulation, good-quality blastocyst, and OPR were 50.5%, 42.1%, 15.8%, 24.7% after Ca-AOA, while those of Sr-AOA were 48.6% (P = 0.01), 35.7%, 16.4%, 26.0%, 16.4%, respectively. Thus, the 2PN rate was significantly higher in Sr-AOA. In TESE-ICSI cases, those after Ca-AOA vs Sr-AOA were as follows: 28.6% vs 33.8%, 17.6% vs 35.3% (P = 0.05), 1.4% vs 12.9% (P = 0.01), 26.9% (14/52) vs 54.2% (13/24) (P = 0.05), 9.62% (5/52) vs 41.7% (10/24) (P = 0.01), respectively. The rates of blastulation, good-quality blastocyst, CPR and OPR were remarkably higher in Sr-AOA. Among 16 patients in whom no fertilization was obtained with Ca-AOA in preceding cycles, 15 patients yielded at least one normal fertilization by Sr-AOA. Sr-AOA was assessed in patients who experienced failed or low fertilization between September 2013 and December 2021 at a fertility center. Efficiency of Sr-AOA was considered as a legitimate option for cases with failed or low fertilization by Ca-AOA with both of ejaculated and testicular sperm. Interestingly pre- and post-implantation development was significantly improved by Sr-AOA in TESE-ICSI.

IMPACT STATEMENT: Because of the availability of largest clinical data and safety concern, Ca-AOA remains the first means of treatment. However, based on the current results, Sr-AOA is recommended for patients who have no improvement by Ca-AOA.

SUPPORT: none

P-86 6:30 AM Monday, October 24, 2022

IN VITRO MATURATION OF OOCYTES: A BREAK-THROUGH FOR Treating INFERTILITY in INACTIVATING MUTATION OF THE LUTEINIZING HORMONE/CHORIONGONADOTROPIN RECEPTOR. Michael Grynenberg, M.D., Ph.D., Julie Labrosse, M.D., Isabelle Cedrin Durnerin, M.D., Maëllis Peigné, M.D., Ph.D., Christophe Sifer, M.D. Hôpital Antoine Béclère, Clamart, France; Jean Verdier Hospital, Reproductive medicine, Bondy, France; Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine, Assistance Publique–Hôpitaux de Paris (AP–HP), Hôpital Universitaire Paris Centre, Centre Hospitalier Universitaire (CHU) Cochin, Paris, France; Jean Verdier Hospital, France.

OBJECTIVE: LH plays a fundamental role in female reproductive physiology and is responsible for steroidogenesis, oocyte maturation, ovulation and subsequent progesterone production by the corpus luteum. LH binds to the LH receptor (LHCGR) and couples the latter to downstream signal transduction pathways. Maturation of inhibiting mutations of the LHCGR lead to the impossibility to obtain final oocyte maturation both during natural cycles and after ovarian stimulation for in vitro fertilization purposes. Therefore, egg donation represents the only option for treating their infertility. The present clinical case aims to report a novel inactivating homozygous luteinizing hormone/choriongonadotropin receptor (LHCGR) mutation and a possible option for treating infertility of these patients with their own oocytes.

MATERIALS AND METHODS: Retrieval of immature oocytes was performed transvaginally under ultrasound scan without previous hCG priming. After 48h of incubation in an IVM medium, metaphase 2 oocytes were inseminated by ICSI and cleavage stage embryos were frozen. Frozen/thawed embryos transfer was performed after endometrial preparation using hormonal replacement therapy.

RESULTS: The 35-year-old nulliparous patient presented with primary spaniomorenorrhea but timely and spontaneous onset of secondary sexual characteristics. Serum LH levels were high (ranging from 15 to 30 IU/L) and to a lesser extent so were FSH levels. The ovarian reserve was normal for age, as assessed by serum AMH levels and ultrasound. There was no argument for polycystic ovarian syndrome, 21-hydroxylase deficiency, Cushings syndrome or hyperprolactinemia. Two previous attempts of controlled ovarian stimulation with gonadotropins and ovulation trigger with hCG and GnRH-agonist had failed, resulting in low estradiol levels despite correct follicular growth on ultrasonography and absence of ovulation after trigger. However, genetic analysis identified a novel homozygous inactivating LHCGR mutation (exon 6, c.470A>G) which had never been described previously. IVM was performed. A total of 7 oocytes were obtained after IVM, resulting in 4 Day 3 embryos. All embryos were frozen. Subsequently, 2 Day 3 embryos were replaced after endometrial preparation by hormone replacement therapy. The patient became pregnant and gave birth to a healthy baby. Two Day 3 embryos remain.

CONCLUSIONS: We report the first live birth after in vivo maturation (IVM) in a patient with a novel homozygous inactivating LHCGR mutation (exon 6, c.470A>G).

IMPACT STATEMENT: We describe a novel inactivating LHCGR mutation with subsequent live birth after IVM. As a growing number of gonadotropin receptor mutations are identified, this successfully achieved live birth places IVM as the only reliable option for these patients to conceive with their own eggs.

P-87 6:30 AM Monday, October 24, 2022

NICOTINAMIDE MONONUCLEOTIDE (NMN) IN VITRO SUPPLEMENTATION IMPROVES DEFICIENCIES IN NUCLEAR AND CYTOPLASMIC COMPETENCE OF GERMINAL VESICLE OOCYTES. Aitor Galbete Urrutia, B.S.c., Maria Marchante Cuevas, M.Sc., Amparo Másfud Giner, Ph.D., Jessica Martinez Carmona, B. Sc., Maria F. Insua, B.S.C., M.D., Ph.D., Antonio Pellicer, MD Ph.D, Sonia Herrera, Ph.D., Maria Jose Escribife Perez, PhD, Instituto de Investigación Sanitaria La Fe, Valencia, Spain; IVI, Madrid, Spain; IVI Foundation, Valencia, Spain; IVIEMA Foundation, Valencia, Spain; IVI Foundation - IIS La Fe, Valencia, Spain; IVIRMA, Valencia, Spain; IVIEMA Foundation, Valencia, Spain; IVI Foundation - IIS La Fe, Valencia, Spain; IVIRMA, Valencia, Spain.

OBJECTIVE: To test the effect of in vitro supplementation with nicotinamide mononucleotide (NMN) on nuclear and cytoplasmic competence of germlinal vesicle (GV) oocytes, according to age.

MATERIALS AND METHODS: This is an experimental, prospective randomized study, performed on GVs collected after COS, retrieval and denudation, from Dec 2021 to Apr 2022, after signed informed consent (IRB approval 2102 FIVI 013 SH).

Patients were classified according to age and AMH levels as young (<35y and ≥ 1.2 mg/mL) or aged (≥ 35y and/or < 1.2 mg/mL). Each GV was randomized into experimental (NMN) or control group. Briefly, 487 GV were individually cultured in 25 μl SCSCM-NXC (Vitrolife) with or without 100μM NMN in, Embryo Slides at 37°C, 5% CO2 and 5% O2 in an EmbryoScope. After 24-28h, GV reaching the MII (rMII) were activated with A23187 (4 μm, 5 min) and gave birth to a healthy baby. Two Day 3 embryos remain.

RESULTS: NMN supplementation improved RR in aged women (63.4% vs. 43.9%; p = 0.006) but did not affect the young groups (48.6%).

IMPACT STATEMENT: NMN supplementation improved RR in aged women (63.4% vs. 43.9%; p = 0.006) but did not affect the young groups (48.6%). Indeed, t1PB occurred significantly earlier in control aged group (19.5±2.3h; 95CI: 18.8-20.2h) than in the NMN-aged or young groups (20.8±2.3h; 95CI: 20.5-21.1h).
In NMN-aged women, rMII extruded tPB1 later than controls (19.5 ± 2.3h vs. 21.0 ± 2.1h), by longer MI duration (16.4 ± 2.0h vs. 15.0 ± 1.1h; p < 0.01) without affecting the permanence at GV (4.5 ± 2.3h).

In younger women, NMN supplementation did not modify tPB1 (20.7 ± 2.5h), but NMN-rMII lasted less at GV (4.6 ± 2.1h) and longer MI duration (16.2 ± 1.9h) than their matched controls (5.9 ± 2.2h and 14.7 ± 1.9h, respectively). Moreover, NMN also improved NOAR in the young (38.5% vs. 73.9%, respectively; p = 0.03), but not in the older women (56.4%).

CONCLUSIONS: In ≤ 35y women, 100µM NMN supplementation did not modify nuclear competence, but improved cytoplasmic competence of GV, while in the aged allowed GV to display a similar competence to that of young women. NMN supplementation extends MI duration regardless age, and reduces permanence at GV in young women. However, the biological relevance of these variables on oocyte competence remains unknown.

IMPACT STATEMENT: Since NAD+ decreases with age and the NMN supplementation enhances NAD+ biosynthesis, our results suggest that may overcome some oocyte competence limitations.

RESULTS: When women were divided into who generated (benefited) or not BSTC from GV rescue, no significant differences were observed in demographic variables: aged (34.0 ± 0.3y); or reproductive ones: AMH levels (2.2 ± 0.3 ng/mL), number of follicles ≥ 14mm (8.1 ± 0.3), number of retrieved MII (5.1 ± 0.3) and GV (4.5 ± 0.2), and RR (0.70 ± 0.05); however, differences were observed, in rR (67.2% vs. 39.3%), improving the rMII RR to 1.1 ± 0.6, in benefited women.

34% women had RR ≥ 75%, ranged within Vienna Consensus’s values. In them, MII rescued is near to that expected by folliculometry (RR: 1.2 ± 1.0; 95IC: 0.9-1.4); and so, GV rescue had not to be applied. Instead, in women with MII RR < 75%, rMII RR was significantly higher in benefited (0.83 ± 0.19) than in non-benefited women (0.69 ± 0.29; p = 0.02); maybe due to higher rR.

Out of 41 women with rMII RR > 80%; in 13 women (32%), GV rescue yielded 1.5 ± 0.5 (95IC: 1.2-1.8) extra BSTC. In 5 women (12%), cycle was not lost, as 1.6 ± 0.5 BSTC came only from rMII: 8 women added 1.5 ± 0.5 extra BSTC to those from MI (2.6 ± 1.1 MII BSTC).

CONCLUSIONS: The GV rescue approach is not applicable to all women. It would be a complementary strategy to conventional IVF protocols when woman has < 38y and from whom MI RR is < 75%. Also, we recommend to complete the GV approach with ICSI when rMII RR > 80%. Thus, 1/3 women might obtain GV-derived BSTC.

IMPACT STATEMENT: Besides the MI RR proposed by the Vienna Consensus, the rMII RR, can be a useful complementary performance indicator to identify women that will potentially benefit from GV rescue.

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**Table:**

<table>
<thead>
<tr>
<th>N (%)</th>
<th>Fluorescence intensity</th>
<th>Fraction Bound</th>
<th>Short Lifetime</th>
<th>Long Lifetime</th>
<th>Redox ratio (NADH int/ FAD int)</th>
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<tr>
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<td>NADH</td>
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<td>MII</td>
<td>100 (57%)</td>
<td>0.03 ± 0.01</td>
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<td>GV</td>
<td>75 (45%)</td>
<td>0.02 ± 0.02</td>
<td>0.015 ± 0.001</td>
<td>0.73 ± 0.004</td>
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<td>Patients &lt; 35y</td>
<td>123 (53%)</td>
<td>0.73 ± 0.003</td>
<td>0.49 ± 0.007</td>
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<td>Patients ≥ 35y</td>
<td>107 (47%)</td>
<td>0.73 ± 0.002</td>
<td>0.47 ± 0.01</td>
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<td>pValue</td>
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RESULTS: A total of 175 GV s reached MII stage. Several FLIM parameters representative of mitochondrial function were significantly different in GV s that matured to MII compared to those that showed maturation failure. FLIM imaging was able to significantly distinguish between oocytes from young and AMA women.

CONCLUSIONS: GV s that matured exhibit a different metabolic profile compared to those that failed. Similarly, GV s from older women display diminished mitochondrial activity.

IMPACT STATEMENT: FLIM may be able to discern which GV from patients can reach MII. This could be a valuable tool for patients to obtain extra mature oocytes for their cohort.

FROZEN EMBRYO TRANSFER CYCLES MAY IMPROVE PREGNANCY RATES. Fang Li, M.D./Ph.D.1, Muhammet Rasit Ugur, Ph.D.2, Fayek Shamma,2 Ahmad Hammoud, MD.3, Hanh N. Cottrell, MD.4, Sule Dogan, PhD5, Rochester general hospital, Rochester, NY; 2IVF Michigan, Bloomfield Hills, MI; 3TFV Michigan, Ypsilanti, MI.

OBJECTIVE: To evaluate pregnancy outcome of frozen embryo transfer, compared to fresh embryo transfer between two groups of patients: advanced reproductive age (≥35 yo) vs. young reproductive age (<35 yo).

MATERIALS AND METHODS: In this study, we reviewed 2249 infertile patient’s files in our IVF center from 2016 to 2018, who underwent ICSI, and either frozen or fresh transfer. The patients with advanced reproductive age (≥35 yo) vs. young reproductive age (<35 yo) were analyzed separately. Each age group were classified into two subgroups: patients who underwent frozen embryo transfer (FET, n=1438), and fresh embryo transfer (ET, n=811).

RESULTS: In this study, we reviewed 2249 infertile patient’s files in our IVF center from 2016 to 2018 (excluding the PGT (preimplantation genetic testing) case), who underwent ICSI, and either frozen or fresh transfer. Patients with advanced reproductive age (≥35 yo) vs. young reproductive age (<35 yo) were analyzed separately. Each age group was classified into two subgroups: patients who underwent frozen embryo transfer (FET, n=1438), and fresh embryo transfer (ET, n=811).

CONCLUSIONS: The pregnancy outcomes were significantly better in FET cycles, compared to ET cycles in both group of patients. The significance is even greater for people with advanced reproductive age. During the latest pandemic, freeze all cycles proved to benefit patients without compromising the higher pregnancy rates. A control prospective study should be conducted for further conclusions.

IMPACT STATEMENT: There is long term controversial of FET vs. ET. With the increase rate of PGT and pandemic impact, the requirement of FET increased significantly. This research reassures the advantage of FET overweight other factors, and will improve the application of FET and outcome.

SUPPORT: None

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Table 1. Outcomes of FET and ET cycles in both groups

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<th>Number of the FET case</th>
<th>Number ET case</th>
<th>Total</th>
<th>pregnancy rate of FET (%)</th>
<th>pregnancy rate of ET (%)</th>
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<tbody>
<tr>
<td>Group A (≥35)</td>
<td>582</td>
<td>259</td>
<td>841</td>
<td>61.0</td>
<td>47.5</td>
</tr>
<tr>
<td>Group B (&lt; 35)</td>
<td>856</td>
<td>552</td>
<td>1408</td>
<td>68.5</td>
<td>62.0</td>
</tr>
<tr>
<td>Total</td>
<td>1438</td>
<td>811</td>
<td>2249</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CONCLUSIONS: The trend to increased male: female live birth SSR coincides with the wider application of blastocyst transfer in this study. Both blastocyst developmental stage and blastocyst grade significantly predict male sex.

IMPACT STATEMENT: Understanding the potential reasons for sex-ratio imbalance following fertility treatment helps us develop strategies to balance SSR in the future. How to reach a natural sex ratio by balancing blastocyst and cleavage stage embryo transfer deserves future investigation.

SUPPORT: None.

P-92 6:30 AM Monday, October 24, 2022

COMPARISON OF LABORATORY OUTCOMES FROM DIFFERENT SPERM SOURCES USING FRESH AND FROZEN DONOR EGGS IN A SINGLE HIGH VOLUME LABORATORY. Haleigh Silz, MS,1 Laura Reed, BS,1 William B. Schoolcraft, MD,2 Jason E. Swain, PhD, HCLD1 1CCRM Colorado, Lone Tree, CO; 2CCRM Fertility Laboratory, Lone Tree, CO.

OBJECTIVE: Use of frozen donor eggs for ART has increased substantially. The convenience of using frozen donor eggs in advantageous and addresses limitations present with fresh donor egg cycles. However, compared to fresh donor cycles, the number of frozen eggs provided per cycle is low. Thus, high developmental competence of frozen eggs is critical to ensure success, especially with certain sperm sources. Fertilization and blastocyst development from fresh and frozen donor eggs following injection with varying sperm sources were compared.

MATERIALS AND METHODS: Data from ICSI cycles using fresh or frozen donor egg over a 21 month period were examined. Cycles using fresh ejaculated (Ejac) and testicular sperm (TEST) were analyzed separately. Rates of fertilization (fert) per mature egg as well as good quality blastocyst (GQB) development >3BB per 2PN were compared on days 5, 6 and 7. Data were analyzed using Fisher’s Exact test, p<0.05.

RESULTS: In fresh donor eggs, fert rates differed by sperm source with TESE sperm yielding lower rates than Ejac. Using frozen eggs, no difference in fert was noted between sperm sources. Fert rates using just Ejac sperm or just TEST sperm did not differ between egg types. Using either fresh or frozen donor eggs, GQB rates were lower for TESE sperm than Ejac on all days. No differences were noted using just TEST sperm between fresh or frozen eggs. Using Ejac sperm, frozen donor eggs yielded lower GQB on all days. A higher increase in GQB from D6 to 7 was obtained using frozen eggs than fresh eggs. Overall, GQB was higher for fresh eggs on D5 (34.1% vs. 24.9%) D6 (60.4% vs. 51.1%) and D7 (61.6% vs 56.4%) compared to frozen eggs p <0.005.

<table>
<thead>
<tr>
<th></th>
<th>Fresh Donor Egg</th>
<th>Frozen Donor Egg</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>1277</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>2532</td>
<td>26</td>
</tr>
<tr>
<td>Fert rate (%)</td>
<td>82.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>60.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>D5 GQB (%)</td>
<td>34.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>D5/6 GQB (%)</td>
<td>62.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>36.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>D5/6/7 GQB (%)</td>
<td>63.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>36.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Different letter superscript indicates significant difference between sperm source within an egg type. Different numeric superscript indicates significant difference within a sperm type between egg sources.

CONCLUSIONS: Testicular sperm yielded lower blastocyst rates in both fresh and frozen donor eggs compared to ejaculated sperm. Frozen donor eggs yielded fewer high quality blastocysts than fresh eggs on all days examined and did not catch up by day 7, indicating that slower development was not the only issue. Frozen donor eggs may benefit from extended observations, checking development later on day 6 or on day 7 to ensure all blastocysts are identified.

IMPACT STATEMENT: Frozen donor eggs display reduced blastocyst formation compared to fresh donor eggs using different sperm sources and may benefit from extended culture.

P-93 6:30 AM Monday, October 24, 2022

OPTIMAL INTERVENTION TO OBTAIN SPERM WITH GOOD DNA QUALITY – ROLE OF MACS VS MICROFLUIDICS IN SPERM SORTING. Krishna Mantravadi, Dr., MBBS, PGDHOM, Masters in clinical embryology,1 Akshay Vinodrao Tayawade, MSc. in Clinical Embryology,2 Durga Gedela, Rao Dr., MRCOG 1Oasis fertility, Hyderabad, India; 2Oasis Fertility, Visakapatnam, India; 3Oasis Fertility, Hyderabad, India.

OBJECTIVE: In Individuals with raised Sperm DNA Fragmentation Index (DFI), which sperm selection technique, Magnetic Activated Cell Sorting (MACS) or Microfluidics Sperm Sorting (MF) helps obtain sperms with good DNA quality.

MATERIALS AND METHODS: This is an ongoing observational cohort study conducted at a private teaching hospital between November 2020 and October 2021. Men undergoing IVF cycles were randomly allocated to MACS (58) or MF (30) sperm sorting. Sperm DFI testing was performed on neat samples and post processed samples. Couples with one failed IVF, sperm count >5millions/ml, and raised Sperm DFI (>25%) were included in the study. Sperm DFI testing was performed by SCSA method. Based on randomization, MACS or MF was done as per the manufacturer’s instruction. DFI assessment was done on neat and post intervention samples. The efficiency of the sperm processing method to reduce the DFI value post intervention was the primary outcome. We also evaluated the percentage of samples whose DFI values were <15, 15-25, and >25% respectively post intervention. MedCalc® Software Version 20.022 was used for statistical analysis.

RESULTS: MF group showed an average Pre- Interventional DFI Value of 24.75% & Post-Interventional DFI Value of 5.19%. The mean Rate of Change in DFI was observed to be 81.39% (P=0.008), with the highest frequency of 100% and a lower frequency of 6.06%.

MACS group showed an average Pre-Interventional DFI Value of 44.44% & Post-Interventional DFI Value of 21.56%. The mean Rate of Change in DFI was observed to be 54.47% (P=0.007), with the highest frequency of 100% and a lower frequency of 3.70%.

Post-Interventional DFI Value Distribution:

- MICROFLUIDICS
- 52 samples had DFI <15%
- 1 sample - 15% - 25%
- 5 samples - >25%
- 8 samples had DFI <15%
- 8 sample - 15% - 25%
- 14 samples - >25%

- MF sperm sorting seems to be efficient in offering a better rate of change in DFI values. Irrespective of the DFI value of neat samples, a higher proportion of semen samples seem to have a DFI value of less than 15% in the MF sperm sorting group post intervention.

CONCLUSIONS: Microfluidics seems like a beneficial intervention to optimize sperm selection for Individuals with raised sperm DFI. MF sperm sorting seems to be efficient in offering a better rate of change in DFI values. Irrespective of the DFI value of neat samples, a higher proportion of semen samples seem to have a DFI value of less than 15% in the MF sperm sorting group post intervention.

IMPACT STATEMENT: For individuals with a history of failed implantation and raised sperm DFI, MF sperm sorting seems to be a beneficial intervention to obtain sperm with good DNA quality.

P-94 6:30 AM Monday, October 24, 2022

SPERM CONCENTRATION, SPERM MOTILITY AND TOTAL MOTILE SPERM COUNT ARE NOT AFFECTED BY CORONAVIRUS DISEASE 2019 (COVID-19) INFECTION. Melis Golce Kocer Yazici, MD, PhD1, Mert Yesiladali, MD, PhD,1 Ece Gumusoglu, MD, PhD,2 Oya Alagöz, MD,1 Rukuet Attar, MD, PhD,1 Gazi Yildirim, MD,3 Erkut Attar, MD, PhD,1 Yeditepe University Hospital, Istanbul, Turkey; 2Yeditepe University Hospital, Istanbul, Istanbul, Turkey.

OBJECTIVE: The purpose of this study is to compare the parameters of sperm analysis in a group of healthy sperm donors before and after Coronavirus Disease 2019 (COVID-19) infection.

<table>
<thead>
<tr>
<th>_parameter</th>
<th>Pre-COVID-19</th>
<th>Post-COVID-19</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm concentration (millions/ml)</td>
<td>250 ± 50</td>
<td>250 ± 50</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Sperm motility (% motile)</td>
<td>50 ± 10</td>
<td>50 ± 10</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Total motile sperm count (million)</td>
<td>25 ± 5</td>
<td>25 ± 5</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Different letter superscript indicates significant difference between group post intervention.
TABLE 1.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>N</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Covid Abstinence (Day)</td>
<td>4.5385</td>
<td>13</td>
<td>1.85362</td>
<td>0.5140</td>
<td>0.607b</td>
</tr>
<tr>
<td>Post-Covid Abstinence (Day)</td>
<td>4.2308</td>
<td>13</td>
<td>1.53590</td>
<td>0.42598</td>
<td></td>
</tr>
<tr>
<td>Pre-Covid Volume (mL)</td>
<td>3.9462</td>
<td>13</td>
<td>1.99065</td>
<td>0.55211</td>
<td>0.889b</td>
</tr>
<tr>
<td>Post-Covid Volume (mL)</td>
<td>3.9846</td>
<td>13</td>
<td>2.09239</td>
<td>0.58032</td>
<td></td>
</tr>
<tr>
<td>Pre-Covid Concentration (M/mL)</td>
<td>55.8689</td>
<td>13</td>
<td>37.86822</td>
<td>10.50275</td>
<td>0.313a</td>
</tr>
<tr>
<td>Post-Covid Concentration (M/mL)</td>
<td>64.8634</td>
<td>13</td>
<td>43.96596</td>
<td>12.19396</td>
<td></td>
</tr>
<tr>
<td>Post-Covid A+B (%)</td>
<td>41.3077</td>
<td>13</td>
<td>21.70017</td>
<td>6.01854</td>
<td>0.852a</td>
</tr>
<tr>
<td>Post-Covid A+B (%)</td>
<td>41.9231</td>
<td>13</td>
<td>20.35707</td>
<td>5.64604</td>
<td></td>
</tr>
<tr>
<td>Post-Covid TMSC (M)</td>
<td>112.5763</td>
<td>13</td>
<td>94.04360</td>
<td>26.08300</td>
<td>0.570a</td>
</tr>
<tr>
<td>Post-Covid TMSC (M)</td>
<td>127.5823</td>
<td>13</td>
<td>96.70131</td>
<td>26.82012</td>
<td></td>
</tr>
</tbody>
</table>

**P-95** 6:30 AM Monday, October 24, 2022

**MONOZYGOTIC TWINS AFTER IVF: CAN TIME-LAPSE TECHNOLOGY PREDICT MONOZYGOTIC TWIN PREGNANCY?**

Carlos Augusto Zarate Nisell, M.D., Arias Santos Gomes, B.Sc., Hamilton De Martim, B.Sc., Tatiana CS. Bonetti, PhD., Pedro AA. Monteleone, MD, PhD, Monteleone Human Reproduction Center, São Paulo, Brazil; Centro de Reprodução Humana Monteleone, São Paulo, Brazil; Universidade Federal de São Paulo, São Paulo, Brazil.

**OBJECTIVE:** The purpose of this study was to evaluate morphokinetic of embryos that resulted in monozygotic twin pregnancies (MZTP) after a single embryo transfer (SET), with matched time-lapse data of embryos that resulted in a singleton pregnancy (SP) after SET.

**MATERIALS AND METHODS:** The study included semen analysis from eligible sperm donors aged 25-56 who had abstinence of 3-9 days and provided sperm before and after COVID-19 infection. Data were obtained from the patients who applied to our infertility clinic for semen analysis or in vitro fertilization (IVF) treatment. Ejaculate volume (mL), average concentration (M/mL), percent motility (percent), and total motile sperm count (M) were the primary outcomes. Data were compared and analyzed by paired samples t test and Wilcoxon’s test.

**RESULTS:** A total of 13 qualified sperm donors met inclusion criteria for this study. There was no significant difference in concentration, motility, or total motile sperm count between the patients’ semen parameters before and after the infection (p>0.05) (Table 1).

**CONCLUSIONS:** COVID-19, a novel coronavirus disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has sparked a global pandemic that hit the world in 2020, offering a huge challenge to healthcare systems and affected populations (1). One of the known effects of SARS-CoV-2 infection is invasion or damage to the male reproductive system. To enter host cells, the virus uses the transmembrane serine protease 2 (TMPRSS2) and the angiotensin-converting enzyme 2 (ACE2) receptor (2). Furthermore, ACE2 is extensively expressed in testicular tissue, and SARS-CoV-2 has been found in semen (3). SARS-CoV-2 can also infect cells through the host cell receptor CD147 (basigin, BSG), a transmembrane glycoprotein crucial for the blood–testis barrier’s integrity (BTB) (4). Sperm quality measures were not significantly different in qualified, otherwise healthy sperm donors prior to COVID-19 infection and after recovery.

**IMPACT STATEMENT:** SARS-CoV-2 infection has no impact on sperm concentration, motility, or total motile sperm count in healthy, eligible donors.

**REFERENCES:**
1. https://doi.org/10.1016/j.scitotenv.2020.138996,
2. https://doi.org/10.1007/s40618-022-01764-z,
3. https://doi.org/10.1001/jamanetworkopen.2020.8292,
4. https://doi.org/10.1016/j.ydbio.2013.05.023

**IMPACT STATEMENT:** Division occurring at the blastocyst stage (70-75%) is believed to account for mostly of MZTP. The division shortly after fertilization (20-30%) or in later stages of pregnancy are supposed to be minority (1-2%). Thus, time-lapse technology would allow us to observe embryo splitting in most blastocysts which become MZTP. More than a decade after the time-lapse imaging surge, there are rare report of ICM splitting videos. In the time-lapse videos reviewing, no sign of embryo splitting or doubled inner cell mass (ICM) were observed. It is also interesting that all blastocyst which become MZTP had inner cell mass classified as A or B in the morphological evaluation.

**CONCLUSIONS:** Embryo morphokinetics whose result in MZTP are similar to SP. There are no sign which indicates embryo splitting or doubled ICM until the fifth day of embryo development, evaluated by time-lapse videos.

**IMPACT STATEMENT:** Division occurring at the blastocyst stage (70-75%) is believed to account for mostly of MZTP. The division shortly after fertilization (20-30%) or in later stages of pregnancy are supposed to be minority (1-2%). Thus, time-lapse technology would allow us to observe embryo splitting in most blastocysts which become MZTP. More than a decade after the time-lapse imaging surge, there are rare report of ICM splitting in the literature. Our study corroborates with others on the absence of morphokinetic differential or visual signal of ICM splitting in blastocyst at fifth day of development that became MZTP. Thus, the theory about the timing of embryonic division generating MZTP appears not to be consistent with more recent assisted reproductive practices.

**SUPPORT:** No financial support was required.

**REFERENCES:**
ULTRAFAST WARMING PROTOCOL DEMONSTRATES SIMILAR OUTCOMES AND SIGNIFICANTLY DECREASES EMBRYOLOGY WORKLOAD COMPARED TO STANDARD WARMING PROTOCOLS, A RANDOMIZED CONTROL TRIAL WITH EUPLOID BLASTOCYSTS. Tyl H. Taylor, PhD, Jessica Nicole Manns, MS, Isabel Katz, BS, Jennifer L. Patrick, MS, PhD, Taylor Holt, PA-C, Seth E. Katz, M.D. REACH, Charlotte, NC; Reproductive Endocrinology Associates of Charlotte, Charlotte, NC; Reproductive Endocrinology Associates of Lone Tree, CO; CCRM Fertility Network, Lone Tree, CO.

OBJECTIVE: Procedures within the IVF lab have become more complex and time-consuming resulting in embryologist fatigue. One of these procedures is embryo warming. Embryo warming requires 14 minutes of embryology bench time due to the movement of the embryo through TS (thawing solution), DS (dilute solution), and WS (washing solution). Therefore, we have modified the standard warming technique to merely moving the embryo to TS solution for 1 min and then immediately to culture media. This method eliminates the need for DS and WS steps and decreases the overall time to complete the warming process. It is the objective of this study to compare outcomes of embryos warmed with the standard protocol (14 minutes) versus embryos warmed with the ultrafast protocol (1 min).

MATERIALS AND METHODS: All embryos were warmed with FujiFilm® warming media. Only patients undergoing a frozen embryo transfer (LET) of a single euploid blastocyst were included in this study. Patients were randomized between two groups: embryos warmed with the standard protocol (Group 1: 1 minute TS, 4 minutes DS, 8 minutes WS, and transfer to culture media) and embryos warmed using the ultrafast protocol (Group 2: 1 minute TS and transfer to culture media). All blastocysts were transferred utilizing standard of care protocols and pregnancy rates, implantation rates, and embryology time savings were compared between groups.

RESULTS: A total of 200 patients and 200 blastocysts were randomized between the two groups, 94 in group 1 and 106 in group 2. The average age between group 1 and group 2 was not significant, 36.1 ± 4.2 and 36.9 ± 5.4, respectively (NS). Pregnancy rate between group 1 and group 2 was not significant, 69/94 (73.4%) and 83/106 (78.3%), respectively (NS). Implantation rate between group 1 and group 2 was not significant, 51/96 (53.1%) and 67/106 (63.2%), respectively (NS). Regarding embryology time savings, the total time for embryologists to warm was 1316 minutes and 106 minutes for group 1 and group 2, respectively (P < 0.0001).

CONCLUSIONS: This study demonstrated that a significantly quicker embryo warming technique provides comparable pregnancy and implantation rates, while saving 13 minutes of tech time per warming. Further studies are needed to determine if this protocol can be utilized across different vitrification and warming procedures.

IMPACT STATEMENT: Altering warming protocol to 1 min in TS saves tech time and does not impact pregnancy or implantation rates.

SUPPORT: none

P-96 6:30 AM Monday, October 24, 2022

SPERM PARAMETERS AMONG SELENE SAMPLES PROCESSED BY MICROFLUIDICS COMPARED TO DENSITY GRADIENT CENTRIFUGATION (DGC): A SECONDARY ANALYSIS OF A DOUBLE-BLINDED PROSPECTIVE RANDOMIZED TRIAL. Prachi N. Godiwala, MD, Jane L. Kwieragba, BSc, TS; Emilie Almanza, BS; John Nulsen, MD; Claudio A. Benadiva, MD, HCLD; Daniel R. Grow, MD, MHC, Alison Bartolucci, PhD; Lawrence Engmann, MD Center for Advanced Reproductive Services, Farmington, CT; Center for Advanced Reproductive Services, Farmington.

OBJECTIVE: Microfluidics has been shown to improve post-processing sperm parameters and avoid damage to sperm DNA compared to DGC in retrospective studies. We aim to compare post-preparation sperm parameters among semen samples processed by microfluidics compared to DGC.

MATERIALS AND METHODS: This was a secondary analysis of data collected for a double-blinded randomized controlled trial examining euploidy rates among embryos created from sibling oocytes injected with sperm processed via microfluidics or via DGC. Male partners produced fresh semen samples which were divided into two aliquots for processing via DGC or via a microfluidics device (ZyMot Multi [850uL] Sperm Separation Device). In DGC processing, fresh ejaculate was placed into a 90% gradient and centrifuged; the pellet was then transferred into sperm wash media to record the post-preparation count and motility. In microfluidics processing, 850uL of the raw semen sample was inserted into the inlet port of the device and sperm was allowed to traverse the chamber for 30 minutes; the post-preparation parameters were recorded from sperm reaching the outlet chamber. The primary outcomes were the post-processing sperm concentration and motility. Paired t-tests were used for continuous variables, reported as mean ± SEM. A two-sided p-value of <0.05 was considered significant.

RESULTS: Semen samples were analyzed from 104 male partners. 26.9% of participants carried a diagnosis of male factor infertility. The mean age of the male partner was 37.3 ± 0.4 years. The mean pre-processing concentration was 62.6 ± 4.3 million/mL and the mean pre-processing motility was 53.2 ± 1.7%. The mean post-processing concentration was significantly higher in the microfluidics group compared to the DGC group (19.0 ± 2.0 million/mL versus 11.3 ± 1.4 million/mL, p < 0.01). The mean post-processing motility was also significantly higher in the microfluidics group compared to the DGC group (46.8 ± 0.6% versus 87.7 ± 1.8%, p < 0.01).

CONCLUSIONS: Microfluidics sperm processing improves post-processing concentration and motility compared to DGC.

IMPACT STATEMENT: Microfluidics sperm processing improves post-processing semen parameters, which may translate into improved embryologic outcomes in the IVF laboratory.

SUPPORT: The randomized controlled trial from which the data used in this study was collected is funded by ZyMot(TM) / DnNow via a grant awarded to our fertility center.
EVALUATION OF OOCYTE FERTILIZATION AND IN VITRO EMBRYO DEVELOPMENT AFTER SPERM PREPARATION USING ZYMOT® PRIOR TO INTRA-CYTOPLASMIC SPERM INJECTION (ICSI) AND IN VITRO FERTILIZATION (IVF). Said Daneshmand, MD,1 Kevin S. Richter, PhD,2 Hanna L. Callies, MA,1 Shannon Kokjohn, MSc4 San Diego Fertility Center, San Diego, CA; 3Fertility Science Consulting, Silver Spring, MD.

OBJECTIVE: To compare ICSI/IVF oocyte fertilization rates and in vitro embryo development associated with the use of Zymot®, versus conventional semen preparation methods, prior to selecting sperm for injection.

MATERIALS AND METHODS: Records of ICSI/IVF cycles performed at a single infertility treatment center from January 2019 through December 2020, during which time the center gradually shifted toward incorporating ZyM® for sperm preparation into ICSI/IVF protocols, were reviewed retrospectively. Cycles using non-ejaculated sperm (i.e., biopsied or aspirated) were excluded from the analysis. Sperm preparation was conducted according to conventional methodology (n=519), or with the use of the ZyM® Sperm Separation Device (n= 141).

ICSI fertilization outcomes, subsequent embryo development to the blastocyst stage, and confirmation of euploidy by next-generation preimplantation genetic testing for aneuploidy (PGT-A) were evaluated and compared between conventional sperm preparation or ZyM® by two-sample t-test.

RESULTS: Compared to cycles using conventional sperm preparation methods, ZyM® cycles used donor oocytes and cryopreserved semen significantly less frequently. The average age of patients undergoing autologous IVF was more than a year younger for ZyM® versus conventional sperm preparation cycles. Despite being significantly younger, the ZyM® group did not exhibit increased fertilization or euploid blastocyst formation compared to conventional sperm preparation.

<table>
<thead>
<tr>
<th></th>
<th>Conventional</th>
<th>ZyM®</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donor oocyte</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cryopreserved semen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oocytes retrieved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fertilization (2pn/oocyte)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Euploid blastocysts per 2pn</td>
<td></td>
<td></td>
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</tbody>
</table>

Conclusions: We were unable to confirm any benefits to either oocyte fertilization or in vitro embryo development through the blastocyst stage resulting from incorporation of ZyM® into ICSI/IVF treatment protocols. While there may be identifiable subgroups that experience a more substantial benefit, our results suggest that there is little or no benefit to incorporating ZyM® across the general IVF population.

IMPACT STATEMENT: Our results cast doubt on the utility of general application of ZyM® in the IVF laboratory.

E-POSTER ABSTRACT SESSION: 11
OBJECTIVE: Increased sperm DNA fragmentation (SDF) is one of the leading causes of male infertility. Conventional methods for sperm preparation have induced questioning of sperm recovery rates. The microfluidic sperm sorting (MSS) technique selects highly motile sperm with lower levels of SDF compared to density-gradient centrifugation (DGC) technique. This study aimed to compare MSS to DGC technique in couples with repeated implantation failure (RIF) and high SDF referred to a PGT-A (preimplantation genetic testing for aneuploidies) cycle.

MATERIALS AND METHODS: This retrospective study included couples who had at least 2 previous failed ICSI cycles despite transfer of good quality embryos. In their new cycles, couples who accepted the technique were assigned to the MSS group (92 cycles with 310 embryos) and the rest were managed with DGC (151 cycles with 378 embryos). Unexplained pregnancy was achieved, a subsequent FET (frozen embryos transfer) cycle was scheduled for those with available euploid embryos detected with PGT-A. Female patients were aged <43 years, had BMI <35, no gynecological or medical disorders. Males with a SDF ≥30% were included. A maximum of 3 FET cycles of each patient were included. Statistical analyses were performed using SPSS, version 22.0 (SPSS Inc Chicago IL, USA). Mann Whitney U test, Pearson’s chi square test and fisher’s exact test were used for comparisons. p-value of < 0.05 was accepted as significant.

RESULTS: There was no difference in fertilization & euploidy rates, number of patients with surplus frozen embryos, mean number of euploid embryos per patient, number of live births (LB) in the first cycle & subsequent cycles, clinical miscarriage, and cumulative live LBs per aspirate of patients with surplus frozen embryos, mean number of euploid embryos. In their new cycles, couples who accepted the technique over DGC group. The number of blastocysts per mature oocyte (M2) (1.62 ± 1.47 vs. 0.87 ± 1.36 < 0.001) was significantly higher in the MSS group than DGC. The number of blastocysts per mature oocyte (M2) (0.62 ± 0.25 vs. 0.43 ± 0.34 p:0.01) was also significantly higher in the MSS group compared to the DGC group.

CONCLUSIONS: MSS technique increases blastulation rates however it does not improve euploidy and LB rates compared to DGC in couples with high SDF and RIF.

IMPACT STATEMENT: MSS provides a higher number of top-quality blastocysts when compared to DGC. However, unaltered euploidy and LB rates may require further evaluation. Studies focusing on confounding factors to embryonic genomic status in the presence of high SDF are needed.

<table>
<thead>
<tr>
<th></th>
<th>DGC</th>
<th>MSS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of LB / OPU in 1. cycle (%)</td>
<td>48/151 (31.7)</td>
<td>39/92 (42.4)</td>
<td>0.09</td>
</tr>
<tr>
<td>No of LB in subsequent cycles</td>
<td>15/40 (37.5)</td>
<td>10/29 (34.4)</td>
<td>0.8</td>
</tr>
<tr>
<td>Cumulative LB per aspirated cycle (%)</td>
<td>63/151 (41.7)</td>
<td>49/92 (53.2)</td>
<td>0.08</td>
</tr>
<tr>
<td>Clinical Miscarriage per aspirated cycle (%)</td>
<td>13 (8.6)</td>
<td>9 (9.7)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

P-103 6:30 AM Monday, October 24, 2022

DOUBLE HOMOLOGOUS IUI WITH COMBINATION OF TWO SPERM PREPARATION METHOD IMPROVES SUCCESS RATE IN IUI CYCLES. C Jyothi Budhi, M.B.B.S. 4 Charulata Chatterjee, phd 4 Direcor, Secunderabad, India; 1Scientific Head and Consultant Embryologist, Secunderabad, India.

OBJECTIVE: This study aims to evaluate the single Vs double IUI in controlled ovarian stimulation cycle –COH and to evaluate the effects of combining two methods on improving the efficacy of sperm preparation.

MATERIALS AND METHODS: It is a Retrospective study done at our center. 1041 couples undergoing COH for an IUI cycle within twelve months were included in this study. The primary outcome measure was clinical pregnancy.

Inclusion criteria for women were age below 35 years with functional Fallopian tube/s and no other noted uterine or ovarian abnormalities. Men with post-wash total motile sperm count of at least 10 million were included in the study. All women underwent COH and ovulation tracking was done with ultra sound scan. Insemination were performed either once or twice depending upon ovulation status and as decided earlier with couples. In case of double IUI density gradient processed sperm were inseminated in pre ovulatory phase and phases were processed through swim up technique and then inseminated after ovulation.

RESULTS: Out of 1041, three couples dropped the treatment in between due to personal reason and 512 couple underwent double IUI where as 526 couple single IUI was done. The overall clinical pregnancy rate was 16% and 11% [p= 0.001] for double Vs single IUI respectively.

CONCLUSIONS: A combination of two sperm preparation methods resulted in higher recovery rates of mature motile spermatozoa and helped to improve success rate. A large group study is recommended to support this observation.

IMPACT STATEMENT: Intra Uterine Insemination- [IUI] is preferred fertilization treatment for unexplained and moderate male factor sub fertility. Incorporation of double insemination and two sperm preparation method (double density gradient and swim up) might help to improve outcome.

SUPORT: not funded by any one.

A SIMPLE IN VITRO INCUBATION OF A SPERM SAMPLE WITH MYO-INOSITOL CAN HELP PREDICT THE CLINICAL OUTCOMES OF AN ICSI CYCLE. Patrizia Rubino, MS. 3 Katlin A. Doody, MD. 4 James Patrick Toner, MD, 2 Caroline Moon, BS. 2, Kohar Mazmanian, M.S., 3 Lisa Guan, B.A., 3 Riccardo Gambioli, MS. 3 Vittorio Unfer, MS. 3 Tih Tan, MS 4 HRC Pasadena, Pasadena, CA; 2 Keck School of Medicine, University of Southern California; 3 Emory School of Medicine, GA; 4 HRC Fertility - Pasadena, Pasadena, CA; 5 Lo.Li.Pharma, Roma, Italy.

OBJECTIVE: Paternal mitochondria are selectively degraded in the zygote and should not affect embryo development. However, it is known that reactive oxygen species (ROS) damage the mitochondrial membrane. Myo-inositol (MI) is thought to improve sperm mitochondrial function in vitro by raising the mitochondrial membrane potential (MMP). This is associated with an increase in prospective motility (PM). Post incubation with MI, sperm samples with minimal change in PM (low responders - increase of PM 0%-30%) are considered having high MMP, while medium and high responders (increase of PM 31%-60% and 61%-100% respectively) are considered having lower MMP.

The purpose of this study was to evaluate if the sperm sample’s response in vitro to MI can be predictive of clinical outcomes of an ICSI cycle.

MATERIALS AND METHODS: Prospective experimental study (NCT03677011) involving couples with female age ≤ 35 undergoing an ICSI cycle with preimplantation genetic diagnosis for aneuploidies (PGT-A). On the day of ICSI, 0.5-1ml of the sperm sample was incubated for 30 min with a 2mg/ml solution of MI (Andrositol® test, Lo.Li.Pharma, Rome). PM changes were evaluated by computer assisted sperm analysis and sperm samples were classified as low, medium or high responders. Male partners with a sperm volume ≤ 1 ml, a sperm count ≤ 5 X 10^6/ml and a total sperm motility ≤ 10% were excluded from the study. All patients were consulted and the study was approved by the WGC IRB.

Primary outcome was the Fertilization rate (FR). Secondary outcomes were blastocyst formation rate (BR), euploidy rate (ER), embryo implantation rate (IR) and abortion rate (AR).

To demonstrate the superiority of group 1 (low responders) versus group 2 (medium and high responders) samples for FR, based on a maximum absolute increment of 10% with a standard deviation of 30%, a power of 80% and a confidence of 95% a minimum of 112 cycles per group were required. Considering a mean FR of 70% the higher confidence limit was ≥ 80%.

RESULTS: All cycles were freeze all PGT-A cycles. IRRs were calculated on subsequent frozen embryo transfers (FET). A total of 272 cycles were enrolled, 23 were excluded because they did not meet the inclusion criteria, 137 samples were low responders (group 1), 112 were medium and high responders (group 2). Female age, number of oocytes retrieved, FR, ER, IR and AR were similar between group 1 and 2 (31.8±3.0 vs 31.7±4.2, 12.2±5.5 vs 12.0±5.6, 30.8% vs 80.6%, 51.2% vs 46.6%, 65.7% vs 66.1%, 16% vs 15% respectively). The BR was significantly higher in group 1 (66.1% vs 61.0% p=0.02). There was also a significantly higher number of cycles with no euploid embryos available for transfer in group 2 (24% vs 12% p=0.01).

CONCLUSIONS: Cycles where sperm samples were classified as euploid and medium responder (low MMP) showed a significantly lower BR and a tenfold increase in duration of transfer period compared to high MMP (4.7 days vs 5.9 days) leading to a significant difference in clinical outcomes. The Andrositol® test has been shown effective in identifying compromised sperm samples.

SUPPORT: Lo.Li.Pharma.
OBJECTIVE: The oxygen consumption rate (OCR) of individual human oocytes can be measured by a novel metabolic microsensor, and used to assess oocyte aerobic metabolism. Such a noninvasive assay may be valuable to assess human oocyte competence in clinical settings. Here, we examined the impact of maternal body mass index (BMI) and age on the OCR of metaphase II (MII) stage human oocytes. Our objective was to determine whether maternal BMI and age impact the human oocyte metabolic activities, and evaluate the feasibility of using the novel microsensors to noninvasively evaluate oocyte competence.

MATERIALS AND METHODS: Following routine ovarian stimulation and oocyte retrieval, immature oocytes at the germinal vesicle (GV) stage were vitrified and stored in liquid nitrogen and used for research with IRB approval (WCG IRB#: 20142468). The oocytes were warmed and placed into in-house made Oocyte Handling Medium for Maturation (OHM-Mat) for 27-30 h. Oocytes reached to MII stage were individually evaluated using an electrochemical microsensor platform at 37 °C for 30 minutes in a sealed microfluidic chamber. OCR were obtained from each oocyte and comparisons were made between normal weight (NW; n = 12) BMI between 18.5 to 25 and overweight (OW, n = 10, BMI > 25) patients as well as age reported by the patients. Categorical data were analyzed using Student’s t-test and Pearson correlation test. Data are presented as mean ± standard deviation.

RESULTS: Oocyte OCR in OW was higher than that of oocytes in NW (6.88 ± 2.52 vs. 3.38 ± 0.87 fmoles s⁻¹/oocyte, P < 0.001). Maternal age did not affect oocyte OCR for combined groups (r = 0.22, P = 0.34) or for NW (r = -0.14, P = 0.66); however, OCR was negatively associated with OW patient age (r = -0.72, P < 0.02).

CONCLUSIONS: Oocytes from overweight donors have an approximately 50% higher oxygen consumption rate when compared to oocytes from normal-weight donors, indicating differences in aerobic metabolism. Although maternal age did not affect the OCR of oocytes from NW women, the OCR of oocytes from overweight donors decreased with increasing maternal age.

IMPACT STATEMENT: The use of a novel microsensor provides new opportunities to assess how maternal factors impact oocyte metabolism. OCR, based on the measurement from individual human oocytes, may provide useful insight into the relationships among maternal BMI and age and oocyte metabolic activity. This novel device also provides opportunities to examine other parameters that may impact patient IVF outcomes.

P-105 6:30 AM Monday, October 24, 2022
A NON-COMMERCIAL WITNESSING SYSTEM: A JOURNEY TO CREATE A BAR CODE SYSTEM FROM DISH LABELS TO MICROSCOPIC BAR CODES NEXT TO THE EMBRYO. Oscar Perez, Ph.D.1, Hannalie H. Adriaanse, B.S.1, Gabriella Navarrete, B.S.1, Linda Lay, B.S.1, Breanna Tilley, MSc.1, Jessica Kozlowski, B.S.C.2, Ravi Gada, M.D.2, Samuel J. Chantilis, M.D.1, Dallas Fertility Center, Dallas, TX;2Dallas Fort Worth Fertility Associates, Dallas, TX.

OBJECTIVE: The complexity of the procedures in the IVF laboratory requires a witnessing system to decrease the risk of human errors. Current quality control practices include a second person in a double witnessing protocol in gamete collection, insemination, and embryo transfer procedures. Commercial electronic witnessing systems have provided an alternative option for increasing the security level of matching samples in the laboratory; however, blastocyst biopsy, cell loading, and individual embryo freezing have not been covered entirely due to the complexity of the microscopic level. The objective of this study was to create a non-commercial wireless witnessing system (DFC-WS).

MATERIALS AND METHODS: A software engineer helped to create a witnessing software, a witnessing server database, and wireless connectivity. A bar code system was added to the software. The tools to complete the scanning consisted of bar code readers, tablets, label printers, and paper and plastic labels for scanning laboratory procedures, such as tubes, charts, dishes, and cryopreservation labels, and lately, a laser system to create a microscopic bar code labels on the plastic dishes.

The andrology laboratory initiated the complexity of the electronic witness system. Andrologists needed a short time to become familiar with this introductory witnessing system. The following steps consisted of the oocyte retrieval procedures matching patient ID, dishes, and ultimately matching the sperm (Tube) and oocytes (dish). The evaluated event’s purpose consisted of matching samples. The witness system covered andrology and the IVF procedures. Recently, FET procedures were covered by scanning bar codes of the embryologist names to verify freezing straws before thawing. The last procedure was the frozen embryo transfer. The patient ID, embryos, and dishes were covered wireless. A commercial laser system was an alternative to help match individual embryos and cells for biopsy and freezing purposes. It could create microscopic barcodes for the biopsy, cell loading and freeze directly on the plastic dishes.

RESULTS: The witnessing software recorded the time of each scanning process, the confirmation of matching events, and ultimately, the completion of procedures. The system was prepared to detect errors and interrupt the process in case of mismatching. Since establishing the DFC-WS, no mismatching errors were detected in the andrology and IVF laboratories. A barcode reader detected microscopic bar codes of at least 20 microns and transmitted and matched the information of individual embryos and cells in the working dish. Creating a bar code witnessing system is cheaper than the ones available in the IVF market.

CONCLUSIONS: Introducing a witnessing system provides a high-security level of traceability and confidence between the matching events in the andrology and IVF laboratories. Patient care is improving with a high level of security between laboratory procedures.

IMPACT STATEMENT: A witnessing system should be incorporated into the protocols of IVF laboratories. Its implementation minimizes adverse mismatching events.

COMMENTS

P-106 6:30 AM Monday, October 24, 2022
HOW MANY CLONES WILL BE OBTAINED FROM A SPERM? Laura Escrich, PhD.1, Aitor Galbete Urrutia, B.Sc.1, Andrea Oller, B.Sc.1, Rosa Bautista-Llacer, B.Sc.1, Xavier Vendrell, PhD.2, Maria Jose Escriba Perez, PhD.1, Noelia Grau, PhD.1, IVIIRMA Valencia, Valencia, Spain;2Instituto de Investigación Sanitaria La Fe, Valencia, Spain; Sistemas Genómicos; Sistemas Genómicos; IVIIRMA-Valencia, Valencia, Spain.

OBJECTIVE: To determine the number of sperm clones (or androcytes) that does not compromise the chromosomal stability.

MATERIALS AND METHODS: The androgenote is a biological construct, unipaternal in origin (from a genetic point of view), generated in brief by the MII enucleation and subsequent intracytoplasmic sperm microinjection. After 16-20h culture, the androgenote was assessed by in brief by the MII enucleation and subsequent intracytoplasmic sperm microinjection. After 16-20h culture, the androgenote was assessed by

RESULTS: This study included 8 androgenotes; NGS results were obtained by in brief by the MII enucleation and subsequent intracytoplasmic sperm microinjection. After 16-20h culture, the androgenote was assessed by

COMMENTS

Androgenotes were cultured until day 3. Then, constituent cells, onward called androcytes, were isolated and counted; one androcyte was studied for 5-chromosome (13, 18, 21, X, Y) by FISH, to determine ploidy (i.e., haploid =23X or 23Y- or diploid); remaining sister androcytes were individually tested for 24-chromosome aneuploid by NGS.

Retrospective analysis of all sister androcytes, informed us on euploid or aneuploid; the proportion of each informs on uniformity or mosaicism intra androgenote. These variables were related to number of androcytes which were checked for normality, and analyzed by a t-test.

RESULTS: This study included 8 androgenotes; NGS results were obtained in 71 out of 76 androcytes. Three androgenotes were uniform euploid (37.5%) and 5 were mosaic, as formed by euploid/aneuploid androgenotes; three androgenotes had euploid / compensatory aneuploid androgenotes and two androgenotes had euploid / different aneuploidies androcytes. No uniform or mosaic aneuploid androgenotes were observed.

Euploid androgenotes had fewer aneuploid than mosaic ones (8.3±0.3 aneuploids; 95CI: 6.9-9.8 vs. 11.4±0.9 aneuploids; 95CI: 9-13.8; p=0.04)

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CONCLUSIONS: Under a haploid unipaternal condition, the chromosome stability is strongly dependent on the number of androcytes, limiting the number of sperm clones to eight. Since no uniform / mosaic aneuploid androgenotes were observed, the origin of aneuploidies might be mitotic in origin.

IMPACT STATEMENT: Our proof-of-concept studies on the androgenote model, to define the number of mitosis that does not compromise the chromosome stability intra androgenote is critical. This study defines that the number of chromosomally stable sperm clones or androcytes might be eight.

P-107 6:30 AM Monday, October 24, 2022

URINARY E3G MONITORING WITH THE MIRA FERTILITY TRACKER DURING COH AS AN ALTERNATIVE TO SERUM E2. Gary S. Nakhuda, MD,1 Ning Li, MS,2 Zheng Yang, Ph.D.,2 Sylvia M. Kang, MS MBA2 1Olive Fertility Centre, Vancouver, BC, Canada; 2Quanovate Tech Inc., San Ramon, CA.

OBJECTIVE: A commercially available, direct to consumer, FDA-registered device called the Mira Fertility Tracker (“Mira”), measures quantitative urinary hormone levels via immunofluorescence for ovulation monitoring with a comparable accuracy to clinical immunanlyzers.

While Mira is marketed for use in physiological cycles, the ability to quantify estrone 3-glucuronide (E3G), the urinary metabolite of estradiol (E2), may provide an alternative to serum E2 measurements during IVF.

MATERIALS AND METHODS: A prospective, observational pilot study of patients undergoing superovulation for IVF or oocyte cryopreservation was performed. Inclusion criteria required an AMH of 1-3.5 ng/ml and use of an antagonist protocol. Patients were provided with the Mira device and test wands and were asked to test their first morning urine each day of stimulation. Management decisions during were based solely on routine clinical population. Management decisions during were based solely on routine clinical parameters, not uE3G results. Typically, the first serum E2 was assessed on day 6 of stimulation, with subsequent blood samples and ultrasounds performed as necessary.

Analysis was performed with scatter plots of uE3G and E2 to examine trends during stimulation, and a joint distribution map of uE3G and E2 was created. Spearman correlation of daily uE3G and E2.

RESULTS: Results for 22 patients were analyzed. Mean values for the following parameters were as follows:

- Age: 37.0 years (29-43, SD 3.9)
- Days of stimulation: 8.9 (8-11, SD 1.1)
- uE3G samples/patient: 8.7 (5-11, SD 1.8)
- E2 samples/patient: 3.1 (2-4, SD 0.7)
- Scatter plots of uE3G/day and E2/day displayed a monotonically increasing pattern, as did the pairwise uE3G vs E2 scatter plot.

The result regression equation was as follows: $E2 = -161.85 + 6.11[uE3G]$. The Spearman correlation between pairwise uE3G & E2 was calculated as 0.82.

CONCLUSIONS: The uE3G dynamics were comparable to that of serum E2 with a Spearman correlation of 0.82. Thus, at-home urine monitoring of uE3G is a viable alternative to serum E2 measurements during COH that is potentially more patient friendly and convenient. Further studies are required for additional validation in the general IVF population.

IMPACT STATEMENT: U3G is a potential alternative to serum E2 testing during IVF.

P-108 6:30 AM Monday, October 24, 2022

EARLY PREGNANCY OUTCOMES IN A HORMONE REPLACEMENT THERAPY AND NATURAL CYCLE FROZEN EMBRYO TRANSFER FOLLOWING IN-VITRO FERTILIZATION TREATMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS. Marika Raff, MD,1 Emily A. Jacobs, MD,2 Karen M. Summers, MPH CHES,2 Patrick Ten Eyck, MS PhD,2 Amy E. Sparks, PhD,3 Bradley J. Van Voorhis, MD,2 Abey Eappen, M.B.B.S., PH.D.3 1University of Iowa Carver College of Medicine, Iowa City, IA; 2University of Iowa College of Medicine, Iowa City, IA; 3University of Iowa Center for Advanced Reproductive Care, Iowa City, IA; 4University of Iowa Carver College of Medicine, Iowa City, IA; 5UT Southwestern Dallas, Dallas, TX.

OBJECTIVE: To synthesize results of studies analyzing outcomes in early pregnancy using hormone replacement therapy (HRT) and natural cycle (NC) protocols in IVF frozen embryo transfers (FET).

MATERIALS AND METHODS: Data Sources: PubMed, Cochrane registry, Embase, Scopus, and Web of Science were searched through Jan 10, 2022: Search Terms: (natural OR stimulated OR hormone OR modified OR artificial) AND (frozen OR thawed OR vitrified OR warmed OR cryopreserved) AND embryo transfer AND transfer. Study Selection: We included observational cohort studies with data for early pregnancy outcomes following IVF frozen embryo transfer utilizing hormone replacement therapy and natural cycle. Data Extraction and Synthesis: Three reviewers independently extracted data on relevant baseline characteristics and clinical outcomes and used NIH criteria for quality assessment. Outcomes: Miscarriage rate, implantation rate, clinical pregnancy rate, live birth rate. Methods: Meta-analyses for comparisons of proportions were performed using the R functions metacon and meta, respectively, from the meta package (https://cran.r-project.org/web/packages/meta/index.html). Composite estimates for odds ratios (OR) and their 95% confidence intervals (CI) were calculated for outcomes in each study and used the random effects weights for calculating the aggregate statistics. Further, we performed subgroup analysis based on euploidy status of the embryo. Statistics for the heterogeneity of each set of studies are included in each plot. Forest, funnel, and meta-regression plots were produced comparing differences of maternal outcomes, age, and BMI between HRT and NC treatments. Meta-analysis of outcomes set of studies. The forest plots summarize group statistics with counts, means, and standard deviations.

RESULTS: Seventy-two studies met inclusion criteria for the combined analysis of outcomes of interest in our study. For the primary outcome of miscarriage rate, 63,036 women who underwent HRT-FET and 42,628 who underwent NC-FET were included. Pooled data suggested that the miscarriage rate in women undergoing HRT-FET was significantly higher than in those undergoing NC-FET, OR (95% CI) 1.3 (1.1-1.5). We also observed a significant reduction in live birth rate [0.8 (0.8-0.9)] in women undergoing HRT-FET.

CONCLUSIONS: In this systematic review and meta-analysis of women undergoing frozen embryo transfer following IVF treatment, there was a significant increase in miscarriage rate and a significant decrease in live birth rate in a hormone replacement therapy cycle compared to a natural cycle FET.

IMPACT STATEMENT: The use of HRT has increased over the past decade with improvements in technology and live birth rates. Frozen embryo transfers are commonly performed in a hormone replacement therapy cycle, where there is an absence of corpus luteal function and suppression of relaxin and vascular endothelial growth factor. This may result in dysfunction of the endometrium, leading to sub-optimal early pregnancy outcomes. The use of natural cycle FET may improve early pregnancy outcomes following IVF treatment.

P-109 6:30 AM Monday, October 24, 2022

IS THERE AN INFLUENCE OF RECIPIENT AGE IN OOCYTE DONATION CYCLES OUTCOMES AFTER CONSTANT OR INCREASING ESTROGEN DOSE FOR ENDOMETRIAL PREPARATION? Gabriella Mamede Andrade, PhD1, Adriana Bos-Mikich, PhD,2 Fernanda KUNRATH, Robin, Master Nursing,1 Carolina Lumentz Martellos, Ms,1 Luiza Mezzomo Donatti, Master,1 Marília Korbes Rockenbach, Biomedicine degree,4 Nilo Frantz, M.D.1 1Nilo Frantz Reproductive Medicine; 2Federal University of Rio Grande do Sul; 3Nilo Frantz Reproductive Medicine; 4Nilo Frantz Medicina Reprodutiva, Porto Alegre, Brazil.

OBJECTIVE: Endometrial preparation is a key factor for successful ART outcomes, particularly in oocyte donation (OD) cycles. Estrogen (E2) administration may follow different protocols, including E2 constant dose (CD) or increasing dose (ID), implying in differences on endometrial preparation and receptivity. Until now, no study has considered the recipient age effect on OD cycles success following CD or ID E2 administration. The objective of the present study is to investigate possible differences OD cycles outcomes after CD or ID endometrial preparation taking into consideration the recipients’ age.
MATERIALS AND METHODS: A total of 220 OD cycles from 2018 to 2020 were retrospectively included in the study. Cycles were divided in two groups according to CD_E2 administration, CD_E2 group (n=144) and ID_E2 group (n=76). CD_E2 recipients received 6mg/day and ID_E2 recipients started with 3mg/day and increased to 6mg/day, due to insufficient endometrial response with 6 mg/day. These groups were split into three age categories (≤39, 40-44 and ≥45 years old). Outcomes in terms of positive beta human chorionic gonadotropin test (h-hCG)+, clinical pregnancy, delivery and miscarriage rates were compared among groups by Fisher’s exact test using Graphpad Prism. P value ≤ 0.05 was considered significant.

RESULTS: Overall CD_E2 patients presented a significantly higher h-hCG+ rate (65.5%) when compared with ID_E2 recipients (44.7%), p=0.0041. Clinical pregnancy, delivery and miscarriage rates did not present any significant differences. Among the age groups, was observed a significant increase in h-hCG+ for patients aged ≥45 years old in CD_E2 (p=0.05), compared with ID_E2 patients (64.8% vs 40%, respectively). Non-significant differences were observed among all age groups for clinical pregnancy, delivery and miscarriage rates.

CONCLUSIONS: Previous reports demonstrated that recipient age exerts a deleterious impact on pregnancy rates, an effect possibly related to an endometrial aging process. Constant dose of E2 administration seems to have a positive effect on pregnancy establishment for patients aged ≥45 years in OD cycles. Therefore, recipient age should be taken into account when choosing the endometrial preparation protocol in those cases.

IMPACT STATEMENT: Positive human chorionic gonadotropin test rate is higher in older patients under estrogen constant dose, compared with increasing dose protocol. Based on that, the patient age must be taken into consideration when choosing the endometrial preparation protocol, particularly in oocyte donation cycles.

SUPPORT: This study was financially supported by Nilo Frantz Reproductive Medicine.

E-POTER ABSTRACT SESSION: 12

P-111 6:30 AM Monday, October 24, 2022

ARTIFICIAL INTELLIGENCE FOR INTRAUTERINE INSEMINATION AND TIMED INTERCOURSE.

Almog Luz, B.SC.,1 Rohi Hoveritz, B.SC.,2 Ariel Hoveritz, M.D.,3 Micha Baum, M.D.,1 Ettie Maman, M.D.1,3 Tel-Aviv, Israel;1 FertilAI, Israel; 1IVF Unit Shamir Medical Center, Israel; 3Sheba Medical Center, Israel; 2Sheba Medical Center, Ramat Gan, Tel Aviv, Israel.

OBJECTIVE: The aim of the study is to investigate whether artificial intelligence (AI) can support physician decision for optimizing the timing for intra uterine insemination (IUI) or intercourse in spontaneous cycles.

MATERIALS AND METHODS: The dataset consist of 2041 natural cycles (NC) for frozen embryo transfers with complete data for at least 2 visits including women age and hormonal levels (Estrogen, Progesterone and LH) for each visit. The data was taken from a lab serving 50 different physicians, each with his/her own practice. Ovulation date was calculated by the treating physician decision. The dataset was split to train, validation, and test sets. For the test set, all charts were reviewed by two independent experts, who determined ovulation date independently of the treating physician to achieve the best prediction model.

Two algorithms were trained as part of the study: 1. An NGBoost machine learning (ML) model that estimates the probability of ovulation occurring in each cycle day based on the available cycle visits data.

2. A treatment management state machine algorithm that uses the ML model after receiving a new visit’s data to determine if an optimal insemination day can be returned, or another blood test should be performed, in which case the optimal day to perform the additional test is supplied. Failures were split to two types:

1. A “Miss” was defined as the algorithm declaring it missed the insemination window defined as -1 and -2 relative to the ovulation (day 0).

2. An “Error” was defined as the algorithm supplying an insemination date that isn’t within the insemination window.

Both algorithms were jointly tuned to minimize failures under an average test days restriction of 3 days.

RESULTS: The treatment management algorithm declared a miss in 5.2% of cases, and provided an accurate prediction within the insemination window in 95.3% of the remaining cases, the prediction was made in days -4 (1%), -3 (33%), -2 (40%) and -1 (26%) relative to the ovulation. It took an average of 2.95 test days to reach a prediction.

CONCLUSIONS: To the best of our knowledge, this is the first AI algorithm designed to predict ovulation based on blood tests. According to our results the ovulation prediction model was able to predict accurately the “insemination window” in 95.3% of the cases with 5.2% miss rate, we believe those stats can be further improved by using the patient average cycle length.

IMPACT STATEMENT: Timing intercourse or IUI during spontaneous cycle is a challenge for many women trying to conceive. We expect that introducing the capabilities of AI into the management of spontaneous cycle follow-up will enable both women trying to conceive spontaneously and treating physician to improve accuracy and efficiency of ovulation prediction and accordingly increase the chance of conception and fertility control in these cycles.

P-112 6:30 AM Monday, October 24, 2022

SEGMENTATION-BASED CLASSIFICATION OF HUMAN BLASTOCYST USING DEEP LEARNING.

Elena Paya Bosch, Ph.D. Student,1 Alejandro Vergara, B.S.,2 Lorena Bori Arnal, PhD Student,1 Fernando Meseguer Estornell, M.S.,3 Valery Naranjo, Ph.D.,4 Marcos Meseguer, Ph.D.1 IVIRMA Global, Valencia, Spain; 3Universitat Politècnica de València; 4IVIRMA Global, Valencia, Spain; 2Universitat Politècnica de València, Valencia, Spain.
OBJECTIVE: This work aimed to build an automatic system with Geri® time-lapse images for evaluating blastocyst morphology based on deep learning algorithms. Also, we studied to what extent the models emulate the skill of a trained specialist through the influence of segmentation of blastocyst structures.

MATERIALS AND METHODS: We developed a single-center retrospective study to automate embryo evaluation with different approaches. The database consisted of 375 images at 111.5 hours post-insemination (hpi). There are 129 with 928 × 928 and 246 with a size of 1440 × 1440, all acquired with Geri® technology. Images were divided into three classes depending on the quality of the embryo according to ASEBIR criteria (A = high; B = medium, and C = low-quality). The segmentation ground truth was prepared using a pixel-level annotation in four classes: background, TE, ICM, and blastocoele.

Our goal is to develop a semantic segmentation model and a classification model using the segmented images and compare the results with a classification model with the raw data. In this way, we could study the influence of the blastocyst structures in the final decision: (1) We trained a U-Net architecture for the segmentation task. The convolutional encoder part extracts features from input images to capture context and reduces dimensionality. The decoder reconstructed images assigning a label to each pixel. (2) We used the pre-trained Xception to train a segmentation-based classification model. The input consisted of four images from each structure of the blastocyst. (3) We trained a conventional classification model without morphology information.

RESULTS: The metrics used to evaluate the system performance were precision, recall, and accuracy. Segmentation-based classification model obtained values of 0.71, 0.70, and 0.70, respectively. Conventional classification model achieved values of 0.6, 0.58, and 0.63, respectively. In addition, we calculated the Dice and Jaccard metrics that evaluate the performance of the segmentation model by comparing the similarity between images and obtained values of 0.99 and 0.98, respectively.

CONCLUSIONS: The proposed segmentation model applied by first time on Geri® time-lapse images outperforms the state-of-the-art studies, and the need to add structure information to the model was corroborated. We can conclude that deep learning algorithms analyze blastocyst as a trained specialist, giving a score to each part. Our system achieved promising results; therefore, it could be a valuable tool for supporting embryologists by providing objectivity to embryo selection and considerable time reduction.

IMPACT STATEMENT: This study demonstrated that frozen euploid transfers with between 0 and 9 laser pulses were all concordant, albeit chaotic due to the karyotype of the cell line.

CONCLUSIONS: This novel biopsy system provides an alternative to laser-based embryo biopsy which is faster, easier to learn, and less expensive than conventional biopsy. The PGT-A results after re-biopsy with the novel biopsy system revealed fewer abnormalities in 8/23 embryos when compared to the initial conventional biopsy. More embryos will need to be biopsied and analysed to confirm these findings in a larger cohort.

IMPACT STATEMENT: PGT-A is a widely accepted method for reducing time to pregnancy, the miscarriage rate and the risk of genetic disorders in offspring. Our laser-free novel biopsy system provides a simpler, potentially safer and more accurate alternative to conventional embryo biopsy.
WHAT 400 REBIONPSIED EMBRYOS SHOW US: TECHNICAL AND CLINICAL OUTCOMES. María DEL MAR NOHALES Córcoles, PhD,1 Pilar Campos, Embryologist,2 Maria Fernanda Insua, PhD,3 Marcos Meseguer, PhD,4 Diana Beltrán, Master,5 Arantzazu Delgado Mendive, PhD5 1IVIRMA VALENCIA, Valencia, Spain; 2IVIRMA VALENCIA, Valencia, Spain; 3IVIRMA Valencia, Valencia, Valencia, Spain; 4IVIRMA Global, Valencia, Spain; 5IVIRMA Valencia, Valencia, Valencia, Spain.

OBJECTIVE: To evaluate the real impact of the rebiopsy in terms of survival, efficiency and clinical outcomes in embryos with a first inconclusive result after the trophectoderm biopsy.

MATERIALS AND METHODS: This retrospective study analyses in a total of 400 blastocysts the impact of a second biopsy and an extra round of vitrification in blastocysts with an inconclusive chromosomal assessment after trophectoderm biopsy in a private IVF center from 2016 to 2021. Embryos that were rebiopsied were further classified as euploid, mosaic, abnormal or inconclusive. Clinical outcomes of the embryos rebiopsied were compared to the ones of the embryos with a diagnostic yielded in the first round of biopsy. χ² tests were performed and P<0.05 was considered statistically significant.

RESULTS: From 5171 PGT-A cycles, 517 embryos had an inconclusive result (2.87% of the overall embryos biopsied). Four-hundred blastocysts survived intact to the warming procedure, reexpanded and had quality enough to be biopsied and analyzed in a second round (N=400/517; survivor rebiopsied blastocysts: 77.37%). A successful diagnosis was obtained in 384 of the rebiopsied embryos (92.2%); 374/384 (97.4%) of these embryos were diagnosed as euploid embryos. A lack of diagnosis was obtained in 34 of the reanalyzed blastocysts. However, still a percentage of embryos had a repeated lack of diagnosis in this second round (4%, N=16/400). Finally, just 0.09% of the initial biopsied embryos had “no diagnosis” (N=16/18028). The following data was obtained:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group 1 (n=66)</th>
<th>Group 2 (n=229)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at retrieval, years</td>
<td>32.6 (4.0)</td>
<td>35.8 (4.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Blastocyst survival at TBR</td>
<td>333/361 (92.2%)</td>
<td>410/416 (98.6%)</td>
<td>0.79</td>
</tr>
<tr>
<td>Blastocyst survival at transfer</td>
<td>76/77 (98.7%)</td>
<td>410/416 (98.6%)</td>
<td></td>
</tr>
<tr>
<td>Transfers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total transfers</td>
<td>71</td>
<td>392</td>
<td></td>
</tr>
<tr>
<td>Total per patient</td>
<td>1.08 (0.8)</td>
<td>1.71 (0.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Embryos per transfer</td>
<td>1.07 (0.3)</td>
<td>1.05 (0.2)</td>
<td>0.45</td>
</tr>
<tr>
<td>Outcomes per transfer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biochemical pregnancy rate, n (%)</td>
<td>46 (64.8)</td>
<td>240 (61.2)</td>
<td>0.57</td>
</tr>
<tr>
<td>Clinical pregnancy rate, n (%)</td>
<td>41 (57.7)</td>
<td>191 (48.7)</td>
<td>0.16</td>
</tr>
<tr>
<td>Live birth or ongoing pregnancy rate, n (%)</td>
<td>36 (50.7)</td>
<td>162 (41.3)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

OUTCOMES PER TRANSFER

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group 1 (n=66)</th>
<th>Group 2 (n=229)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biochemical pregnancy rate, n (%)</td>
<td>39 (79.6)</td>
<td>174 (76.0)</td>
<td>0.59</td>
</tr>
<tr>
<td>Clinical pregnancy rate, n (%)</td>
<td>35 (71.4)</td>
<td>146 (63.8)</td>
<td>0.31</td>
</tr>
<tr>
<td>Live birth or ongoing pregnancy rate, n (%)</td>
<td>32 (65.3)</td>
<td>132 (57.6)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

* Values are in means (standard deviation) unless stated otherwise.

CONCLUSIONS: Rebiopsy of blastocysts with inconclusive results increases the yield of embryos available for transfer therefore it can be considered a valid approach to offer to the patients. Still a percentage of embryos will have a lack of diagnosis due to the IVF laboratory procedures or inherent to the genetic platform. Even though the limited number of cases does not allow to draw conclusions, the implantation ability of the rebiopsied blastocysts could be compromised or, at least, penalized.

IMPACT STATEMENT: Even if our results exhibit lower clinical outcomes than those obtained in the embryos biopsied once, the rebiopsy of undiagnosed blastocyst shows that the majority are euploid embryos and they contribute to increase the cumulative live birth.

SUPPORT: None

P-115 6:30 AM Monday, October 24, 2022

MEDIA DROP NON-INVASIVE PGT-A AS AN ALTERNATIVE TO BLASTOCYST RE-BIOPSY. Kalyn Trowbridge, BS,1 Blair R. McCallie, PhD,2 Jason C. Parks, PhD,3 Laura Reed, BS,3 Rachel Makloski, RN,4 William B. Schoolcraft, MD,5 Mandy Katz-Jaffe, PhD6 1Castle Rock, CO; 2CCRM Genetics, Lone Tree, CO; 3CCRM Genetics, Lone Tree, CO; 4Lone Tree, CO.

OBJECTIVE: Current methods for the re-testing of no result PGT-A embryos require a second biopsy of additional TE cells. However, the biopsy of excessive TE cells (≥10) has been shown to have an adverse impact on embryonic developmental competence and the probability of achieving a live birth. The aim of this study was to develop a non-invasive alternative to blastocyst re-biopsy for PGT-A no results seeking re-testing.

MATERIALS AND METHODS: Surplus cryopreserved PGT-A tested blastocysts (n=50) were donated with patient consent for protocol validation.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group 1</th>
<th>Group 2</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First round of biopsy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transferable blastocysts (euploids + mosas)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscarriage rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live birth rate</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome</th>
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<tr>
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</tr>
<tr>
<td>Pregnancy rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscarriage rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live birth rate</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS: The use of an alternative non-invasive technique to re-test PGT-A embryos could be a valid approach for patients who seek a new attempt at pregnancy without the need for a second biopsy of additional TE cells.
Following successful validation, infertility patients were consented under an approved IRB protocol to perform media drop PGT-A on no result embryos (n=49). Blastocysts were warmed and cultured for 7-8 hours prior to collection and processing of the media drop for PGT-A (VeriSeq™ Vitrolife). In total, 25 clinical, media drop, no result PGT-A cases have been performed with 23 (92%) resulting in DNA amplification and a PGT-A result. Of these 23 media drop samples with PGT-A results, 11 were euploid and 12 euploid. To date, there have been two frozen embryo transfers, both resulting in clinical pregnancies with fetal heart tone, one currently in the first trimester and the other mid-gestation.

CONCLUSIONS: Media drop PGT-A is a non-invasive, reliable and reproducible protocol for re-testing of no result embryos. Our clinical data demonstrates that cell-free DNA is present in media drops following embryo culture and can be utilized for PGT-A as a non-invasive alternative to re-biopsy. Avoiding the removal of additional TE cells that otherwise may have impacted future developmental competence, allows for the embryo to have the best opportunity for implantation and establishing a viable clinical pregnancy.

IMPACT STATEMENT: A non-invasive approach to re-testing of no result embryos successfully avoids a second biopsy and allows for PGT-A results to be obtained and the best possible chance of implantation.

SUPPORT: None

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**P-117** 6:30 AM Monday, October 24, 2022

**BIOSPY TECHNIQUE, DAY OF EMBRYO BIOPSY AND BLASTOCYST STAGE ARE ASSOCIATED WITH THE RISK OF INCONCLUSIVE CHROMOSOMAL ASSESSMENT AFTER EMBRYO BIOPSY: ANALYSIS OF 18028 Biopsied Blastocysts, Maria DEL MAR NOHALES Córcoles, PhD,1 Aila Coello, PhD,2 Angel Martin Bastida, M.SC.,2 Maria J. De Los Santos, PhD,3 Arantza Guindel Mendive, PhD,4 Maria Fernanda Insua, PH.D.5 IVIRMA VALENCIA, Valencia, Spain; 2 Valencia, Spain; 3IVI Foundation - Health Research Institute La Fe, Valencia, Spain; 2IVI RMA Valencia, Valencia, Valencia, Spain; 3IVIRMA Valencia, Valencia, Spain; 4IVIRMA Valencia, Valencia, Valencia, Spain.

OBJECTIVE: To identify blastocyst features and laboratory procedures related with the probability of obtaining an inconclusive result after blastocyst trophectoderm biopsy.

MATERIALS AND METHODS: Retrospective study performed in a single IVF laboratory center from January 2016 to December 2021. Trophectoderm biopsies were analysed by NGS_SNP calling. Inconclusive chromosomal assessment was analysed in relation to i) the blastocyst biopsy methodology (flicking vs pulling), ii) the day of biopsy (day 5 vs day 6), iii) the blastocyst developmental stage (blastocysts hatching out of the zona; iHB, or completely hatched; HB), iv) trophectoderm (TE) quality (good or poor). Categorical variables are shown as rate. Chi-squared tests were performed to assess statistically significant differences. P-value<0.05 was considered statistically significant.

**RESULTS:** During the study timeframe, a total of 18028 blastocyst from 4150 patients were biopsied for PGT-A. The overall diagnostic rate was 97.1%, with 517 blastocysts receiving inconclusive reports. Flicking methodology was applied in 14920 biopsied embryos, 348 of them were blastocysts with no diagnosis after blastocyst biopsy (23.3%). Pulling methodology was performed in 3108 biopsied embryos, 169 of them had also a no diagnosis (5.4%, showing p<0.001 between both methodologies). Regarding the day of biopsy, the rate of inconclusive results was 2.66% (N=313/11744) on Day 5 and 3.25% (N=204/6284) on Day 6 (p<0.05). The blastocyst stage was strongly associated with the chance of achieving a conclusive diagnosis, as the rate of inconclusive results was 2.67% (N=412/15557) when iHB were biopsied and 4.17% (N=972/2324) when HB were biopsied (p<0.001). On the contrary, a worse TE quality did not result into higher rates of inconclusive diagnosis (good N=266/9630; 2.76%; poor N=251/8398, 2.98%; p>0.05).

CONCLUSIONS: Blastocyst biopsy involved a very low risk of inconclusive chromosomal assessment (2.67%). In our hands, the day of TE biopsy, the expansion degree and the TE biopsy technique represent the main variables affecting the DNA analyzed for the blastocyst diagnosis.

**P-118** 6:30 AM Monday, October 24, 2022

**STANDARD INSEMINATION (SI) IN IVF PATIENTS WITHOUT MALE FACTOR INFERTILITY (MFI) MAY INCREASE THE EUPLOIDY RATE (ER) AMONG PRE-IMPLANTATION GENETICALLY TESTED BLASTOCYSTS FOR ANEUPLOIDIES (PGT-A).** Arti Taggar, M.D., M.PH, Lawrance Engmann, MD, Stephanie M. Hallisey, MD, Daniel R. Grow, MD, MHCM, Claudio A. Benadiva, MD, HCLD, Allison Bartolucci, PhD University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT.

OBJECTIVE: Available publications on the effects of intracytoplasmic sperm injection (ICSI) on ERs demonstrate conflicting outcomes.1,2 We aim to explore a large academic practices’ use of ICSI among patients with normospermia undergoing a controlled ovarian hyperstimulation in vitro fertilization (COH IVF) cycle with a trophectoderm biopsy for PGT-A.

MATERIALS AND METHODS: COH IVF cycles were selected after the universal use of Next-Generation Sequencing (NGS) for PGT-A in our clinic from October 2017-March 2022 and included women ages 18-42 undergoing cycles utilizing PGT-A with partners without MFI. Cycles were excluded if PGT-A was used for any known risk for chromosomal abnormalities such as single gene defects or rearrangements. Only the first chronological cycle meeting inclusion criteria per individual was included. Cycles using ICSI were compared to cycles utilizing SI for oocyte fertilization. Our primary
Table 1: Correlation of the mtDNA ratio with ploidy status in Day 5/6 blastocysts

<table>
<thead>
<tr>
<th>Blastocyst age</th>
<th>Euploid</th>
<th>Mosaic</th>
<th>Aneuploid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total #</td>
<td>(%)</td>
<td>mtDNA</td>
</tr>
<tr>
<td>Day 5</td>
<td>220</td>
<td>90 (41%)</td>
<td>0.00219&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Day 6</td>
<td>141</td>
<td>41 (29%)</td>
<td>0.00182&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a,b,c</sup> Values with different superscript letters within the same column or row are significant different (p<0.05)

RESULTS: As shown in Table 1. The euploid and mosaic rates in Day 5 blastocysts were significantly higher than that in Day 6 blastocysts while the aneuploid rates of blastocysts were on the contrary. The significant differences in mtDNA ratios were found among three different ploidy blastocysts (aneuploid > mosaic > euploid) in both Day 5 and Day 6 blastocysts. The mtDNA ratios in Day 5 blastocysts were higher than that in Day 6, but the differences were not statistically different.

CONCLUSIONS: Our results indicate that Day 5 blastocysts contained significantly higher rates of euploidy and mosaic, lower rates of aneuploidy compared to Day 6 blastocysts. The mtDNA quantity was associated with different ploidy status (aneuploid, mosaic, euploid) and may affect the early stage of embryo development. More studies are needed to investigate the relationship between mtDNA quantity and embryo implantation potential.

IMPACT STATEMENT: This study may develop a novel biomarker for embryo selection by using mtDNA quantity in trophectoderm.

FOOTNOTES

P-119 6:30 AM Monday, October 24, 2022

**CORRELATION OF MITOCHONDRIAL DNA QUANTITY AT THE BLASTOCYST STAGE WITH DIFFERENT PLOIDY STATUS.** Tao Tao, PH.D.,<sup>1</sup> Devon A. Dickson, B.Sc., M.Sc.,<sup>1</sup> Wensheng Qin, Ph.D.,<sup>1</sup> Alfonso Del Valle, MD, FRCS(C)<sup>1</sup> The Fertility Partners/The Toronto Institute for Reproductive Medicine, Toronto, ON, Canada;<sup>2</sup> Lakehead University, Thunder Bay, ON, Canada;<sup>3</sup> The Fertility Partners/The Toronto Institute for Reproductive Medicine, Toronto, Canada.

OBJECTIVE: A wide attention has been drawn recently to the use of mitochondrial DNA (mtDNA) quantity in trophectoderm cells as a biomarker for embryo viability. The purpose of this study was to determine whether the mtDNA is associated with embryo ploidy status and embryo age.

MATERIALS AND METHODS: This study included 361 blastocysts which underwent PGT-A testing for aneuploidy in our clinic in 2021. It was approved by The Institutional Scientific Advisory Board. The mtDNA ratio was defined as the ratio of mitochondrial DNA to autosomal (chromosome 1-22) DNA. Whole-genome amplification, NGS, and data analysis were performed by Sequence46 using the Ion ReproSeq™ PGS Kit and Ion Reporter™ software (Thermo Fisher Scientific). An ANOVA test was used to compare the variations of the mean mtDNA ratios between Day 5 and Day 6 blastocysts and among different ploidy status. The percentages of different ploidy embryos were analyzed by using the Chi-square test. P<0.05 was considered statistically significant.

RESULTS: The euploid and mosaic cycles without MFI were not different. Summary statistics are shown in the table below.

<table>
<thead>
<tr>
<th>Blastocyst Age</th>
<th>Total #</th>
<th>mtDNA # (%)</th>
<th>mtDNA # (%)</th>
<th>mtDNA # (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 5</td>
<td>220</td>
<td>90 (41%)</td>
<td>0.00219&lt;sup&gt;a&lt;/sup&gt;</td>
<td>57 (26%)</td>
</tr>
<tr>
<td>Day 6</td>
<td>141</td>
<td>41 (29%)</td>
<td>0.00182&lt;sup&gt;a&lt;/sup&gt;</td>
<td>32 (23%)</td>
</tr>
</tbody>
</table>

<sup>a,b,c</sup> Values with different superscript letters within the same column or row are significant different (p<0.05)

CONCLUSIONS: Previous studies included patients with MFI, were limited in sample size, used fluorescence in situ hybridization, or used microarray-based comparative genomic hybridization screening methods for chromosomal abnormalities. Our study incorporates the more contemporary use of NGS platforms in a population without MFI and showed that SI improved oocyte utilization and therefore euploid rates per oocyte retrieved.

IMPACT STATEMENT: Clinicians should consider that SI maximizes embryo utilization and that ICSI may not offer any additional benefit to patients undergoing COH IVF cycles without MFI.

REFERENCES:
3. Tao Tao, PH.D., 1
4. Wensheng Qin, Ph.D., 1
5. Alfonso Del Valle, MD, FRCS(C) 1
6. The Fertility Partners/The Toronto Institute for Reproductive Medicine, Toronto, ON, Canada; 2
7. Lakehead University, Thunder Bay, ON, Canada; 3
8. The Fertility Partners/The Toronto Institute for Reproductive Medicine, Toronto, Canada.

P-120 6:30 AM Monday, October 24, 2022

**THE EFFECT OF THE DAY OF BLASTOCYST FORMATION ON ONGOING PREGNANCY RATES IN PATIENTS RANDOMIZED TO FRESH OR FREEZE-ALL.** Leah A. Kaye, B.A.,<sup>1</sup> M.D.,<sup>2</sup> Melody A. Rasouli, MD, MBA,<sup>3</sup> Kajal Verma, MD,<sup>2</sup> Forest C. Garner, MS,<sup>2</sup> Carrie E. Bedient, MD,<sup>1</sup> Bruce S. Shapiro, M.D., PH.D.<sup>3</sup> 1University of Connecticut Health Center, Las Vegas, NV; 2University of Nevada, Las Vegas, School of Medicine, Las Vegas, NV; 3Fertility Center of Las Vegas, Las Vegas, NV.

OBJECTIVE: To characterize the effect of the day of blastocyst formation (day 5 or 6) on transfer outcome in fresh and frozen embryo transfers (FET).

MATERIALS AND METHODS: After conventional ovarian stimulation with exogenous gonadotropins, consented first-time IVF patients were randomly assigned to fresh transfer or else cryopreservation of all embryos followed by thaw for transfer in subsequent FET cycles. FET cycles were artificially prepared with exogenous estradiol and, after sonographic confirmation of adequate endometrial development, intramuscular progesterone was initiated 5 days before the expected day of transfer. All transfers occurred at the expanded blastocyst stage. All transfers occurred at the expanded blastocyst stage. Luteal support was continued in pregnant patients until 10 weeks gestation. Pre-implantation genetic testing, use of a gestational carrier, and patients >40 years of age or with diminished ovarian reserve were excluded. Ongoing pregnancy rates were compared using Fisher’s exact test. P<0.05 was considered significant.

RESULTS: There were 204 transfers. Two transfers of day 7 blastocysts, one with ongoing pregnancy, were excluded due to too few data for meaningful analysis, and the remaining 202 transfers were included in this analysis (105 fresh, 97 FET). Patients were 31.7±3.8 years of age, had 18.0±2.2

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antral follicles and 15.5±7.3 oocytes collected. Transfer outcome frequencies are shown in Table 1. Among fresh transfers, the ongoing pregnancy was significantly greater with day 5 transfer than with day 6 transfer (64.2% vs 37.5%, RR=1.71, P=0.0327). Among thaw transfers, this difference was smaller and not statistically significant (88.9% vs 72.1%, RR=1.23, P=0.0737).

Table 1: Outcome frequencies and rates.

<table>
<thead>
<tr>
<th></th>
<th>Day 5 blastocysts</th>
<th></th>
<th>Day 6 blastocysts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ongoing</td>
<td>Not Ongoing</td>
<td>Total</td>
</tr>
<tr>
<td>Fresh transfers</td>
<td>52 (64.2%)</td>
<td>29 (35.8%)</td>
<td>81</td>
</tr>
<tr>
<td>Thaw transfers</td>
<td>32 (88.9%)</td>
<td>4 (11.1%)</td>
<td>36</td>
</tr>
<tr>
<td>Totals</td>
<td>84</td>
<td>33</td>
<td>117</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The day of blastocyst formation appears to have a greater effect following fresh transfers than FET.

IMPACT STATEMENT: Previous assessments of the effect of the day of blastocyst formation were based on retrospective analyses, and therefore subject to various biases due to non-random treatment assignment.

SUPPORT: None.
**E-POSTER ABSTRACT SESSION: 13**

**P-121** 6:30 AM Monday, October 24, 2022

**DOES POORLY EXPANDED THAWED EUPLOID EMBRYO AFFECTS GOOD EXPANDED EUPLOID EMBRYO IN TWIN EMBRYO TRANSFER?** Samar Gamal, B.Sc., 1 Hager Abu Elmagd, B.Sc., 1 Hanaa Ahmed Alkhader, MBCH, 1 Hosam H. Zaki, M.B.B.CH., M.D., M.Sc. 1 2Al-Azhar University; 3Ganin IVF lab Director, Cairo, Egypt; 4Ganin Fertility Center, Cairo, Egypt.

**OBJECTIVE:** To assess whether poorly expanded embryos negatively affect good expanded embryos when transferred together as the expansion rate is the main predictor of the clinical outcomes of ICSI.

**MATERIALS AND METHODS:** We recorded and collected data on thawed euploid blastocysts transferred throughout January 2021 to February 2022. We categorized the transferred thawed euploid blastocysts into 3 groups and compared their clinical outcomes. After thawing, embryos with a > 60% expansion rate were considered to have good expansion whereas poor expanded embryos were those with an expansion rate from 0 to < 60%.

The three groups were as follows:
- **Group A:** single good expanded euploid blastocysts.
- **Group B:** two thawed good expanded blastocysts.
- **Group C:** one good expanded blastocyst with one poor expanded blastocyst.

The transfer of two euploid embryo was performed upon patient’s request or in cases of repeated clinical failure.

One-way analysis of variance (ANOVA) was used to compare the categorical and numerical variables between the study groups. The differences were considered significant if the p-value was ≤ 0.05. Our outcome measures included pregnancy and implantation rates.

**RESULTS:** The average ages of the females were 32.57 ± 4.8 years old for group A, 30.27 ± 5.03 years old for group B, and 30.9 ± 6 years old for group C. Data are presented as means ± standard deviation.

The clinical outcomes of the study’s groups are shown in the table below:

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Pregnancy rate</th>
<th>Embryo grade</th>
<th>Implantation rate</th>
<th>Pos HCG</th>
<th>CPR</th>
<th>MZT</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>162</td>
<td>90/162 55.55%</td>
<td>84/104 80.76%</td>
<td>19/47 40.42%</td>
<td>0.000027</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>104</td>
<td>90/104 55.55%</td>
<td>107/208 54.14%</td>
<td>25/94 26.5%</td>
<td>&lt; .00001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>47</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N refers to the number of cases
Good expansion : ≥60%
Poor expansion : ≤60%

The result is significant at p < 0.05

**CONCLUSIONS:** Our findings suggest that there is a potential negative effect of embryos with poor re-expansion degree on good expanded embryos when transferred together as shown in the third group. The transfer of two good expanded euploid embryos yielded significantly higher pregnancy rate compared to single euploid embryo transfer. Moreover, there was no significant difference in the implantation rate between the transfer of single good embryos and the transfer of two good expanded embryos. To the best of our knowledge, this study is the first to compare the transfer of three different groups of thawed euploid blastocysts based on their number and expansion degree.

**IMPACT STATEMENT:** The transfer of poorly expanded thawed euploid embryos may affect the clinical outcomes of ICSI if transferred together with good expanded embryos.

**P-122** 6:30 AM Monday, October 24, 2022

**IMPACT OF EMBRYO TRANSFER CATHETER LOADING TECHNIQUE ON CLINICAL OUTCOMES FOLLOWING SINGLE EUPLOID BLASTOCYST TRANSFER.** Michael Abeyta, BS, 1 William B. Schoolcraft, MD, 2 Jason E. Swain, PhD, HCLD 1 1CCRM San Francisco, Menlo Park, CA; 2CCRM Colorado, Lone Tree; 3CCRM Fertility Network, Lone Tree, CO.

**OBJECTIVE:** Embryo transfer catheter loading approach has been shown to impact clinical outcomes. Prior studies have indicated that media volume or size/placement of air bubbles may impact success rates. Rinsing of the catheter prior to embryo loading may also be impactful. However, prior studies did not always control for uterine environment or embryo quality. The outcomes following transfer of a single euploid blastocyst in a frozen embryo transfer cycle were compared using two catheter loading approaches.

**MATERIALS AND METHODS:** Data was retrospectively analyzed for frozen embryo transfers using single euploid blastocysts (>3BB) formed on day 5, 6 and 7 of culture. Transfers utilized the Wallace Sureview 18gm catheter attached to a 1cc TB syringe and EmbryoGlue. Method 1 (n=166) of catheter loading entailed flushing medium through the catheter to pre-rinse and then loading the embryo within a column of medium flanked by 2 air bubbles. As a result, the catheter above the embryo was back-filled with media up to the syringe. Method 2 (n=110) of catheter loading did not rinse the catheter but used the same amount and arrangement of media and bubbles. As a result, the catheter had a column of air above the embryo to the syringe. Injection volume of both approaches was ~30ul. Transfers were performed in similar fashions and outcomes compared. Because day of blastocyst formation is potentially impactful on outcomes, day of blastocyst formation between the two approaches was compared. Rates of positive HCG (Pos HCG), clinical pregnancy rate (CPR) and monzygotic twinning (MZT) were compared. Differences were examined using Fishers Exact test, p<0.05

**RESULTS:** No significant differences existed between the 2 catheter loading approaches with regard to the day of blastocyst utilized for transfer. No statistically significant differences were noted in the rates of positive HCG, CPR or MZT between the two catheter loading techniques examined.

**CONCLUSIONS:** Using a single euploid blastocyst transfer for a frozen embryo transfer as a model to control for embryo and uterine quality, clinical outcomes were not affected by the two catheter loading techniques examined. While other catheter loading approaches that alter transfer volume and/or size/placement of air bubbles may impact outcomes, the presence/absence of media above the embryo and pre-rinse of the catheter in this study were not impactful.

**IMPACT STATEMENT:** Pre-rinsing of the embryo transfer catheter and media back-fill had no impact on clinical outcomes following single euploid blastocyst transfer in a frozen embryo transfer cycle.

<table>
<thead>
<tr>
<th>Avg. Female Age</th>
<th>% D5 blast</th>
<th>% D6 blast</th>
<th>% D7 blast</th>
<th>Pos HCG</th>
<th>CPR</th>
<th>MZT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Method 1</strong></td>
<td>35.9</td>
<td>65.1%</td>
<td>30.7%</td>
<td>4.2%</td>
<td>86.7%</td>
<td>75.3%</td>
</tr>
<tr>
<td><strong>Method 2</strong></td>
<td>35.7</td>
<td>68.2%</td>
<td>27.3%</td>
<td>4.5%</td>
<td>86.4%</td>
<td>76.4%</td>
</tr>
</tbody>
</table>

**FERTILITY & STERILITY®**

**e161**
ENDOMETRIAL RECEPTIVITY ANALYSIS CAN BE HELPFUL ESPECIALLY IN PATIENTS WITH HISTORY OF HIGH ORDER REPEATED IMPLANTATION FAILURE: REAL WORLD DATA OF SINGLE PRIMARY FERTILITY CENTER IN SOUTH KOREA. Chang-Woo Choo, M.D. Seoul, AA, South Korea.

OBJECTIVE: This study was designed to evaluate the clinical utility of ERA test and to set an effective indication about the subgroup of patient who can get help from the test.

MATERIALS AND METHODS: This was a prospective study performed by single clinician at single primary fertility center. From January 2019 to December 2021, a total of 47 ERA test were performed for the patients suffered from RIF. The test was indicated to the patients with 1) no endometrial pathology, 2) moderate to good quality embryo, 3) 3 or more times of failed previous ET cycles in spite of corrected immunologic, thromboembolic, hereditary etiology of RIF, 4) 3 or more times of failed previous ET cycles with preimplantation genetic test for aneuploidy (PGT-A). The patients' endometrial tissues were obtained by reference protocol suggested by test provider, every cycles were performed at hormone replacement cycle. After checking the result, next embryo transfer (ET) procedure was performed with exactly same way with ERA test, and embryo transfer timing was personalized according to the recommendation of the test result. We checked the pregnancy result of next 4 consecutive embryo transfer cycles and also measured the basal characteristics of the patients.

RESULTS: The basal characteristics of the patients were as below. Women's age were 38.0±4.08 years old, the minimum was 31 and the maximum was 46, and the number of their previous failed ET cycles were 8.98±4.47, the minimum was 4 and the maximum was 22. Only 29.8% of total cases showed receptive endometrium, 46.8% were pre-receptive, 12.8% were early-receptive, 6.4% were late-receptive and 4.3% were post-receptive. The result was detailed checked by age distribution, for the patients under 35 years old, receptive were 33.3% and for the patients aged from 35 to 39 years old, receptive result were 46.7%, and for 40 or older patients, receptive were 11.8%. The ERA test result were analyzed by the number of previous failed ET cycles. Because this study was performed only to the patient with at least 4 or more times of previous failed ET cycles, for the patients with 4 to 6 times of previous failed ET cycles 35.3% were receptive (47.1% of pre-receptive, 5.9% of early-receptive, 11.8% of late-receptive, 0% of post-receptive). On the contrary, for the patients with 7 or more times of previous failed ET cycles, only 19.0% were receptive (52.4% of pre-receptive, 19.0% of early-receptive, 19.0% of late-receptive, 9.5% of post-receptive). Cumulative pregnancy rates (7.5% vs 5.7%, p<0.001), number of previous in-vitro fertilisation (IVF) attempts (2.23±1.32 vs 2.15±1.18 p=0.849) and endometrial thickness (9.92±1.85 mm to 10.30±1.72 mm, p=0.112), Number of women with positive human chorionic gonadotropin (hCG) 10th day following ET (37.5% vs 54.7%, p=0.734), clinical pregnancy rate (48.1% vs 49.1, p=0.911) and abortion rates (7.5% vs 5.7%, p=0.753) were similar in both groups.

CONCLUSIONS: Our results indicate that excess serum progesterone on day of ET do not have detrimental effects on clinical pregnancy rates.

IMPACT STATEMENT: P4 levels > 60 ng/mL on the day of ET do not exert any effect on clinical outcomes in artificially prepared FET cycles.

SUPPORT: none

REFERENCES: none

P-125 6:30 AM Monday, October 24, 2022

ANTI-MÜLLERIAN HORMONE (AMH) CAN BE A PREDICTABLE PARAMETER OF CLINICAL OUTCOMES AFTER SINGLE VITRIFIED BLASTOCYST TRANSFER CYCLES (SVBT). Mungunshagai Baatarsuren, MSc., 1 Kitazato, Japan. 2 Naka medical, Japan. 3 Mongolian Academy of Medical Sciences, Mongolia; 4 Ojinmed IVF Center, Ulaanbaatar, Mongolia; 5 International University of Health and Welfare, Narita, Japan.

OBJECTIVE: Anti-Müllerian hormone (AMH) serum level significantly correlates with an ovarian reserve and useful quantitative marker in in-vitro fertilization (IVF) cycle. Recent studies reported AMH serum level positively correlated with clinical outcomes, which used standard ovarian stimulation protocol often. Clomiphene-citrate (CC) based minimal stimulation protocol is one of the mild stimulations, which uses low dose or no gonadotropin. This study aims to investigate the correlation between clinical outcomes and AMH serum level after CC based minimal stimulation.

MATERIALS AND METHODS: Retrospective study involved 384 patients who underwent clomiphene-citrate based minimal stimulation and were treated with 6mg/d of estradiol valerate and then with 2x50mg subcutaneous progesterone once endometrium was ≥7mm. Serum P4 was measured on the morning of FRET. A maximum of two blastocysts were transferred on the 6th day of P4 supplementation. For each cycle with a >60ng/mL of P4 level on the day of ET, two subsequent cycles with 9-30ng/mL P4 were matched with respect to female age, number and quality of blastocysts transferred and the cycle rank.

RESULTS: Baseline characteristics of women with low progesterone levels were not significantly different than women with ≥60 ng/ml progesterone concentrations in terms of age (33.7±4.72 vs 33.81±4.63, p=0.792), number of previous in-vitro fertilisation (IVF) attempts (2.23±1.32 vs 2.15±1.18 p=0.849) and endometrial thickness (9.92±1.85 mm to 10.30±1.72 mm, p=0.112). Number of women with positive human chorionic gonadotropin (hCG) 10th day following ET (37.5% vs 54.7%, p=0.734), clinical pregnancy rate (48.1% vs 49.1, p=0.911) and abortion rates (7.5% vs 5.7%, p=0.753) were similar in both groups.

CONCLUSIONS: Our results indicate that excess serum progesterone on day of ET do not have detrimental effects on clinical pregnancy rates.

IMPACT STATEMENT: P4 levels > 60 ng/mL on the day of ET do not exert any effect on clinical outcomes in artificially prepared FET cycles.

SUPPORT: none

REFERENCES: none
In multivariable logistic regression analysis, the AMH serum level significantly correlated with implantation rate (aOR 0.86, 95% CI: 0.76–0.98, p=0.03), clinical pregnancy rate (aOR 0.83, 95% CI: 0.73–0.93, p=0.002) and live birth rate (aOR 0.88, 95% CI: 0.79-0.99, p=0.04), and the women’s age significantly correlated (p<0.05), concomitantly.

CONCLUSIONS: We found correlation between AMH serum level and clinical outcomes. Although the basal AMH serum level can be used as a predictor of clinical outcomes after CC based minimal stimulation for ICSI/IVF cycle.

IMPACT STATEMENT: This is a first report of correlation between AMH serum level groups and clinical outcome, and showed possible prediction of clinical outcomes for SVBT after CC based minimal stimulation protocol.

SUPPORT: None

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**TABLE 1.**

<table>
<thead>
<tr>
<th></th>
<th>Same MD N=416</th>
<th>Switch MD N=868</th>
<th>P value</th>
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</thead>
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<tr>
<td>Age (yrs)</td>
<td>34.31</td>
<td>34.87</td>
<td>0.16</td>
</tr>
<tr>
<td>AMH (ng/ml)</td>
<td>95%CI (33.92-34.69)</td>
<td>95%CI (34.61-35.12)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>5.21</td>
<td>4.69</td>
<td>0.13</td>
</tr>
<tr>
<td>Embryo quality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Good quality (4-6AA, AB, BA, BB)</td>
<td>330/416 79.3%</td>
<td>305/868 77.4%</td>
<td>0.22</td>
</tr>
<tr>
<td>% Fair quality (4-6BC, CB)</td>
<td>62/416 14.9%</td>
<td>158/868 18.2%</td>
<td></td>
</tr>
<tr>
<td>% Poor quality (4-6CC)</td>
<td>24/416 5.8%</td>
<td>38/868 4.4%</td>
<td></td>
</tr>
<tr>
<td>Endometrial thickness (mm)</td>
<td>9.25</td>
<td>9.34</td>
<td>0.34</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>316/416</td>
<td>647/868</td>
<td>0.59</td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>76.0%</td>
<td>74.5%</td>
<td></td>
</tr>
<tr>
<td>Clinical pregnancy loss rate</td>
<td>271/416</td>
<td>564/868</td>
<td>0.89</td>
</tr>
<tr>
<td>Clinical pregnancy loss rate</td>
<td>65.4%</td>
<td>65.0%</td>
<td></td>
</tr>
<tr>
<td>Ongoing pregnancy rate</td>
<td>39/271</td>
<td>88/564</td>
<td>0.72</td>
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<tr>
<td>Ongoing pregnancy rate</td>
<td>229/416</td>
<td>473/868</td>
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</table>

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**P-126 6:30 AM Monday, October 24, 2022**

**REPRODUCTIVE OUTCOMES AFTER SWITCHING PHYSICIANS IN THE SETTING OF PRIOR FAILED EMBRYO TRANSFER.** Stephanie Willson, MD, Nola Herlihy, MD, Cheri K. Margolis, MD, Leah M. Roberts, MD, Pavan Gill, MD, Andres Reig, MD, Paul A. Bergh, M.D., Marie D. Werner, MD, IVI-RMA New Jersey, Basking Ridge, NJ; IVIRMA New Jersey, Basking Ridge, NJ; IVI-RMA New Jersey, Basking Ridge.

OBJECTIVE: The objective of this study is to investigate whether switching physicians after a failed embryo transfer improves pregnancy outcomes in a subsequent embryo transfer.

MATERIALS AND METHODS: This was a retrospective cohort study conducted at a single high-volume infertility clinic from January 2010 to March 2022. All patients who underwent a euploid single embryo transfer (SET) resulting in failed implantation and returned for a second euploid SET were included. Those patients whose endometrial linings were <7mm were excluded. Patients were stratified according to whether the same physician performed both transfers or whether a different physician performed the second transfer. The primary outcome was ongoing pregnancy rate, as defined by patient’s discharge to obstetrical care at ≥8-9 weeks of gestation. Statistical comparisons were done using Student’s t-test and chi square.

RESULTS: A total of 1,284 embryo transfers were included, 416 (32%) of which had their second SET performed by the same physician and 868 (68%) of which had their second SET performed by a different physician. In the study population that failed their first euploid transfer, there was no statistically significant difference in ongoing pregnancy rate (55.0% vs 54.7%, p=0.852), nor in any of the secondary outcomes.

CONCLUSIONS: Switching physicians for embryo transfer does not improve pregnancy outcomes. Patients may be reassured that ongoing pregnancy rates remain high for the subsequent ET after a failed ET, regardless of the physician performing the procedure.

IMPACT STATEMENT: Failure of implantation can leave patients frustrated and physicians looking for alternative methods. Patients and providers can be reassured that reproductive outcomes remain unchanged regardless of the transferring physician in subsequent cycles following failed embryo transfer.

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**P-127 6:30 AM Monday, October 24, 2022**

**EFFECT OF AUTOLOGOUS PLATELET-RICH PLASMA TREATMENT ON REFRACTORY THIN ENDOMETRIUM DURING THE FROZEN-EMBRYO TRANSFER CYCLE: A SINGLE ARM SELF-CONTROLLED TRIAL IN 100 PATIENTS.** So Yeon Shin, MD, Jihyang Kim, MD, Hwang Kwon, MD, Jung Ryeol Lee, MD, PhD, Jeeyyun Kim, M.D., Ji Eun Shin, B.S., M.D., Hwa Seon Koo, MD, Donghee Choi, M.D., Chan Park, M.D., CHA Bundang Medical Center, CHA University, Seonam-nam-si, Gyeonggi-do, Korea, Republic of (South); Fertility Center, CHA Bundang Medical Center, CHA University, Seonnam-nam-si, Gyeonggi-do, Korea, Republic of (South); Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South); Fertility Center, Seonnam-nam-si, Gyeonggi-do, Korea, Republic of (South).

OBJECTIVE: Platelet-rich plasma (PRP), as cutting-edge technology, is widely applied in regenerative medicine, including cartilage repair, alopecia, and management of diabetic foot ulcers. Patients with refractory thin endometrium, defined as less than 7mm of the endometrial thickness (EMT) unresponsive to standard treatment options, were associated with reduced incidence of pregnancy rate and often resulted in cycle cancellation. PRP emerged as a new therapeutic option to improve implantation rate and pregnancy outcome. The aim of this study is to identify the effect of intrauterine autologous PRP infusion on implantation and pregnancy in patients with refractory thin endometrium.

MATERIALS AND METHODS: Ninety-one women who had a history of two or more failed IVF cycles and refractory thin endometrium were recruited for this study. No woman had successful on-going pregnancy in the previous cycle. The main inclusion criteria were EMT <7mm with more
than two cycles of medical therapy, such as high dose estradiol valerate, transvaginal sildenafil, or pentoxifylline with vitamin E. The Patients were treated with intrauterine infusion of autologous PRP between cycle days 7 and 14 in their hormone replacement therapy-frozen embryo transfer (HRT-FET) cycle. PRP was administered at a 3-day interval until the EMT reached 7mm. After 3 times of PRP administration, ET was performed regardless of whether the EMT reached 7mm. The primary outcomes were the on-going pregnancy rate. The secondary outcomes were the implantation rate and EMT increment compared with the previous cycle without PRP infusion. The outcome data were compared with those of the previous cycles.

**RESULTS:** Mean age of the patients was 38.6±3.9 years old at the treatment cycle. The on-going pregnancy rate showed 20.9% (19/91) in the PRP treatment cycle, significantly higher than in the previous cycle. The implantation rate was significantly improved in the PRP treatment cycle than in the previous cycle (16.4 vs. 3.1%, respectively, p < 0.001). The mean EMT after PRP treatment showed 6.07±1.45mm, which was significantly increased by 0.83 mm (p < 0.001). There were no procedure-related adverse events.

**CONCLUSIONS:** The intrauterine autologous PRP infusion is a safe and effective treatment for patients with refractory thin endometrium. The impact of bed rest of older patients or lower quality blastocysts may be insignificant to see if bed rest may impact less than ideal patient populations.

**IMPACT STATEMENT:** Autologous PRP treatment could improve the pregnancy outcomes of women with refractory thin endometrium with repeated implantation failure (RIF). This treatment could be a promising option for the treatment of refractory thin endometrium. Further study is necessary to confirm the treatment effect on other indications such as idiopathic RIF.

**SUPPORT:** None

### P-128 6:30 AM Monday, October 24, 2022

**IMPACT OF BEDREST VERSUS IMMEDIATE AMBULATION FOLLOWING TRANSFER OF A SINGLE EUPLOID BLASTOCYST.** Haleigh Silz, MS, Laura Reed, BS, William B. Schoolcraft, MD, Jason E. Swain, PhD, HCLD, 1CCRM Colorado, Lone Tree, CO; 2CCRM Colorado, Lone Tree, CO; 3CCRM Fertility Network, Lone Tree, CO.

**OBJECTIVE:** Previous studies have indicated that immediate ambulation following embryo transfer (ET) has no negative impact on resulting pregnancy rates or successful clinical outcomes. Several studies suggest that bed rest following ET may even be detrimental. However, prior studies have not always controlled for day of transfer, embryo quality or number of embryos transferred. Additionally, previous studies have usually examined fresh transfers and time of bedrest has been relatively short (<30minutes). The impact of 1 hour of bed rest following transfer of a single euploid blastocyst in a frozen ET (FET) cycles was examined.

**MATERIALS AND METHODS:** Data were retrospectively collected over a 6 month period. To control for the impact of embryo quality, only patients receiving a single day 5 high quality euploid blastocyst (>3BB) in a frozen embryo transfer cycle were utilized. Cycles analyzed were limited to those receiving a single high quality euploid blastocyst (>3BB) in a frozen embryo transfer cycle. PRP was administered at a 3-day interval until the EMT reached 7mm. After 3 times of PRP administration, ET was performed regardless of whether the EMT reached 7mm. The primary outcomes were the on-going pregnancy rate. The secondary outcomes were the implantation rate and EMT increment compared with the previous cycle without PRP infusion. The outcome data were compared with those of the previous cycles.

**RESULTS:** Mean age of the patients was 38.6±3.9 years old at the treatment cycle. The on-going pregnancy rate showed 20.9% (19/91) in the PRP treatment cycle, significantly higher than in the previous cycle. The implantation rate was significantly improved in the PRP treatment cycle than in the previous cycle (16.4 vs. 3.1%, respectively, p < 0.001). The mean EMT after PRP treatment showed 6.07±1.45mm, which was significantly increased by 0.83 mm (p < 0.001). There were no procedure-related adverse events.

**CONCLUSIONS:** The intrauterine autologous PRP infusion is a safe and effective treatment for patients with refractory thin endometrium with repeated implantation failure (RIF). This treatment could be a promising option for the treatment of refractory thin endometrium. Further study is necessary to confirm the treatment effect on other indications such as idiopathic RIF.

**SUPPORT:** None

### P-129 6:30 AM Monday, October 24, 2022

**OVARIAN PLATELET-RICH PLASMA TREATMENTS MAY REINSTATE OVULATION IN PERIMENOPAUSAL WOMEN AND SIGNIFICANTLY DECREASES SERUM FSH.** Theodore Saydah, BS, Zoe Strong, BA, Alicia Broussard, PHD, Edward J. Nejat, MD, FACC, Janelle Luk, M.D., Jesse J. Hade, M.D., Kirsten Mortimer, BA 1Generation Next Fertility, New York, NY; 2ReproSource.

**OBJECTIVE:** To evaluate perimenopausal women with severely diminished ovarian reserve and anovulation coupled with low AMH and elevated FSH who desire pregnancy using their own oocytes. Autologous platelet-rich plasma (PRP) is a novel medical treatment employed to improve the function and health of different tissues within the body by enhancing the healing and anti-aging process. It has been used in other fields such as orthopedics, cardiology, plastic surgery, and dermatology. In this preliminary study, our objective is to measure the effect of Ovarian PRP treatments on the ovulation, oocyte yield, and embryo yield of patients who are historically anovulatory. Ultimately, we want to determine whether Ovarian PRP treatments can reinstate ovulation in anovulatory patients.

**MATERIALS AND METHODS:** Women (N=8; average age of 40.5) diagnosed with diminished ovarian reserve were treated with PRP over a 3-month period. To control for the impact of embryo quality, only patients receiving a single day 5 high quality euploid blastocyst (>3BB) in a frozen embryo transfer cycle were utilized. Cycles analyzed were limited to those receiving a single day 5 high quality euploid blastocyst (>3BB) in a frozen embryo transfer cycle. PRP was administered at a 3-day interval until the EMT reached 7mm. After 3 times of PRP administration, ET was performed regardless of whether the EMT reached 7mm. The primary outcomes were the on-going pregnancy rate (CPR) and miscarriage were compared. Differences were examined using Fisher’s Exact Test.

**RESULTS:** We found that 63% of patients who are historically anovulatory with mean duration of over 3 normal menstrual cycles and or 6 months from their last menstrual cycle, with an average starting FSH = 70.63 mIU/mL and undetectable AMH <0.015 ng/mL, will resume ovulation following PRP treatment. After the first ovarian PRP treatment (n=8), 25% of patients ovulated, with one spontaneous pregnancy. Following 2 PRP treatments (n=6) 50% of patients ovulated but produced no usable embryos. Following 3 PRP treatments (n=2), 1 eligible embryo for transfer was formed. Following 4 PRP treatments (n=1), 1 eligible embryo for transfer was formed. Furthermore, while starting average FSH for the cohort (n=8) was 70.63 mIU/mL, after 2 PRP treatments, average FSH for the cohort (n=6) was 36.85 mIU/mL, which is a 48% decrease in serum FSH (p = 0.039).

**CONCLUSIONS:** Ovarian PRP treatment is effective in inducing ovulation in historically anovulatory patients who desire pregnancy through IVF. Our research indicates that additional treatments have a cumulative effect with increased rates of ovulation in patients who undergo more than 2 treatments, as well as a significant decrease in FSH after 2 treatments.

**IMPACT STATEMENT:** Autologous PRP treatment is effective in inducing ovulation in histologically anovulatory patients who previously did not have a live birth following an IVF cycle. Our research indicates that additional treatments have a cumulative effect with increased rates of ovulation in patients who undergo more than 2 treatments, as well as a significant decrease in FSH after 2 treatments. Ultimately, we want to determine whether Ovarian PRP treatments can reinstate ovulation in perimenopausal patients.

**SUPPORT:** None

### P-130 6:30 AM Monday, October 24, 2022

**AFTER FAILING IN VITRO FERTILIZATION (IVF) WHAT IS THE SUCCESS RATE OF CONTROLLED OVARIAN STIMULATION (COH) AND INTRAUTERINE INSEMINATION (IUI)? A RETROSPECTIVE STUDY.** Faisal Alorf, MD, Michael H. Dahan, M.D. 1Mcgill University health center, Montreal, QC, Canada; 2Division of Reproductive Endocrinology and Infertility, McGill University Health Care Center, Montreal, QC, Canada.

**OBJECTIVE:** To evaluate the live birth rate after COH IUI for patients who previously did not have a live birth following an IVF cycle.

**MATERIALS AND METHODS:** Retrospective evaluation of data of patients treated at an academic fertility center between October 2008 and April 2018. Patients had a previous history of one or more IVF cycles that did not result in a live birth and subsequently underwent COH IUI with gonadotropins, letrozole or unstimulated. All subjects had at least one patent fallopian tube, did not have severe male factor infertility (less than 2 million Total Motile Sperm Count (TMSO)) and had a standard indication for IVF. Subjects received free IVF and when the government coverage for IVF ended, ovulation induction was started. The on-going pregnancy rate was significantly improved in the PRP treatment cycle than in the previous cycle (16.4 vs. 3.1%, respectively, p < 0.001). The mean EMT after PRP treatment showed 6.07±1.45mm, which was significantly increased by 0.83 mm (p < 0.001). There were no procedure-related adverse events.

**CONCLUSIONS:** Immediate amputation following transfer of a single, high quality euploid blastocyst in a frozen embryo transfer cycle has no benefit on resulting clinical outcomes.
they elected to continue care with COH IUI which remained covered. Data is presented as mean±SD. Chi squared tests or independent sample t tests were performed and multivariate logistic regression was used to model predictors of ongoing pregnancy with COH IUI after failed IVF. Ongoing pregnancy (OP) was either a live birth or a viable third trimester pregnancy. A failed IVF did not result in a live birth.

RESULTS: 550 subjects who failed 1-3 fresh IVF cycles and any resultant embryo transfers subsequently underwent a total of 991 COH IUI cycles. The OP rate after the first IUI cycle was 4.72% (N=26, 3 multiple gestation). The cumulative OP rate for all IUI cycles was 7.45% per patient (N=41/550 ongoing/patients, 3 multiples) and the OP rate per cycle was 4.13% (N=41/991 ongoing/cycles, 3 multiples).

The only discriminator using t-tests of OP was younger female age at treatment (36.6±3.9 vs. 37.6±4.3 years), P=0.037. When using multivariate logistic regression to find predictors of OP with IUI after failing IVF while controlling for confounding effects, none of the factors modeled were significant including: female age, male age, infertility diagnosis, number of previous pregnancies, number of failed IVF transfers, total motile sperm count pre and post processing, total FSH stimulation dose, and maximum endometrial thickness (p>0.05 all).

CONCLUSIONS: OPs with COH IUI after failed IVF occur but are not common. This could be considered, with proper counselling. Cost effectiveness will be modulated by price of COH IUI and medication used and should be studied in a location specific manner.

IMPACT STATEMENT: Patients should be counselled regarding the low OP rate with COH IUI if they have previously failed IVF.

P-132 6:30 AM Monday, October 24, 2022

COMPARISON OF LIVE BIRTH RATES (LBRS) BETWEEN GONADOTROPIN RELEASING HORMONE (GnRH)-ANTAGONIST, GnRH-AGONIST, AND PROGESTINE PRIMED OVARIAN STIMULATION (PPOS) PROTOCOLS IN POSEIDON GROUP-1 PATIENTS. Ruya Tez, MD, 1 Murat Enden, MD, 1 Esra Uyanik, MD, 2 Gurkan Bozdag, M.D., 2 Sezcan Munusoglu, M.D. 1 Hacettepe University; 3Konya Karapinar State Hospital, Ankara, Turkey; 4Koc University, School of Medicine, Istanbul, Turkey.

OBJECTIVE: POSEIDON Group-1 refers to young infertile women (<35 years old), with acceptable ovarian reserve (AFC ≥ 5; AMH ≥ 1.2ng/ml), and unexpected poor (<400 cyto) or suboptimal (4–9 oocytes) response to conventional ovarian stimulation (COS). We aimed to determine the effect of GnRH-agonist, GnRH-agonist and PPOS protocols on LBR in POSEIDON group-1 patients.

MATERIALS AND METHODS: Retrospective cohort study. A total of 643 consecutive couples undergoing their first intra cytoplasmic sperm injection (ICSI) cycle at tertiary academic center during January 2014-July 2021 were included. Inclusion criteria were meeting POSEIDON group-1 criteria and exclusion criteria were azoospermia, pre-implantation genetic testing and fertility preservation cycles, hypogonadotropic hypogonadism, and body mass index (BMI)>35 kg/m². Primary outcome measure was LBR. For COS recombinant-FSH and human menopausal gonadotropin were used alone or in combination. Gonadotropin starting dose was adjusted according to patient’s age, BMI and ovarian reserve. For pituitary suppression, fix GnRH-antagonist (n=490), long GnRH-agonist (n=116) or PPOS (n=37) were used. Final oocyte maturation was triggered when ≥2 follicles ≥17mm with recombinant-hCG (250 mgc) (n=516) and/or GnR agonist (0.2 mg, Triptorelin) (n=127). One or two embryos were transferred either on day 3 (n=232) or day 5/6 (n=322). While either fresh (n=476) or frozen-embryo (n=78) ET was performed in GnRH-agonist and GnRH-agonist cycles, only frozen-embryo ET was performed in PPOS cycle.

RESULTS: Median number of oocytes retrieved (6, 6, and 5, p=0.35, respectively), median number of embryos transferred (1.1, and 1, p=0.1, respectively), cycle cancelation rates (12.7, 15.5, and 24.3%, p=0.12, respectively), and LBRs per started cycle (29.6, 19.8, and 24.3%, p=0.1), respectively) were comparable among GnRH-agonist, GnRH-agonist and PPOS protocols. However, dose of total gonadotropin used was found significantly lower (~300IU) and the duration of stimulation was found significantly shorter (~1 day) in GnRH-agonist protocol. In logistic regression, when treatment year, female age, BMI, indication of IVF, number of previous cycles, AFC, fresh or frozen-embryo ET, pituitary suppression protocol, type of gonadotropin, type of trigger, number of oocytes retrieved, day of ET, number of transferred embryos were taken as covariates only day of ET (OR=1.6, 95%CI 1.1-2.5, p=0.03) remained to be significant predictors of LBR. Whereas pituitary suppression protocol was not an independent predictor on LBR.

CONCLUSIONS: For patients with unexpected hypo-response, diagnosed as POSEIDON group-1, LBRs are comparable among the GnRH-agonist, GnRH-agonist and PPOS protocols. To reduce the treatment burden, it is recommended to use GnRH-agonist protocol with fresh embryo transfer. Lack of cumulative delivery rate data per aspiration cycles is a limitation. Further randomized controlled trials are warranted.

IMPACT STATEMENT: Type of pituitary suppression does not affect LBRs in POSEIDON group-1 patients.

SUPPORT: None

E-PAPER ABSTRACT SESSION: 14

P-131 6:30 AM Monday, October 24, 2022

EFFECT OF DELAYED CHANNEL DISSOLUTION IN OOCYTES AFTER ICSI ON FERTILIZATION AND EMBRYO DEVELOPMENT. Charulata Chatterjee, phd.1 Jyothi JYOTHI. Budi, MRCOG 2 1Scientific Head and Consultant Embryologist, Secunderabad, India; 2Director, Secunderabad, India.

OBJECTIVE: To evaluate the relation of delayed channel dissolution in oocytes after intracytoplasmic sperm injection (ICSI) with Fertilization rate and embryo quality.

MATERIALS AND METHODS: Materials and Methods: A Randomized study conducted at Ferty9 Fertility Center for one hundred and sixty two couples undergoing ICSI were included in the study. Mode of oolemma breakage, channel formation and timing of channel dissolution with oocyte restoration after ICSI, division was made in two groups.

Group 1 is positive channel formation and normal restoration immediately after ICSI.

Group 2 is delayed channel dissolution after ICSI (+2mins).

RESULTS: Total of 1782 oocytes were retrieved from 162 oocyte pick up cycles. Out of 1782 oocytes 1426 oocytes were mature with one intact polar body. In 1027 injected oocytes channel dissolved immediately whereas in 399 oocytes it was delayed restoration of channel. Group 2 oocytes were cultured separately. In Group 1 fertilization rate was 88.9% [ 914/1027] where as in Group 2 fertilization rate was 70.92% [ 283/399] Fertilization rate was significantly low in Group 2 [ p <0.0001] In Group 2 ≥40% fragmentation is observed

CONCLUSIONS: This small group study suggests oocytes with delayed channel dissolution after ICSI affects the fertilization rate and embryo quality. Checking aneuploidy rate might help in transferring those embryos. Further large group study can conclude about transferring those embryos with or without aneuploidy status and its impact on the pregnancy rate.

IMPACT STATEMENT: The purpose of this study was to observe fertilization rate and embryo quality in injected oocytes which displayed delay in channel dissolution.

SUPPORT: not funded by any one

P-133 6:30 AM Monday, October 24, 2022

ENDOMETRIAL SAMPLING IN IVF/ICSI: AN INDIVIDUAL PARTICIPANT DATA BASED REVIEW. Nienke E. Van Hoogenhuijze, M.D., M.Sc.,1 Gemma Lahoz Casarramona, MD,1 Rui Wang, MD, PhD,2 Cynthia Farquhar, FRANZCOG FRCOG MD MPH,1 Mohan Kamath, PhD,1 Nicholas Raine-Fenning, Associate Professor,1 Sine Berntsen, MD,5 Anja Bisgaard Pinborg, MD, PhD,7 Hasan Ali Ali Inal, MD,8 Ernest Hung Yu Ng, M.D.,9 Sze Man Mak, Assistant Professor,10 Wellington P. Martins, D.PHIL., M.D., M.SC.,1 PHD,11
Monzygotic Twins in Human Assisted Reproduction: A Consequence of Zona Pellucida Manipulations. Wei-Hua Wang, PhD, ¹Craig Witz, MD, ²Ghassan Haddad, M.D., ³Daniel Williams, MD ⁴Aspirehi-Houston Laboratory, Houston, TX; ⁵Houston Fertility Institute, Houston, TX; ⁶Houston Fertility Institute, Tomball, TX; ⁷Houston Fertility Institute, Houston, TX.

OBJECTIVE: To investigate whether occurrence of monzygotic twin (MZT) in human in vitro ferritization (IVF) and embryo transfer is associated with artificial zona pellucida (ZP) manipulations.

MATERIALS AND METHODS: A retrospective cohort study was performed in a private fertility clinic. This study includes 5387 clinical pregnancies (cardiac activity under ultrasonography) after single embryo transfer from 2016-2021 (373 from fresh embryo transfers and 5014 from frozen embryo transfers). Out of fresh embryo transfers, 29 pregnancies had blastocyst biopsy, while others did not undergo any ZP manipulations. All frozen embryo transfers had either biopsy and/or blastocyst collapse by using laser biopsy, while others did not undergo any ZP manipulations. All frozen embryo transfers had either biopsy and/or blastocyst collapse by using laser biopsy, while others did not undergo any ZP manipulations.

RESULTS: There were statistically significant differences between the MZT and other pregnancies as regarding miscarriage rate and live birth rate.

IMAPCT STATEMENT: The use of triploline 0.1mg to progesterone in fresh antagonist ICSI cycles as a luteal phase support was associated with higher clinical pregnancy rate.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. (%)</th>
<th>Study (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy rate</td>
<td>8/45 17.8%</td>
<td>20/45 46.4%</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>6/117 5.1%</td>
<td>28/118 23.7%</td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>5/45 11.1%</td>
<td>19/45 42.2%</td>
</tr>
<tr>
<td>miscarriage rate</td>
<td>2/45 4.4%</td>
<td>4/45 8.9%</td>
</tr>
<tr>
<td>Live birth rate</td>
<td>4/45 8.9%</td>
<td>16/45 35.6%</td>
</tr>
<tr>
<td>Progesterone level</td>
<td>Median (Range)</td>
<td>35.9 (15.3-127.8)</td>
</tr>
</tbody>
</table>

A significant P value was considered when it is <0.05.

Two patients in the control group were tubal ectopic pregnancy.

P-135 6:30 AM Monday, October 24, 2022

Single Dose Triptorelin 0.1 Mg As a Luteal Phase Support in Antagonist Intracytoplasmic Sperm Injection (ICSI) Cycles. sherif M. Badran, MD, ¹Kamal M. Zahran, MD, ¹Tarek Farghaly, MD, ¹Azza Abouelfadle, MD, ¹Moustafa M. Abouelela, MD, ¹Ihab M. Elnashar, MD ²Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; ³Faculty of Medicine, Department of Clinical Pathology, Assiut university, Assiut, Egypt.

OBJECTIVE: To compare the effect of luteal phase support using progesterone and triptorelin versus progesterone alone on the reproductive outcomes of antagonist ICSI cycles.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control (n = 45)</th>
<th>Study (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy rate</td>
<td>8/45 17.8%</td>
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</tr>
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<td>Live birth rate</td>
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<td>16/45 35.6%</td>
</tr>
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</table>

A significant P value was considered when it is <0.05.

Two patients in the control group were tubal ectopic pregnancy.

Median (Range) 35.9 (15.3-127.8) 135.4 (31.0-300.8) 0.000*
single embryo transfer. With regards to fresh blastocyst transfer, the rate of MZT following of biopsy was significantly higher than blastocysts that did not undergo any ZP manipulation (3.4% vs. 0.29%; p=0.025). All frozen blastocysts underwent ZP manipulation (either blastocyst biopsy and/or blastocyst collapse before freezing). The rate of MZT was significantly higher in those blastocysts that did not undergo partial ZP cutting to expand the ZP opening after warming than blastocysts that underwent partial ZP cutting (2.79% vs 0.48%; p=0.00001). Furthermore, when the ZP opening was enlarged using ZP cutting following warming, there was no difference in rates of MZTs between biopsied and non-biopsied blastocysts (0.86% vs. 0.48%; p=0.109).

CONCLUSIONS: Our data suggest that ZP manipulations by biopsy, assisted hatching and blastocyst collapse (which creates smaller ZP openings) are associated with an increase in the rate of MZT in both fresh and frozen embryo transfers. This appears to be mitigated by creating a larger opening in the ZP post warming. As cryopreservation, blastocyst collapse and embryo biopsy are routine laboratory procedures, we would recommend creating a larger opening in the ZP post warming, prior to frozen embryo transfer to lower the risk of MZT associated with routine ZP manipulations.

IMPACT STATEMENT: This study may provide recommended method and/information to reduce the rate of MZT associated with human IVF.

SUPPORT: NA

P-136 6:30 AM Monday, October 24, 2022

INTRACYTOPLASMIC SPERM INJECTION (ICSI) DOES NOT IMPROVE OUTCOMES IN NON-MALE FACTOR PATIENTS. Deina R. Bossa, M.D., 1 Kevin J. Doody, M.D. 1,2 University of Texas Southwestern Medical Center, Dallas, TX; 3 CARE Fertility, Bedford, TX.

OBJECTIVE: Intracytoplasmic sperm injection (ICSI) is a method to improve fertilization among couples with male factor infertility. ICSI increases the cost of IVF cycles. The rate of ICSI is increasing among IVF cycles with non-male factor infertility. The purpose of this study was to examine if ICSI use increased the live birth rate among couples undergoing IVF with non-male factor infertility using the most recent SART national summary report.

MATERIALS AND METHODS: SART 2020 preliminary national summary report was filtered for live birth rates among first transfer, own egg cycles using all cycles types (minimal stimulation, natural cycle, conventional stimulation, and in vitro maturation) and all fertility diagnoses in the report. Gestational carrier cycles were excluded. Live birth rates were stratified by age group per the report (<35, 35 – 37, 38 – 40, 41 – 42, >42). Fertility diagnoses were then grouped into “male factor” and “non-male factor”. The live birth rate among male factor and non-male factor diagnoses was calculated when ICSI was excluded and with only ICSI use. The non-ICSI live birth rate was corrected to account for canceled cycles. Fisher’s exact test was used to calculate statistical significance.

RESULTS: Among couples with male factor infertility, there was a statistically significant increase in the live birth rate when ICSI was used for ages <35, 35 – 37, 38 – 40, and >42 (see Figure 1). Among couples with non-male factor infertility, there was no statistically significant increase in the live birth rate when ICSI was used for ages <35, 35 – 37, 38 – 40, and 41 – 42 (see Figure 2). Among couples with non-male factor infertility and ages >42, there was a statistically significant decrease in the live birth rate with ICSI use (see Figure 2).

CONCLUSIONS: ICSI use is not associated with increased live birth rate among couples with non-male factor infertility.

IMPACT STATEMENT: Increased cost of ICSI must be balanced against evidence based benefits to its use. This study shows that ICSI use does not provide increased benefits in couples with non-male factor infertility.

P-137 6:30 AM Monday, October 24, 2022

EFFECTIVE UNIVERSAL WARMING-DILUTION OF BLASTOCYSTS VITRIFIED ON AN OPEN DEVICE SYSTEM. Mitchel C. Schiewe, MS, PhD; Jose R. Vaca, B.S.; Pedro J. Toledo, BS; James Stachecki, PhD; Richard P. Marrs, MD 1 Ovation Fertility, Newport Beach, CA; 2 ART Lab, Beverly Hills, CA; 3 California Fertility Partners, Los Angeles, CA; 4 Innovative Cryo Enterprises II LLC, Wayneville, NC; 5 California Fertility Partners, Los Angeles.

OBJECTIVE: Universal warming protocols for vitrified embryos have been previously validated in our lab for a closed system. The goal of this study is to verify the effectiveness of different non-permeating sugar solutions for post-warming dilution of blastocysts vitrified on an open system when alternatives to their typical commercial products are needed. A prospective, randomized study of patient consented research discard blastocysts (>2BB quality) was conducted in an apriori arrangement of 4 sugar solution treatments post-warming: A) fresh Irvine Sci./FF Vit Warm kit solutions (TS/DS); B) frozen-thawed Irvine Sci./FF TS/DS solutions (i.e., flash frozen in LN2); C) 1M sucrose; and D) 10% honey (commercial grade, multi-floral). Our null hypothesis was that fresh commercial thaw solutions are required to maximize the viability of ultra-rapid vitrified blastocysts.

MATERIALS AND METHODS: Blastocysts vitrified on Cryolocks in Irvine Sci./FF VX Vit kit solutions (30% EG/DMSO) were rapidly warmed in 1 of 4 solution treatment groups. This training study included 30 blastocysts per group accounting evenly for quality and batch effects before randomly assigning the treatment. Solutions A and B were commercial IS/FF products (TS/DS)/methodology, whereas C and D were lab-made, filtered stock LG-

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**Figure 1: Male factor**

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt;35</th>
<th>&lt;35-37</th>
<th>35-37</th>
<th>38-40</th>
<th>41-42</th>
<th>&gt;42</th>
</tr>
</thead>
<tbody>
<tr>
<td># retrievals</td>
<td>567</td>
<td>14298</td>
<td>408</td>
<td>7667</td>
<td>333</td>
<td>6211</td>
</tr>
<tr>
<td>Live birth rate (%)</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0003</td>
<td>0.26</td>
<td>0.0079</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.00001</td>
<td>0.00001</td>
<td>0.26</td>
<td>0.0079</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 2: Non-male factor**

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt;35</th>
<th>&lt;35-37</th>
<th>35-37</th>
<th>38-40</th>
<th>41-42</th>
<th>&gt;42</th>
</tr>
</thead>
<tbody>
<tr>
<td># retrievals</td>
<td>4160</td>
<td>15598</td>
<td>2643</td>
<td>11424</td>
<td>2571</td>
<td>11901</td>
</tr>
<tr>
<td>Live birth rate (%)</td>
<td>0.677</td>
<td>0.1662</td>
<td>0.6183</td>
<td>0.5617</td>
<td>&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.677</td>
<td>0.1662</td>
<td>0.6183</td>
<td>0.5617</td>
<td>&lt;0.00001</td>
<td></td>
</tr>
</tbody>
</table>
pernumery embryos to cryopreserve, AH in early blastocysts can improve rates of BCP, CPR, and LBR for fresh cycle transfers. Although the exact mechanism is unknown, the likely benefit of AH is an enhanced interaction between the harnessed trophectoderm generated by AH and the endometrial epithelium.

IMPACT STATEMENT: AH should be considered for fresh Day 5 early blastocyst transfers, especially in patients with poor prognosis or slow blastocyst development.

SUPPORT: None

P-139 6:30 AM Monday, October 24, 2022
SINGLE STEP VERSUS SEQUENTIAL CULTURE MEDIUM: WHICH IS BETTER FOR OLDER PATIENTS TO IMPROVE BLASTOCYST QUALITY AND ENUPLAUPH RATE? A PROSPECTIVE STUDY. Manar Hozyen, MSc.1 Amr Elshimy, BSc.2 Yasmin sayed Azzouz, BSc.1 Hosam H. Zaki, M.B.B.CH. M.D., M.SC.2 1Ganin Fertility Center IVF lab, Cairo, Egypt; 2Ganin Fertility Center, Cairo, Egypt.

OBJECTIVE: To determine if embryos from older ICSI patients will develop better in one type of embryo culture medium over the other.

MATERIALS AND METHODS: This study of 1120 mature oocytes (MII) from 143 couples that underwent ICSI from June 2020 to April 2021. Female age ≥37 years, had at least one MII, and all patients had ejaculated sperm with normal parameters according to WHO 2010. PGT-A was done for high-quality blastocysts with ≥4BB grade (according to Gardner’s criteria 1999). In total of 481 MII were cultured in continuous single culture-NX media (CSC-NX) with 10% SSS (Irvine Scientific, USA) while 639 MII were cultured in sequential cleavage and blastocyst media with 10% SPS (SAGE, Denmark). Data were analyzed using SPSS (version 23).

RESULTS: There were no significant differences in the female age, number of retrieved, MII oocytes or semen parameters between the two groups. The main results are shown in the table.

CONCLUSIONS: Embryos from ICSI patients over 37 years old had comparable results when cultured in single step or sequential media. In case of PGTa+ results, despite the non-significance in euploidy rates; there is a significantly lower aneuploidy rate in blastocysts cultured in sequential media, which would increase the available embryos for transfer even with the higher mosaicism rate. As the mosaic embryos may develop into normal healthy babies.

IMPACT STATEMENT: Although our study has a relatively low sample size, it sheds light on a better approach in culturing human embryos from older patients undergoing ICSI. As those patients already have smaller number of mature oocytes and good quality embryos and lower chances of pregnancies compared to younger patients, the use of sequential culture media might improve their chances of getting suitable blastocysts for transfer.

P-140 6:30 AM Monday, October 24, 2022
INTRAUTERINE INFUSION OF G-CSF JUST BEFORE EMBRYO TRANSFER MAY IMPROVE THE EMBRYO IMPLANTATION RATE FOLLOWING IVF/ICSI IN PATIENTS WITH RECURRENT IMPLANTATION FAILURE. Chung-Hoon Kim, M.D., Ph.D.1,2 Jei-Won Moon, M.D.1 Sungwook CHOL, M.D.1,2 Shin Yong Moon, M.D., Ph.D.1 1 Fertility Center, Seoul, Korea, Republic of (South); 2Fertility Clinic, Seoul, Korea, Republic of (South).

OBJECTIVE: This study was performed to investigate the effect of intrauterine infusion of granulocyte colony-stimulating factor (G-CSF) just before embryo transfer (ET) on pregnancy and implantation rates following IVF/ICSI in patients with recurrent implantation failure (RIF).

MATERIALS AND METHODS: A total of 115 consecutive IVF-ET cycles in 115 patients with RIF who underwent IVF-ET between May 2018 and Jan 2022 was included in this retrospective cohort study. RIF is defined as the failure to achieve a clinical pregnancy after the transfer of good quality embryos in a minimum of three fresh or frozen cycles to a woman under the age of 40 years. In 50 patients of 115, 100µg (0.3ml) of G-CSF was slowly infused in the uterine cavity using a soft ET catheter 1-2 min before ET. Sixty-five patients who did not receive intrauterine G-CSF infusion before ET were served as controls. In all subjects, embryo glue (hyaluronic acid-
enriched transfer medium, HETM) was used as an embryo media and GnRH antagonist protocol was used for controlled ovarian stimulation (COS). If patients underwent two or more cycles of IVF/ICSI during the study period, charts corresponding to the 1<sup>st</sup> IVF/ICSI cycle were reviewed and data of other IVF/ICSI cycles except 1<sup>st</sup> cycle were excluded from this analysis. Student’s t-test was used to compare mean values. Chi-square test and Fisher’s exact test were used to compare fraction. Statistical significance was defined as P<0.05. All analyses were performed by using SPSS statistical package for Windows, version 11.0.

RESULTS: The demographic characteristics of subjects were comparable between the treatment and control groups. There were no differences in the two groups with respect to total dose and days of gonadotropins used for treatment and control. There were no differences in the study. Autologous MSC in the adipose tissue’s stromal vascular fraction (SVF) was placed in the patient’s uterine cavity to improve endometrial quality. Micro liposuction was performed to obtain 20 ml of abdominal fat. Adipose tissue was washed, mechanically disaggregated, and treated with collagenase type I to isolate SVF. Isolated cells were counted, and trans-myometrial injection. Changes in EMT were monitored for at least three months. Embryos were thawed and transferred during controlled endometrial development cycles. Embryo implantation was determined on Day 14 by serum β-hCG concentrations (>10 mU/ml), and clinical pregnancy was confirmed by the presence of a fetal heartbeat using ultrasound at six weeks.

RESULTS: Fourteen patients underwent the MSC uterine enrichment treatment, which significantly improved the endometrial mean thickness (3.5 ± 2.6 mm, p < 0.0001) in the 14 patients. No adverse effects attributable to the cellular product or its application were reported. Three patients got pregnant spontaneously after MSC application (21.43 %), and 11 patients underwent FET with seven cycles with implanted embryos, giving a current implantation rate of 64.29%. Implanted embryos resulted in six ongoing clinical pregnancies (43.86 %) and one live birth without complications (7.14 %).

CONCLUSIONS: Trans-myometrial implantation of MSC cells in the stromal vascular fraction of adipose tissue improve reproductive outcomes. Here, we demonstrate that using autologous MSC in SVF to enrich the endometrial niche is a novel alternative to endometrial improvement.

IMPACT STATEMENT: MSC application is a novel tool in ART to improve endometrial quality in patients with refractory endometrium or Asherman’s syndrome to achieve pregnancy.

SUPPORT: None

E-PAPER ABSTRACT SESSION: 15

P-141 6:30 AM Monday, October 24, 2022

TRANS MYOMETRAL INJECTION OF AUTOLOGOUS MESENCHYMAL STEM CELLS IMPROVES ENDOMETRIAL QUALITY AND ART RESULTS IN PATIENTS WITH REFRACTORY ENDOMETRIUM OR ASHERMAN’S SYNDROME. Dinorah Hernandez-Melchor, B.Sc.1, Ginna Milena Ortiz, MD.2, Ivan Madrazo, M.D.2, Juan José Suarez, MD.2, Norma Indira Barrera Vargas, M.B.3, M.B.B.S.3, M.SC.3, America Padilla, PhD.3, Esther Lopez-Bayghen, PhD1, Cinvestav-Ipa, Mexico, TL, Mexico; 1Ingenes Mexico, Mexico City, DF, Mexico; 2Instituto de Infertilidad y Genética Puebla SC, Puebla, PU, Mexico; 3CINVESTAV, Ciudad DE Mexico, Mexico; 1Centro de Investigación y Estudios Avanzados IPN, México, EM, Mexico.

OBJECTIVE: In patients with Asherman’s syndrome and other conditions affecting the endometrial layer in the uterus, endometrial dysfunction is the rate-limiting step in ART procedures. Ineffectivity associated with a lack of endometrial responsiveness is a hard-to-treat condition to achieve pregnancy that, to date, has not been solved. Here we explore mesenchymal stem cells (MSC) to regenerate endometrial tissue, support endometrial thickening, and development to allow embryo implantation, and achieve pregnancy in infertile women.

MATERIALS AND METHODS: Women between 32 and 51 years with a history of at least 2 failed IVF cycles and suboptimal endometrial quality (Asherman’s syndrome or persistent refractory endometrium) were enrolled in the study. Autologous MSC in the adipose tissue’s stromal vascular fraction (SVF) was placed in the patient’s uterine cavity to improve endometrial quality. Micro liposuction was performed to obtain 20 ml of abdominal fat. Adipose tissue was washed, mechanically disaggregated, and treated with collagenase type I to isolate SVF. Isolated cells were counted, and trans-myometrial injected. Changes in EMT were monitored for at least three months. Embryos were thawed and transferred during controlled endometrial development cycles. Embryo implantation was determined on Day 14 by serum β-hCG concentrations (>10 mU/ml), and clinical pregnancy was confirmed by the presence of a fetal heartbeat using ultrasound at six weeks.

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CONCLUSIONS: Trans-myometrial implantation of MSC cells in the stromal vascular fraction of adipose tissue improve reproductive outcomes. Here, we demonstrate that using autologous MSC in SVF to enrich the endometrial niche is a novel alternative to endometrial improvement.

IMPACT STATEMENT: MSC application is a novel tool in ART to improve endometrial quality in patients with refractory endometrium or Asherman’s syndrome to achieve pregnancy.

SUPPORT: None

FERTILITY & STERILITY®

P-142 6:30 AM Monday, October 24, 2022

AUTOLOGOUS PLATELET-RICH PLASMA TREATMENT IMPROVES EMBRYO IMPLANTATION AND CLINICAL PREGNANCY RATES IN WOMEN UNDERGOING ASSISTED REPRODUCTION: A PILOT STUDY AND SYSTEMATIC REVIEW. Dinorah Hernandez-Melchor, B.Sc.1, Hector Jesus Carrillo Vidrio, MD.2, Martin Rivera, M.D., M.SC.3, M. Elba Gonzalez-Mejia, MD, PhD,4 Leonardo M. Porchia, PhD,5 America Padilla, PhD6, Esther Lopez-Bayghen, PhD7, Science, Technology and Society Program, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Mexico; 4Benemérita Universidad Autónoma De Puebla, Puebla, PU, Mexico; 5Instituto de Investigaciones en Biología del Desarrollo, Secretaría de Educación Pública, Mexico; 6CINVESTAV, Ciudad DE Mexico, Mexico; 7Centro de Investigación y Estudios Avanzados IPN, México, EM, Mexico.
OBJECTIVE: There are limited options to improve embryo implantation in patients with refractory thin endometrium [endometrial thickness (EMT) <7 mm] and recurrent implantation failure. Some studies have demonstrated a benefit from intrauterine autologous platelet-rich plasma (PRP); however, the results are conflicting. Therefore, we conducted a self-controlled retrospective survey as well as a meta-analysis.

MATERIALS AND METHODS: Women with at least two failed IVF cycles and refractory thin endometrium were enrolled. They were treated three times with an intrauterine infusion of PRP on day 10 of the menstrual cycle within a frozen-thawed embryo transfer cycle. For the meta-analysis, PubMed, SCOPUS, EBSCO, and LILACS databases were searched for studies investigating PRP's effect on implantation and clinical pregnancy rates (IR and CPR, respectively). Random effects were used to calculate the pooled Risk Ratio (RR) and 95% confidence intervals (95% CI). No publication bias was detected.

RESULTS: Thirty-eight patients underwent the PRP treatment, which significantly improved the EMT (2.2±0.7 mm, p<0.001). There was no difference in a net increase in the EMT when stratified by IVF outcome. Only 32 underwent FET, in which 21 cycles the embryos were implanted (63.6%), which was a significantly improved from the previous cycle (vs. 3.13%, p<0.001). CPR also significantly improved with the PRP treatment over the previous cycle (63.64% vs. 3.02%, p<0.001). For the meta-analysis, 19 studies were included. For IR, 15 publications (cases=980 and controls=818) showed there was a significant benefit using PRP (RR=1.74, 95% CI: 1.39-2.17, p<0.001). For CPR, 18 publications (cases=804 and controls=763) showed that using PRP improved CPR (RR=1.73, 95% CI: 1.38-2.17, p<0.001).

CONCLUSIONS: Using a three-dose scheme of intrauterine infusion of autologous PRP improves ART outcomes at three levels: EMT, embryo implantation rate, and clinical pregnancy rate of women suffering from refractory thin endometrium and recurrent implantation failure. Our results agreed with other studies, as shown in the systematic review. This work provides more evidence for PRP use when achieving clinical pregnancy during IVF.

IMPACT STATEMENT: Intrauterine infusion of autologous PRP improves the embryo implantation rate and the clinical pregnancy rate of women suffering from refractory thin endometrium and recurrent implantation failure.

SUPPORT: None

P-144 6:30 AM Monday, October 24, 2022

SUBENDOMETRIAL AUTOLOGOUS PLATELET-RICH PLASMA INJECTION IN PATIENTS WITH UNSUSPICIOUS THIN ENDOMETRIUM UNDERGOING FROZEN-THAWED EMBRYO TRANSFER. Yigit Cakiroglu, M.D., Yunus Aytaç Tohma, M.D., Aysen Yuceturk, M.D., Ozge Karasomatoglu, M.D., Sule Yildirim Kopuk, M.D., Zeynep Ece Utkan Korun, M.D., Caglar Yazicioglu, M.D., Richard T. Scott, Jr., M.D., Bulent Tiras, M.D., Hulusi Bulent Zeyneloglu, M.D., Enel Seli, MD, Acibadem Mehmet Ali University Departments of Obstetrics and Gynecology, Istanbul, Turkey; Bahceci Saglik Grubu, Ankara, Turkey; Acibadem Maslak Hospital Assisted Reproductive Techniques Unit, Istanbul, Turkey; 1TVI RMA New Jersey, Basking Ridge, NJ; 2Femart Clinic, Turkey.

OBJECTIVE: The aim of the current study was to investigate the effects of subendometrial PRP injection on endometrial thickness and pregnancy outcomes in patients with a history of unresponsive thin endometrium undergoing frozen-thawed embryo transfer (FET).

MATERIALS AND METHODS: Women with a history of suboptimal endometrial proliferation (<7 mm) after hormone replacement therapy for FET were offered to participate in the study. Those who accepted and gave consent for subendometrial PRP injection formed Group 1 (n=100). Those who accept the PRP injection formed the control group (Group 2; n=100). Autologous PRP was prepared by centrifugation from peripheral blood, and was injected transvaginally into the subendometrial region under ultrasound guidance within 10 days of the cessation of the menstruation. On the 2-4th days of the second menstrual cycle after the PRP procedure, hormonal treatment was initiated with 14 days of oral estradiol (2×2 mg for 5 days, 3×2 mg for 4 days, and 4×2 mg for 5 days). Women who were found to have adequate endometrial thickness (>7 mm) received vaginal progesterone (8% gel) twice a day and 50 mg intramuscular progesterone twice a day. Embryo transfer was scheduled 116-120 hours after the initiation of progesterone. Pregnancy (positive serum hCG) and sustained implantation (>8 weeks) outcomes were followed.

RESULTS: A total of 200 women (age 36.4±5.8) were included in the study. PRP and control groups were not different in mean age (36.9±5.7 vs 35.9±5.7; p=0.25) or BMI (26.7±5.8 vs 26.0±4.9; p=0.35). PRP treatment resulted in higher endometrial thickness compared to the control group (7.7±1.9 mm vs 6.1±1.2 mm; p<0.01). In the PRP group, 3 women (3.0%) conceived spontaneously and 97 (97.0%) attempted FET; in the control group there were no spontaneous pregnancies. In the PRP group, 33/97 women (34.0% of total) could not undergo ET due to persistent unresponsive thin endometrium or fluid in the endometrial cavity, compared to 75/100 (75% of total) in controls (p<0.001). Pregnancy and sustained implantation rates were 24.7% (24/97) and 14.4% (14/97) of the total for the PRP group, compared to 9.0% (9/100) and 2% (2/100) in controls (p=0.003 and p=0.001, respectively). In the subgroup of patients who had PGT-A followed by euploid single FET, those treated with PRP had 8/18 (44.4%) pregnancy and 6/18 (33.3%) sustained implantation, while patients in the control group had 4/8 (50.0%) pregnancy and 1/8 (12.5%) sustained implantation (p=0.793 and p=0.098 respectively).

CONCLUSIONS: In women with a history of suboptimal endometrial development, subendometrial PRP injection resulted in improved endometrial thickness and a cumulative (spontaneous and following FET) sustained implantation rate of 16.0%.

IMPACT STATEMENT: Subendometrial injection of autologous PRP might be considered in women with unresponsive thin endometrium. For wider clinical application, its clinical efficacy will need to be demonstrated in prospective randomized clinical trials.

P-144 6:30 AM Monday, October 24, 2022

CLUSTER ANALYSIS: RATES OF FAVORABLE AND UNFAVORABLE VAGINAL BLEEDING PATTERNS WITH ONGOING DROSPIRENONE 4MG EXPOSURE BASED ON EARLY BLEEDING PATTERN. David F. Archer, MD, Alicyay Angulo, MD, Patricia Murphy, MD, Megan L. Gilbert, MSN, Michael Krychman, MD, Eastern Virginia Medical School, Norfolk, VA; Chemo Research, S.L., Madrid, Spain; Exelis, Madrid, Spain; Exelis USA Inc, Florham Park, NJ; The Southern California Center for Sexual Health and Surviv- orship Medicine, Newport Beach, CA.

OBJECTIVE: This study aims to determine if the bleeding pattern observed during the first reference period of drosipirenone 4mg exposure (cycles 2-4) could predict the future bleeding pattern with ongoing medication usage.

MATERIALS AND METHODS: A post-hoc analysis was performed on the study data from two phase III clinical trials to assess the efficacy, safety, and tolerability of drosipirenone 4mg. One trial was an open-label study lasting 13 exposure cycles (N=713) and one study was a double-blind comparative trial (N=858) with desogestrel 75mcg (N=332) lasting 13 exposure cycles. Bleeding patterns were considered favorable if they consisted of regular bleeding, infrequent bleeding, or amenorrhea. Other bleeding patterns were considered unfavorable, regular bleeding lasting longer than 14 days was also considered unfavorable. Inconsistent usage was defined as ≥4 missed tablets in a single exposure cycle, or ≥2 consecutive missed tablets. A cluster analysis was used to generate a shift table to determine if the early bleeding pattern was correlated with the future bleeding pattern; rates of favorable and unfavorable bleeding patterns were also calculated.

RESULTS: A favorable bleeding pattern during cycles 2-4 was associated with a favorable bleeding pattern for 94.8%-95.1% of participants in future reference periods. An unfavorable bleeding pattern during cycles 2-4 was associated with an unfavorable bleeding pattern for 36.5% of participants in cycles 5-7, dropping to 28.6% of participants in cycles 11-13. A favorable bleeding pattern was reported by 81.5% of patients in cycles 2-4, 87.8% in cycles 5-7; 91.7% in cycles 7-9; 90.1% in cycles 8-10; and 90.3% in cycles 11-13.

CONCLUSIONS: A favorable bleeding pattern during the first reference period is highly predictive of a persistently favorable bleeding pattern. More than 60% of individuals with an unfavorable bleeding pattern during the first reference period (cycles 2-4) converted to a favorable bleeding pattern during the second reference period (cycles 5-7). By cycles 11-13 90.3% of patients experienced a favorable bleeding pattern.

IMPACT STATEMENT: Nearly all patients experienced a favorable bleeding pattern with continued drosipirenone usage.

SUPPORT: This study was funded by Exelis.
OBJECTIVE: The increase of genetic testing to inform prevention and treatment of hereditary cancer has led to an increase in identifying people having a pathogenic variant—referred to as “at-risk.” At-risk patients of reproductive age and their partners often have concerns (e.g., beliefs about passing the variant to future children, need for discussing family building options, and emotional decision-making). This study explored the impact of the CARING (Communicating About Reproduction and Inherited Genes) tool—a pilot intervention designed to facilitate effective communication about family building concerns and encourage communicated perspective taking (CPT) in light of inherited cancer risk (ICR).

MATERIALS AND METHODS: A single-arm pilot with structured discussion tasks about family building concerns and decisions was completed over two time points (Time 1: May–June 2020 and Time 2: July–September 2020). Social media and snowball sampling were utilized to recruit couples over two time points (Time 1: May-June 2020 and Time 2: July-September 2020). Interviews, couples stated the discussion task helped them discuss each other’s perspectives on family building options and how and why certain options were prioritized and vital to future family building decisions. Second, couples noted the task prompted them to discover and/or confront discordant concerns. Discovering discordant concerns sometimes resulted in highlighting relational conflict, suggesting low levels of CPT. However, discovering discordant concerns was not always negative. For some, learning about their discordant concerns allowed them to take note of their partners’ unique perspectives and identify new options to consider. Finally, couples noted the task helped them work through and agree upon next steps for having children. That is, the discussion task’s focus on discussing concerns about family building and ICR. In contrast to organic conversations, in the dyadic interviews, couples stated the discussion task helped them discuss each other’s perspectives on family building options and how and why certain options were prioritized and vital to future family building decisions. Second, couples noted the task prompted them to discover and/or confront discordant concerns. Discovering discordant concerns sometimes resulted in highlighting relational conflict, suggesting low levels of CPT. However, discovering discordant concerns was not always negative. For some, learning about their discordant concerns allowed them to take note of their partners’ unique perspectives and identify new options to consider. Finally, couples noted the task helped them work through and agree upon next steps for having children. That is, the discussion task’s focus on discussing concerns about family building and ICR.

RESULTS: Analysis revealed three themes. First, at-risk patients and partners noted the discussion task helped them realize concordant concerns about family building and ICR. In contrast to organic conversations, in the dyadic interviews, couples stated the discussion task helped them discuss each other’s perspectives on family building options and how and why certain options were prioritized and vital to future family building decisions. Second, couples noted the task prompted them to discover and/or confront discordant concerns. Discovering discordant concerns sometimes resulted in highlighting relational conflict, suggesting low levels of CPT. However, discovering discordant concerns was not always negative. For some, learning about their discordant concerns allowed them to take note of their partners’ unique perspectives and identify new options to consider. Finally, couples noted the task helped them work through and agree upon next steps for having children. That is, the discussion task’s focus on discussing concerns about family building and ICR. In contrast to organic conversations, in the dyadic interviews, couples stated the discussion task helped them discuss each other’s perspectives on family building options and how and why certain options were prioritized and vital to future family building decisions. Second, couples noted the task prompted them to discover and/or confront discordant concerns. Discovering discordant concerns sometimes resulted in highlighting relational conflict, suggesting low levels of CPT. However, discovering discordant concerns was not always negative. For some, learning about their discordant concerns allowed them to take note of their partners’ unique perspectives and identify new options to consider. Finally, couples noted the task helped them work through and agree upon next steps for having children. That is, the discussion task’s focus on discussing concerns about family building and ICR.

CONCLUSIONS: This tool is the first developed for couples with inherited cancer risk. It is novel as it includes partners of at-risk patients as instrumental stakeholders in reproductive health decision making. By providing structured time and facilitating communication between couples, the CARING tool helps at-risk patients and their partners reach an agreement about completing their families while considering the patient’s inherited cancer risk, ultimately impacting their healthcare decision making.

IMPACT STATEMENT: The CARING tool may aid reproductive and genetic clinicians in pre-counseling sessions with couples interested in family building and assisted reproductive technology.

SUPPORT: Marleah Dean, PhD was supported by an Institutional Research Grant, IRG-17-173-22 from the American Cancer Society.
LOW ANTIMÜLLERIAN HORMONE LEVEL IS NOT ASSOCIATED WITH ANEUPLOIDY IN MISCARRIAGES FROM PREGNANCIES CONCEIVED WITH ASSISTED REPRODUCTIVE TECHNOLOGY. Jenny Lin, BA,1 Phillip A. Romanski, MD, MSc,1 Pietro Bortolotto, MD, MSc,2 Alexis P. Melnick, MD1 New York, NY; 2NewYork-Presbyterian Hospital/Weill Cornell Medical Center, Boston, MA; 3Ronald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY.

OBJECTIVE: Antimüllerian hormone (AMH) level is a well-established quantitative marker of ovarian reserve. However, some studies have shown that low AMH may be associated with increased risk of miscarriage, suggesting that AMH could be associated with oocyte and embryo quality. The objective of this study was to assess the association between AMH level and aneuploidy in miscarriages after undergoing embryo transfer to determine whether AMH may be associated with embryonic aneuploidy.

MATERIALS AND METHODS: All assisted reproductive technology cycles resulting in clinical pregnancy loss (defined as pregnancy loss prior to 20 weeks’ gestation) at our center between 01/01/2012 and 06/30/2021 were analyzed for potential inclusion. Inclusion criteria were AMH ≤ 0.4 ng/mL, measured within one year of ovarian stimulation cycle start, singleton gestation, and cytogenetic analysis of products of conception. Patients with pregnancy conceived via donor oocyte, use of preimplantation genetic testing for aneuploidy, hormonal contraceptive use within 3 months of AMH measurement, or history of chemotherapy and/or radiation were excluded. Patients with AMH > 0.4 to 1.0 and AMH ≥ 1 were age-matched 3:1 to the AMH < 0.4 group. The AMH > 0.4 to 1.0 group did not have enough patients to meet inclusion criteria in the AMH ≥ 1 group; therefore, all patients were included in the AMH < 0.4 group. The primary outcome was the incidence of aneuploid products of conception. A chi-square test was used to compare proportion of aneuploid, mosaic, and euploid products of conception across the three groups.

RESULTS: A total of 33 patients with AMH ≤ 0.4 were included and age-matched to the AMH > 0.4 to 1.0 (n=48) and AMH ≥ 1 (n=99) groups. The proportion of aneuploid products of conception in the AMH ≤ 0.4 group was 63.6% (n=21) compared to 81.3% (n=39) in the AMH > 0.4 to <1 group, and 73.7% (n=73) in the AMH ≥ 1 group, which was not significantly different between the groups (p=0.32). The proportion of mosaic products of conception in the AMH ≤ 0.4 group was 3.0% (n=1) compared to 0.0% (n=0) in the AMH > 0.4 to <1 group, and 2.0% (n=2) in the AMH ≥ 1 group, which was again not significantly different between the groups (p=0.53). Further, there was no significant difference in the incidence of euploid products of conception among the three groups (p=0.21).

CONCLUSIONS: Overall, AMH level was not associated with the incidence of aneuploidy among miscarriage products of conception in our study. Compared to age-matched controls with AMH > 0.4 to < 1 and AMH ≥ 1, patients with AMH ≤ 0.4 did not have significantly different rates of aneuploid, mosaic, or euploid products of conception.

IMPACT STATEMENT: There is limited data to suggest that low AMH increases the risk of miscarriage; our results suggest that there is no association between low AMH and embryo chromosomal abnormalities. Other causes for low AMH associated with miscarriage, such as issues related to the corpus luteum or endometrial microenvironment, should be further explored.

DOES THE TROPHOBLASTIC BIOPSY FOR PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) IMPACT EARLY EMBRYO DEVELOPMENT: AN ASSESSMENT OF EARLY PREGNANCY TRANSVAGINAL ULTRASOUND (TVUS) MEASUREMENTS. Meridith Pollie, BS.1 Phillip A. Romanski, MD, MSc.2 Steven D. Spandorfer, MD3 Weill Cornell Medical Center; 2New York, NY; 3NewYork-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY.

OBJECTIVE: To evaluate the impact of trophoblastic biopsy on early growth of normally developing embryos as measured by TVUS.

MATERIALS AND METHODS: We conducted a retrospective cohort study of infertile patients who underwent a euploid frozen embryo transfer from autologous oocytes resulting in a singleton intrauterine pregnancy and live birth from 2017 to 2019. TVUS measurements of crown-rump length (CRL) and fetal heart rate (FHR) performed after the completed 6th week (6w0d – 6w6d) and completed 7th week (7w0d – 7w5d) of gestation were recorded and analyzed for patients who underwent PGT-A compared to unbiopsied embryos.

RESULTS: Of the 1005 included patients (571 PGT-A, 434 unbiopsied), 607 (60.4%) had a TVUS performed during the 6th week of pregnancy, and 716 (71.2%) had a TVUS performed during the 7th week of pregnancy. Among the 607 patients with a 6th week scan, 5 (1.5%) PGT-A embryos had absent fetal pole compared to 7 (2.6%) unbiopsied embryos, which was not statistically significant (RR 0.57 (0.18-1.79)). The incidence of absent FHR was 4.8% (n=16) of the PGT-A embryos compared to 7.0% (n=19) of the unbiopsied embryos, which again was not statistically significant (RR 0.68 (0.35-1.29)). Similarly, among the 716 patients with a 7th week TVUS, there were no statistically significant differences in mean CRL (12.2 ± 2.4 mm vs 12.0 ± 2.3 mm, β=0.01 (-0.01, 0.02)) or mean FHR (149.1 ± 12.8 bpm vs 147.7 ± 13.6 bpm, β=0.000 (0.00, 0.01)) in the PGT-A groups compared to the unbiopsied embryos.
CONCLUSIONS: Patients with a history of infertility undergoing frozen embryo transfer can be reassured that PGT-A has no association with early embryonic growth as measured by TVUS.

IMPACT STATEMENT: These findings further implicate that a PGT-specific growth curve does not need to be derived in order to accurately monitor first-trimester growth of embryos that have undergone PGT-A.

SUPPORT: N/A

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<td>Unbiopsied (n = 270)</td>
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<td>Fetal heartbeat absent</td>
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<th><strong>7th week of gestation</strong></th>
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<tr>
<td>Unbiopsied (n = 322)</td>
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<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Median cycle day</td>
</tr>
<tr>
<td>Mean CRL</td>
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<tr>
<td></td>
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<tr>
<td>Mean FHR</td>
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P-150 | 6:30 AM Monday, October 24, 2022

YEOUNGER WOMEN WITH DIMINISHED OOCYTE RESERVE (DOR) ARE MORE PRONE TO DELIVER BABIES WITH ANEUPLOIDY AS EVIDENCED BY NON-INVASIVE PREGNATAL TESTING. Nicole Weitz, D.O.,1 Jerome H. Check, M.D., Ph.D.,2 Carrie K. Wilson, B.A.,3 Ann DiAntonio, BSMT (ASCP),3 Megan Oneil, B.A.4 1Philadelphia College of Osteopathic Medicine, Philadelphia, PA; 2Cooper Medical School of Rowan University, Camden, NJ; 3Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ; 4Cooper Institute For Reproductive Hormonal Dis, Mount Laurel, NJ.

OBJECTIVE: To determine the risk of potentially having a baby born with trisomy 13, 18, or 21 in women with DOR.

MATERIALS AND METHODS: All women during a two-year time period who reached 10 weeks gestation with a live fetus, who also had non-invasive prenatal testing (NIPT), (Labcorp or Invitale) and who had serum anti-mullerian (AMH) levels obtained within 6 months of becoming pregnant, were identified. Women were included whether they conceived naturally or by in vitro fertilization-embryo transfer (IVF-ET) including fresh and frozen ETs. Only day 3 ETs were included, and thus there was no pre-implantation genetic testing for aneuploidy (PGT-A). The % of women having an NIPT demonstrating trisomy 13, 18, and 21 was determined according to DOR – serum AMH <1ng/mL vs. normal oocyte reserve (NOR) – serum AMH >1ng/mL.

RESULTS: There were 197 women who met the inclusion criteria. There were 146 with NOR and 51 with DOR. No women with NOR had a positive test for trisomy vs. 3 of 51 (5.9%) for DOR (two with trisomy 21 and one with trisomy 18), ages 39.9, 39.8 and 40.9. Thus, in the DOR group there were no test for trisomy vs. 3 of 51 (5.9%) for DOR (two with trisomy 21 and one with trisomy 18) ages 39.9, 39.8 and 40.9. Thus, in the DOR group there were no women with DOR who will deliver the baby before age 40.5 do not seem to have an increased risk of delivering an abnormal baby from aneuploidy. Though the numbers are small, and thus the results could be fortuitous, there may well be a trend for an increased risk of a baby born with trisomy 13, 18, or 21 if the women will deliver after age 40.5 compared to women with NOR at the same age who had no aneuploidy.

IMPACT STATEMENT: Understanding the differences between hCG values after fresh versus frozen-thawed transfers can assist clinicians in individualizing patient counseling regarding the likelihood of normally progressing pregnancy.

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P-151 | 6:30 AM Monday, October 24, 2022

DOES THE OPTIMAL HCG LEVEL FOR DISCRIMINATING NORMAL FROM ABNORMAL IN VITRO FERTILIZATION (IVF) PREGNANCIES DIFFER BETWEEN FRESH AND FROZEN-THAWED EMBRYO TRANSFERS? A SYSTEMATIC REVIEW. Sharon Galperin, MD,1 Julian A. Gingold, MD, PhD,1 Tova Niderberg, B.A.,2 Christie Leinbach Seaton, BA,3 Staci E. Pollack, M.D., M.S.1 Albert Einstein College of Medicine, Bronx, NY; 2Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY; 3Montefiore’s Institute for Reproductive Medicine & Health, Hartsdale, NY.

OBJECTIVE: To assess the effectiveness of hCG cutoff values in predicting live birth (LB) after fresh and frozen-thawed blastocyst embryo transfers.

MATERIALS AND METHODS: A systematic search of PubMed, Embase, and Google Scholar was conducted to identify studies evaluating hCG levels after IVF and pregnancy outcome. Medical Subject Headings (MeSH) terms included “In Vitro Fertilization”, “human chorionic gonadotropin”, “pregnancy outcome”, and “cutoff”, as well as synonyms. Studies were included if patients were adult females who underwent IVF with blastocyst stage embryo transfer and had a positive serum pregnancy test, measured on Day 12 after embryo transfer. The primary outcome was singleton LB. The data extracted was type of transfer (fresh vs. frozen-thawed), day of hCG measurement, and hCG cutoff calculated from a receiver operating characteristic (ROC) curve.

RESULTS: The search resulted in 1,510 abstracts that were screened and 157 full texts that were reviewed. 4 studies were included that contained a total of 2,334 transfers with positive serum pregnancy tests (356 fresh and 1978 frozen-thawed). There were 1,231 total LBs, with LB rates of 55% and 52% for fresh and frozen-thawed respectively. The two studies of frozen-thawed embryo transfers defined hCG cutoffs >350 IU/L, while the three studies of fresh embryo transfers reported values <300 IU/L. Of the studies that reported the sensitivity of optimal hCG values, sensitivities were 61.2 and 96.1 for fresh embryo transfers and 89.3 and 90.4 for frozen-thawed.

CONCLUSIONS: From this data, it appears that pregnancies resulting in live births after frozen-thawed embryo transfers have higher Day 12 hCG levels than after fresh embryo transfers. However, due to the heterogeneity of the optimal sensitivities reported by these studies, it is difficult to establish an ideal cutoff for hCG values associated with live birth in fresh and frozen-thawed transfers.

IMPACT STATEMENT: These physicians who recommend IVF with PGT-A for women of any age with DOR, and one of the reasons is a presumed higher risk of a baby being born with Down’s syndrome or trisomy 13 or 18. There are couples who because of religious or ethical reasons would be willing to defer the transfer of an embryo that has aneuploidy, but would not be willing to terminate a baby that has trisomy 13, 18, or 21. These women, who may not even need IVF-ET to become pregnant, would be willing to undergo the great expense of IVF-ET and PGT-a for fear that her condition of DOR may result in a greater risk of these abnormalities. These data may allow some of these women to forego the increased expense of IVF-ET and PGT-a with the realization that, at least if the baby will be born before age 40.5, the risk appears no greater than women with NOR. Even women needing IVF-ET to become pregnant may decide not to add extra expense of PGT-a which could also decrease the chance of a pregnancy from a given egg retrieval cycle related to subjecting an embryo with less implantation potential to the possible detrimental effects of cryopreservation or damage from the biopsy itself.
OBJECTIVE: In recent years, the optimal timing of embryo transfer can be obtained by the endometrial receptivity analysis (ERA). Although the clinical use of ERA has improved implantation rate after embryo transfer (ET) in many cases, several cases still have resulted in failure. Therefore, we have built the hypothesis that the implantation timing after embryo transfer may differ from the embryo characteristic. The aim of this study is to evaluate the implantation timing after ET based on embryo characteristics.

MATERIALS AND METHODS: Serum human chorionic gonadotropin (HCG) levels of 8,109 frozen-thawed ET cycles resulted in single birth were retrospectively evaluated. We speculated the implantation timing by drawing logarithmic curve line of serum HCG changes.

RESULTS: The average implantation timing (HCG<50) was 3.2 days after ET. Serum HCG levels after logarithmic conversion (logHCG) changed in parallel regardless of starting HCG levels. The estimated implantation timing varied about 5 days (2.5 days and 7.5 days after ET) based on the starting HCG levels. The ratio of high grade blastocysts (3BB or higher in Gardner’s grading scale) were significantly higher in high-HCG group (90.9%; HCG>900 at 10 days after ET) than in low-HCG group (47.4%; HCG<50). Implantation timing varied about 5 days (2.5 days and 7.5 days after ET) based on the starting HCG levels. The estimated implantation timing after ET. Serum HCG levels after logarithmic conversion (logHCG) changed in parallel regardless of starting HCG levels. The ratio of high grade blastocysts (3BB or higher in Gardner’s grading scale) were significantly higher in high-HCG group (90.9%; HCG>900 at 10 days after ET) than in low-HCG group (47.4%; HCG<50).

CONCLUSIONS: Matured blastocysts tends to be implanted earlier than immature blastocysts.

IMPACT STATEMENT: Implantation timing after ET is different from the embryo characteristics. This fact indicates that we need to think about not only the endometrial receptivity but also the duration to implantation after ET based on embryo characteristics.

SUPPORT: none

REFERENCES: none

*Data collected from the same study

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**TABLE 1.**

<table>
<thead>
<tr>
<th>Number of embryo transfers included</th>
<th>Number of live births</th>
<th>Type of Transfer</th>
<th>hCG Cutoff Value (IU/L)</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<td>Kaspinar et al (2018)</td>
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<td>Fresh</td>
<td>178.5</td>
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**P-153 6:30 AM Monday, October 24, 2022**

**KISSPEPTIN (KISS1) AND KISSPEPTIN RECEPTOR (KISS1R) IMMUNOREACTIVITY IN CHORIO-DECIDUAL TISSUES OF EUPLOID AND ANEUPLOID RECURRENT PREGNANCY LOSSES (RPLS).** Amr O. Abdelkareem, M.D., Sahar M. Gebril, MD, Jefferson Terry, M.D, Ph.D., Mohamed Ali Bedaiwy, MD, PhD, Sohag University, Faculty of Medicine, Obstetrics and Gynecology, Sohag, Egypt; Sohag University, Faculty of Medicine, Histology and Cell Biology, Egypt; University of British Columbia, Department of Pathology and Laboratory Medicine, Vancouver, BC, Canada; University of British Columbia, Obstetrics and Gynaecology, Vancouver, BC, Canada.

OBJECTIVE: KISS1 is a known regulator of gonadotrophin-releasing hormone release from the hypothalamus and is expressed peripherally in the endometrium and placenta. KISS1/KISS1R were previously shown to be less expressed in chorio-decidual tissues of unexplained RPLs, however, little is known about their expression in other types of RPL. (1). Our objective was to evaluate the Immunoreactivity of KISS1/KISS1R in RPLs due to aneuploidy (RPL-An), unexplained RPLs (RPL-Ue) compared to control elective abortions (EL-Ab).

MATERIALS AND METHODS: This is a case control study. Samples from archived chorio-decidual tissues of 3 groups of patients were used. This included RPL-An (n=10), RPL-Ue (n=10) and EL-Ab (n=10). Immunohistochemistry staining was done using 2 previously validated antibodies against KISS1 and KISS1R. Signal intensity and abundance were measured by 2 independent observers using a semi-quantitative assay (Histo-score) and were given a score from 0-4. Scoring was done in syncitiotrophoblast (SyT), cyto-trophoblast (CyT), decidual glands (DeG) and decidual stroma (DeS). Data were analyzed using Kruskal-Wallis test followed by pairs of Mann-Whitney test where appropriate. P-value of less than 0.05 was considered significant.

RESULTS: There was no difference between 3 groups as regards to maternal age and gestational (P = 0.3 and 0.5 respectively). KISS1 Immunoreactivity was similar in SyT, CyT, DeG and DeS of all groups. Only KISS1R was significantly lower in SyT and Cyt of RPL-An and RPL-Ue compared to EL-Ab (P < 0.01) with no difference between RPL-An and RPL-Ue (P = 0.5 and 0.9 respectively). However, KISS1R expression was not different in DeG or DeS among study groups.

**TABLE 1.**

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<td>465</td>
<td>Frozen</td>
<td>411.45</td>
<td>89.3</td>
<td>70.1</td>
</tr>
<tr>
<td>Zhao et al (2017)*</td>
<td>1513</td>
<td>Frozen</td>
<td>410.8</td>
<td>90.4</td>
<td>59.3</td>
</tr>
</tbody>
</table>

---

**REFERENCES: none**

**SUPPORT: none**

**IMPACT STATEMENT: Implantation timing after ET is different from the embryo characteristics. This fact indicates that we need to think about not only the endometrial receptivity but also the duration to implantation after ET based on embryo characteristics.**

**SUPPORT: none**

**REFERENCES: none**
CONCLUSIONS: Kisspeptin receptor is less expressed in chorionic tissues of RPLs whether euploid or aneuploid compared to control.

IMPACT STATEMENT: Current results broaden our understanding of the role played by Kisspeptin and its receptor in early placental development. Whether decreased Kisspeptin activity is the cause, or a sequela of defective placentation needs to be evaluated in future studies.

REFERENCES:

P-154 6:30 AM Monday, October 24, 2022
ACTIVE MANAGEMENT OF PERSISTENT PREGNANCIES OF UNKNOWN LOCATION RESULTS IN A SHORTER TIME TO RESUME FERTILITY TREATMENT. Megan Renee Determan, M.D., PH.D., 1,2 Jennifer B. Bakkensen, MD, 3 Allison S. Komorowski, MD, 4 Mary Ellen Pavone, MD, 4 Lia A. Bernardi, M.D., 4 Kruti P. Maniar, MD 5

OBJECTIVE: To demonstrate that active management of persistent pregnancies of unknown location (PPUL) with dilation and curettage (D&C) followed by methotrexate (MTX) treatment if needed results in a shorter time to resume treatment when compared to empiric MTX for a presumed diagnosis of ectopic pregnancy.

MATERIALS AND METHODS: A retrospective cohort analysis of all patients with a PPUL who received empiric MTX treatment or a D&C from January 2010 to March 2022 at a multicenter group practice was performed comparing baseline demographics and time to next fertility treatment. Statistics were performed via Wilcoxon-Mann-Whitney test.

RESULTS: A total of 831 patients with PPUL received active management: 358 patients (43%) received a D&C compared to 473 patients (57%) who elected MTX treatment. Similar demographics were present for each group with a mean maternal age of 35 years of age, a median gestational age of 5 weeks 6 days, and 56% versus 55% of cases occurring after an embryo transfer, respectively. The time interval from the start of the affected cycle to that of another treatment cycle was significantly different (median 154 days versus 189 days and 56% versus 55% of cases occurring after an embryo transfer). The time interval for starting their next treatment interval was similar to patients who elected for empiric MTX (189 days and 56% versus 180 days and 55%).

OBJECTIVES: To evaluate for CE in patients with IF and RPL may be of particular benefit given high LBR was 73.1%.

MATERIALS AND METHODS: A retrospective cohort analysis of all patients with IF and RPL who underwent endometrial sampling (ES) for CE evaluation at a single academic institution (2014-2020). Pathologic diagnosis was made by the presence of plasma cells, positive CD 138 staining, and/or stromal changes. Treatment and subsequent live birth rates were compared with Chi-square tests.

RESULTS: A total of 653 patients (mean age 35.8) underwent ES to evaluate for CE. Indications included recurrent pregnancy loss (RPL, 43.5%), implantation failure (IF, 30.0%), recent spontaneous, missed, or therapeutic abortion (Ab, 10.4%) and abnormal saline-infused sonogram (SIS, 8.0%). The incidence of CE was 28.3%. Stratified by indication, the incidence was 64.7% for recent abortion, 38.5% for abnormal SIS, 27.8% for RPL, and 14.8% for IF.

OBJECTIVE: To identify incidence of chronic endometritis (CE), examine efficacy of antibiotic regimens, and examine pregnancy outcomes after treatment.

MATERIALS AND METHODS: This retrospective cohort study included patients who underwent endometrial sampling (ES) for CE evaluation at a single academic institution (2014-2020). Pathologic diagnosis was made by the presence of plasma cells, positive CD 138 staining, and/or stromal changes. Treatment and subsequent live birth rates were compared with Chi-square tests.

RESULTS: A total of 653 patients (mean age 35.8) underwent ES to evaluate for CE. Indications included recurrent pregnancy loss (RPL, 43.5%), implantation failure (IF, 30.0%), recent spontaneous, missed, or therapeutic abortion (Ab, 10.4%) and abnormal saline-infused sonogram (SIS, 8.0%). The incidence of CE was 28.3%. Stratified by indication, the incidence was 64.7% for recent abortion, 38.5% for abnormal SIS, 27.8% for RPL, and 14.8% for IF.

Comparison of treatment and outcome:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Pregnancy rate (%)</th>
<th>P value</th>
<th>N</th>
<th>LBR (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent Ab</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated CE</td>
<td>40.0</td>
<td>.369</td>
<td>25</td>
<td>10.0</td>
<td>.528</td>
</tr>
<tr>
<td>No CE</td>
<td>52.4</td>
<td></td>
<td>21</td>
<td>63.6</td>
<td></td>
</tr>
<tr>
<td>Abnormal SIS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated CE</td>
<td>40.0</td>
<td>.717</td>
<td>10</td>
<td>50.0</td>
<td>.039</td>
</tr>
<tr>
<td>No CE</td>
<td>25.0</td>
<td></td>
<td>28</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>IF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated CE</td>
<td>50.0</td>
<td>.977</td>
<td>18</td>
<td>77.8</td>
<td>.438</td>
</tr>
<tr>
<td>No CE</td>
<td>50.4</td>
<td></td>
<td>141</td>
<td>64.8</td>
<td></td>
</tr>
<tr>
<td>RPL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated CE</td>
<td>60.0</td>
<td>.867</td>
<td>45</td>
<td>77.8</td>
<td>.168</td>
</tr>
<tr>
<td>No CE</td>
<td>58.6</td>
<td></td>
<td>174</td>
<td>63.7</td>
<td></td>
</tr>
</tbody>
</table>

Over 90% of patients with persistent CE completed a second course of antibiotics; 59.1% cleared CE. Overall clearance after 1-2 courses of antibiotics was 85.6%. Among all patients who cleared CE and subsequently conceived, the LBR was 73.1%.

CONCLUSIONS: CE is common among infertility patients. About two-thirds of patients cleared CE with an initial antibiotic course, and clearance rates were not different by antibiotic regimen. In patients with IF and RPL, LBR was higher when CE was diagnosed and treated compared to when CE was not diagnosed, although this difference was not statistically significant.

IMPACT STATEMENT: Given high rates of persistent CE, development of more targeted treatment regimens is needed. Diagnosis and treatment of CE in patients with IF and RPL may be of particular benefit given high LBRs after CE clearance in these groups.

P-156 6:30 AM Monday, October 24, 2022
ASSOCIATION BETWEEN THE ABSENCE OF CORPUS LUTEUM AND THE RISK OF PLACENTAL INSUFFICIENCY IN PREGNANT WOMEN AFTER ASSISTED REPRODUCTION PROCEDURES. Maite Garcia Zeman, MD, 1 Laura Suelo, MD, 1 Carlos Sanchez Minano, MD, 1 Natalia Vic, MD, 2 Carolina Salazar, MD, 1 Carla Diaz Martin, MD, 1 Diego Lopez Osa, MD, 1 Heydy W. Uriondo Boudri, MSc, 1 Cristian R. Alvarez Sedo, PhD 1 FERTILIA, Tucuman, Argentina; 2 FERTILIA, TUCUMAN, Argentina.
OBJECTIVE: The main objective was to compare if the presence of corpus luteum (CL) was associated with an increased risk of placental pathologies in spontaneous (SP) and/or assisted reproductive technique (ART: own oocytes -OO- and egg donation -ED-) pregnancies.

The specific objectives were to compare if there was an increased risk (IR) of preeclampsia (PE) and fetal growth restriction (FGR):

- between ART (frozen embryo transfers-FT) (OO+ED) vs. SP pregnancies.
- within ART patients (fresh embryo transfers-FT vs. FET).
- within ED patients (FT vs. FET).
- between OO vs. ED.

MATERIALS AND METHODS: This study included 426 pregnant patients who performed combined first trimester screening for PE, FGR and aneuploidies (2019-2021). Sixty-four four-gest patient after ART and 362 were SP. Multiple pregnancies, high risk for aneuploidies, and pregnancies after ART in another IVF center were excluded.

The risk of PE and FGR between pregnant women (with or without CL) was assessed. The population was divided in 5 groups: 1.- SP; 2.- ED-FT; 3.- ED-FET; 4.- OO-FT; 5.- OO-FET.

The dependent variables were: high risk for PE before 34 weeks and FGR before 37 weeks. For both variables, the cut-off value was 1/150, which was calculated by the Astraia Software (v2.8.0). Relative risk (RR) was calculated.

RESULTS: From the total population: 86% - SP, 6% OO-FT, 2% OO-FET, 3% ED-FT and 3% ED-FET. Within ART patients, 58% were ED-FT and 42% from ED. In pregnant women, 64% of the cases had a CL (SP + OO-FT) and 8% not (OO-FET + ED+FT + ED-FET). The average age of the groups was: 33.3 (SP), 34.5 (OO-FT), 36.8 (OO-FT), 43.5 (ED-FT), 42.1 (ED-FT).

Patients without CL had a statistically significant RR 3.97 (IC: 1.57-10.02) for PE, and RR 3.22 (IC: 1.63-6.39) for FGR compared with patients with CL. FET patients (OO+ED) had a statistically significant RR 4.1 (IC: 4.1-4.19) for PE and RR 3.07 (IC: 1.3-7.03) for FGR compared with SP.

A statistically significant association of high risk for PE in OO-FT vs. OO-FET was observed, however, there was not an association for FGR. No differences were observed between ED-FT vs. ED-FET and OO vs. ED.

CONCLUSIONS: The absence of CL is associated with a major risk of PE and FGR. ART patients who performed FET (without CL) had a major risk of PE and FGR compared with SP. There was observed and increased risk of FGR in ED patients.

IMPAKT STATEMENT: This study analyzed the correlation between the presence of CL and the increased risk of PE and FGR with the aim of providing evidence for the early control of potential placental pathologies.

SUPPORT: None

P-157 6:30 AM Monday, October 24, 2022

METHOTREXATE FOR TREATMENT OF ECTOPIC PREGNANCIES: PRACTICE PATTERNS ACROSS ACADEMIC REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY (REI) PROGRAMS. Michelle Dellalana, BA,1 Katherine Koniaris, MD,2 John Nulsen, MD3 1UConn School of Medicine, Farmington, CT; 2University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT; 3University of Connecticut Health Center, Center for Assisted Reproductive Services, Farmington, CT.

OBJECTIVE: To investigate variations in MTX treatment protocol for ectopic pregnancy in clinical practice.

INTRODUCTION: Ectopic pregnancies are a prevalent and potentially life-threatening risk during the first trimester that can be managed medically or surgically. Methotrexate (MTX), a folate antagonist that inhibits cell-mediated reactions for ectopic pregnancies, ACOG has published three protocols for the administration of MTX to treat ectopic pregnancies: 1) single-dose protocol, 2) two-dose protocol, and 3) fixed multiple-dose protocol. While the two dose and multi-dose regimens are less likely to fail, the single-dose protocol is the most convenient and has the fewest adverse side effects [1]. It has yet to be elucidated in the literature which protocol provides the optimal balance between effectiveness and safety. The objective of this study was to investigate the practice patterns of MTX utilization for the treatment of ectopic pregnancies at REI programs across the country.

MATERIALS AND METHODS: A 16-question survey with branching logic was approved by the University of Connecticut Institutional Review Board and administered via REDCap to first year REI Fellows.

RESULTS: Of the 46 first year REI fellows emailed the REDCap link, 21 completed the survey (45.7%). 17/21 (81.0%) and 4/21 (19.0%) survey respondents were from academic and academic-affiliated private practice infertility clinics, respectively. Infertility clinics from 16 states were represented. The specific number of patients utilized MTX at each clinic was as follows: <250 (9.5%), 251-500 (28.6%), 501-750 (4.8%), 751-1000 (14.3%), and >1000 (42.9%). The number of ectopic pregnancies treated per month at a single clinic was reported as: <1 (19.0%), 1-3 (57.1%), 4-19 (10.0%), and >20 (4.8%). 17/21 (81.0%) survey respondents reported they were familiar with ASRM/ACOG guidelines on MTX administration and 16/21 (76.2%) survey respondents reported following the ASRM/ACOG guidelines. 100% of survey respondents utilized MTX for the treatment of ectopic pregnancies with 33.3% employing both the one-dose and two-dose MTX protocols, 57.1% following only the one-dose protocol, 4.8% utilizing only the two-dose protocol, and one survey respondent using an unknown protocol.

CONCLUSIONS: Although MTX is universally used for the medical management of ectopic pregnancies, there is wide variation in the protocols used by academic REI Programs. The majority of REI Programs appear to utilize the single dose protocol despite the greater efficacy with the two dose and multi-dose protocols.

IMPACT STATEMENT: MTX is the primary treatment for the medical management of ectopic pregnancy, but the protocol used varies across REI Programs in the United States despite the enhanced efficacy with the two dose or multi-dose protocol.

REFERENCES:
https://doi.org/10.1097/AOG.0000000000002559

P-158 6:30 AM Monday, October 24, 2022

FACTORS ASSOCIATED WITH PREGNANCY LOSS AFTER SINGLE EUPLOID EMBRYO TRANSFER. Chelsea M. Canon, MD,1 Devora Aharon, MD,1 Joseph A. Lee, BA,2 Carlos Hernandez-Nieto, MD,2 Richard E. Silfkin, B.A., TS(ABB), CLT(NYS),3 Rose Marie Roth, MSc, TS(ABB), CLT (NYS),3 Christine Briton-Jones, PhD,2 Tanmoy Mukherjee, MD,3 Alan B. Copperman, MD,3 Lucky Sekhon, MD1 Icahn School of Medicine at Mount Sinai, New York, NY; 2Reproductive Medicine Associates of New York, New York, NY; 3Icahn School of Medicine at Mount Sinai/Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Clinical pregnancy loss (CPL) is often attributed to chromosomal copy number errors in the human embryo. When undergoing in vitro fertilization (IVF), preimplantation genetic testing for aneuploidy (PGT-A) can be utilized to select euploid embryos for transfer, thus significantly decreasing the risk of miscarriage. Surprisingly, pregnancy loss after single euploid embryo transfer (SEET) can still occur. This study sought to identify patient and cycle-specific factors associated with CPL after a SEET.

MATERIALS AND METHODS: This study included all patients who conceived a pregnancy from a SEET cycle, at a single academic center from September 2016-March 2022. All PGT-A was performed using next generation sequencing. All patients underwent a synthetic endometrial preparation cycle. Cycles were stratified by outcome: a CPL or an ongoing pregnancy/live birth. Demographic and cycle characteristics were collected (primary diagnosis, oocyte age, partner age, BMI, ovarian reserve, progesterone and estrogen levels prior to transfer, type of estrogen and progesterone medication used, endometrial thickness (EMT), number of previous embryo transfers, semen analysis parameters at ICSI, embryo morphologic parameters, history of prior cycle failures, history of unexplained pregnancy loss, history of pregnancy loss following embryo transfer, history of pregnancy loss following elective embryo reimplantation for indeterminate PGT-A results, and time the embryo was cryopreserved). Cycle outcomes were compared by t-test, Kruskal-Wallis, and chi-square. The groups were analyzed using a multivariate regression analysis.

RESULTS: A total of 5468 pregnancies were included in our analysis. After multivariate regression analysis, poor embryo morphologic quality (OR 1.29, 95% CI 1.11, 1.5), female embryo sex (OR 1.16, 95% CI 1.00, 1.35), high BMI (OR 1.03, 95% CI 1.02, 1.05), thin EMT (OR 1.08, 95% CI 1.04, 1.12), primary diagnosis of polycystic ovarian syndrome (PCOS)/anovulation (OR 1.80, 95% CI 1.27, 2.54), and primary diagnosis of female anatomic problems (OR 1.55, 95% CI 1.08, 2.23) were found to be significantly associated with increased odds of CPL.
CONCLUSIONS: The utilization of PGT-A decreases the risk of miscarriage in women of advanced reproductive age who undergo IVF. However, CPL still occurs after euploid transfer. This study was able to identify embryo morphologic quality, embryo sex, BMI, endometrial thickness, primary diagnosis of PCOS, anovulation, and primary diagnosis of female anatomic problems as factors associated with CPL after a SEET. While mechanisms behind factors such as high BMI, thin EMT, and uterine anomalies being linked to poor reproductive outcome are understood, the link between euploid pregnancy loss and anovulation or female embryo sex requires further investigation.

IMPACT STATEMENT: CPL after SEET is associated with embryo morphologic quality, embryo sex, BMI, EMT, primary diagnosis of PCOS/ anovulation and primary diagnosis of female anatomic problems.

SUPPORT: None

REFERENCES:

P-159 6:30 AM Monday, October 24, 2022

VANISHING TWIN SYNDROME RESULTS IN HIGHER RISK OF MISCARRIAGE EVEN FOLLOWING EUPLOID EMBRYO TRANSFER. Tonie Patrick, RN, William B. Schoolcraft, MD, Mandy Katz-Jaffe, PhD Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Vanishing twin syndrome describes the loss of one twin during pregnancy that typically occurs during the first trimester. Risk factors for vanishing twin syndrome include fetal chromosome abnormalities and the transfer of multiple embryos during an IVF cycle. Outcomes of vanishing twin syndrome IVF pregnancies have been shown to result in more frequent premature delivery and babies with low birth weight. The aim of this study was to investigate the incidence of vanishing twin syndrome following euploid embryo transfers and the probability of pregnancy loss.

MATERIALS AND METHODS: A total of n=1263 incidences of multiple pregnancies were included in this analysis and classified as follows: double euploid embryo transfers with dizygotic twins (n=1,107; mean maternal age = 35.7 ± 3.6 years) and double or single euploid embryo transfers with a monozygotic twinning event (n=156; double embryo transfer = 64; single embryo transfer = 92; mean maternal age = 35.5 ± 3.5 years). Vanishing twin syndrome was defined as the loss of one twin in the first trimester of a documented clinical multiple pregnancy with fetal heart tones. For all IVF cycles, blastocyst euploidy was determined from a trophectoderm biopsy using the VeriSeq platform (Vi-trolife). Biopsied blastocysts were vitrified using the Cryotop method and standard protocols for a hormone replacement frozen embryo transfer (FET) were utilized. Statistical analysis was performed by Fisher’s exact test and two-sided Students t-test, significance at P < 0.05.

RESULTS: Maternal age was comparable between the two twinning groups and also in association with the detection of a vanishing twin within each group. However, the incidence of vanishing twin syndrome was significantly lower in double euploid embryo transfers with dizygotic twins (9.6% vs. 19.2% monzygotic twinning events; P = 0.0008; OR 2.3). Nevertheless, the probability of miscarriage was significantly higher in cases of vanishing twin syndrome for double euploid embryo transfer with dizygotic twins (11.3% compared to 1.1% for ongoing dizygotic twins; P < 0.0001). For double or single euploid embryo transfers with a monzygotic twinning event, the miscarriage rate was trending slightly lower for cases of vanishing twin syndrome (13.3%) compared to ongoing multiple pregnancy with a monzygotic twin event (15.9%).

CONCLUSIONS: In conclusion, vanishing twin syndrome was not associated with maternal age following euploid embryo transfers. In relation to the type of twinning, there was an increased probability of vanishing twin syndrome with a monzygotic event, and a higher risk of pregnancy loss with vanishing twin syndrome after double euploid embryo transfer with dizygotic twins. However, monzygotic twinning carries other significant obstetric risks that outweigh any impact of vanishing twin syndrome in relation to miscarriage.

IMPACT STATEMENT: Vanishing twin syndrome was more significantly prevalent in monzygotic twinning events but only increased the risk of pregnancy loss for dizygotic twins, even with the transfer of two euploid blastocysts.

SUPPORT: None

E-POSTER ABSTRACT SESSION: 17

P-160 6:30 AM Monday, October 24, 2022

THE EFFECT OF SERUM PROGESTERONE LEVEL WITH AND WITHOUT EMPIRICAL PROGESTERONE TREATMENT ON PREGNANCY OUTCOME IN WOMEN WITH UNEXPLAINED RPL. Einav Peero Dr, MD,1 Shaonie Ton-Leclerc, MD,2 Ido Feferkorn, MD,3 William M. Bucket, M.B.B.CH., M.D.,4 McGill University Health Center, Montreal QC, Canada; 1Lachine, QC, Canada; 2Division of Reproductive Endocrinology and Infertility, McGill University Health Care Center, Montreal, QC, Canada; 4Division of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada.

OBJECTIVE: To investigate the effect of serum progesterone levels and progesterone treatment on pregnancy outcomes of women with unexplained repeated pregnancy loss (RPL).

MATERIALS AND METHODS: A retrospective cohort study in tertiary academic hospital based reproductive center. Data were collected from charts of women with RPL seen in our unit between January 2018 and January 2022. In our unit only women with low progesterone levels (less than 40nmol/L) in the early pregnancy (around 6 weeks of gestation) are treated with progesterone (Vaginally 200 mg daily or IM 50 mg daily). Statistical analysis included t-test, Fisher exact test and Mann-Whitney test. Pregnancy outcomes were compared between women treated with Progesterone and women without progesterone treatment during their pregnancy. Primary outcome was live birth rates at term.

RESULTS: The study group included 131 women with RPL. The mean age of the women in the study was 34.7 years (+/-4.1 2SD). The mean BMI of the study population was 25.8 (+/6.8 2SD). The mean gestational number and miscarriage number in the study group were 5.7 (+/-2.3 2SD) and 3.9 (+/-2.1 2SD) respectively. The mean Progesterone was similar between women treated with progesterone and untreated women, as expected (67.7nmol/L vs. 67.8nmol/L, P=0.99). There were no difference between live birth rate at term between the treated and the untreated group (32.7% vs. 34.3%, P= 1).

CONCLUSIONS: In women with history of unexplained RPL and high levels of progesterone in early pregnancy (above 40nmol/L), there is no benefit in treatment with progesterone.

IMPACT STATEMENT: Women with history of RPL might not need progesterone treatment if they have a high level of progesterone; however, larger studies are needed to confirm this assumption.

SUPPORT: None
MOXI and IVF in PhoX). Pregnancy outcome definitions (biochemical and clinical pregnancy loss, ectopic pregnancy, and live birth) were standardized across trials. Associations were estimated using Chi-Square, Fisher’s exact, Wilcoxon rank sum and modified Poisson regression models.

RESULTS: Of 3,285 participants across all trials, 855 (26.0%) achieved a live birth and 456 (13.9%) experienced any pregnancy loss. Among those with a positive pregnancy test, 35.9% [33.3, 38.6; 95%CI] experienced a pregnancy loss, the majority being biochemical (22.1% [19.9, 24.5]) and clinical losses (11.2% [9.3, 13.4]). By diagnosis, overall loss was highest among those with an unexplained infertility (37.7% [32.5, 43.1]) and lowest in male factor infertility (27.7% [15.6, 42.6]). Biochemical, clinical, and overall pregnancy loss did not significantly differ across studies or diagnoses after adjustment for maternal factors (female age, BMI, infertility duration, income, and race). Female and male age were greater in couples experiencing any loss (33.0, 35.0 years) than in those achieving live birth (31.0, 33.0) (p < 0.001). Maternal age ≥ 35 increased risk of pregnancy loss across all studies following adjustment for female factors (RR 1.86 [1.58, 2.20]).

CONCLUSIONS: The risk of pregnancy loss in women with infertility undergoing treatment (35.9%) is greater than previously reported among women without a known diagnosis of infertility (31%). In our study, pregnancy loss varied across infertility diagnoses, but differences were not statistically significant. Despite its large sample size, our study is underpowered to detect small differences across diagnoses. Women age ≥ 35 experienced almost a two-fold greater risk of loss compared to women < 35.

IMPACT STATEMENT: In this well-characterized cohort of couples undergoing infertility treatment, the overall risk of pregnancy loss is greater than that previously reported in women without infertility who were monitored for early pregnancy outcomes. Consistent with findings from other populations, advanced maternal age is a risk factor for pregnancy loss among infertility couples. SUPPORT: U54GM104938 NIGMS and NICHD U10 HD077680

REFERENCES:
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P-163 6:30 AM Monday, October 24, 2022
ULTRASOUND ASSESSMENT OF ENDOMETRIAL ABNORMALITIES DURING ENDOMETRIAL MATURATION FOR FROZEN EMBRYO TRANSFER (FET).
Kaia Schwartz, MD, Laura Detti, M.D. Cleveland Clinic Foundation, Cleveland, OH; *Baylor College of Medicine.

OBJECTIVE: To analyze the endometrial features of patients undergoing medicated endometrial maturation for FET and correlate them with pregnancy outcomes.

MATERIALS AND METHODS: Abnormal endometria were diagnosed by the presence of polyps, cystic lesions, heterogeneous or non-trilaminar morphology. We consecutively evaluated FET cycles with single embryo transfer between 4/1/2021 - 9/30/2021. Endometrial characteristics and patient demographics, including FET outcomes, were collected. Prior to FET preparation, patients underwent cavity evaluation with hysterosalpingogram (HSG), office hysteroscopy, or saline sonohysterogram. Patients deemed to be normal. Evaluation of the endometrial echo was performed by one of seven physicians on duty and verified by a second physician. Outcome measures were: failed conception, early pregnancy loss/biochemical pregnancy, and ongoing pregnancy. R statistical program version 4 was used to perform t-test comparison for continuous variables and chi-square test for the categorical variables. A proportional odds logistic regression model was used to control for confounders.

RESULTS: We identified 164 endometrial echoes within the time period, 18 of which were cancelled and were excluded from analysis. Prior to endometrial maturation, the majority of patients underwent a cavity evaluation with hysteroscopy (63.4%, n=92), followed by SIS (32.4%, n=47) and HSG (4.1%, n=4). Table 1 illustrates the pregnancy outcomes stratified by normal versus abnormal endometria. When controlling for age, BMI, and days between ultrasound and FET, AE patients are 7.27 times more likely to have a poor pregnancy outcome (Biochemical, SAB or no conception) as compared to NE patients (95% CI 3.50 - 15.11).

Table 1

CONCLUSIONS: The presence of endometrial abnormalities on ultrasound in preparation for FET has a significant correlation with poor cycle outcomes and conception rates were decreased by greater than 50%. HSG and office hysteroscopy may not be sufficient for the evaluation of the uterine cavity. Patients with abnormal endometria on lining check ultrasounds have a much higher risk of poor pregnancy outcome if we proceed with FET. These patients may benefit from cancelling the FET and restarting with an alternative endometrial maturation protocol to achieve a normal endometrium.

IMPACT STATEMENT: This study underscores the importance of ultrasound in the evaluation of the endometrium and prediction of FET cycle outcomes.

SUPPORT: None

P-164 6:30 AM Monday, October 24, 2022
ALTERATIONS IN THE SERUM REACTIVE OXYGEN SPECIES (ROS) - ANTIOXIDANT BALANCE AS A CAUSE FOR RECURRENT PREGNANCY LOSS (RPL) PATHOGENESIS: A PILOT STUDY IN THE NORTH-EAST INDIAN POPULATION OF ASSAM.
Parabati Deka Bose, M.Sc., Ph.D.1; Natasha Kashyap, M.Sc.; Chandana Ray Das, MD, Ph.D.1; Ratul Dutta, M.D.2; Anjuma Begum, M.Sc., M.Sc.; Sajoy Bose, M.Sc., Ph.D.3; MBBT Department, Cotton University, Guwahati, India; 3MBBT Department, Cotton University, Guwahati, Assam, India; 3Gauhati Medical College and Hospital, Guwahati, India; 4Down Town Hospitals, Guwahati, India; 5Gauhati University, Guwahati, India.

OBJECTIVE: Recurrent pregnancy loss (RPL) is a major pregnancy complication, affecting 7.46% of the Indian population. Although the role of oxidative stress in pregnancy has been extensively studied, only few studies have correlated alterations in oxidative stress with RPL predisposition in women from India. This work, therefore, aims to study the alterations in the ROS-antioxidant levels between the RPL and MTP cases and to correlate these alterations with RPL predisposition in the study population.

MATERIALS AND METHODS: RPL patients who had undergone three or more spontaneous miscarriages (N=21) and medically terminated pregnancies (MTP) cases (n=35) were enrolled for this study, with informed consent. Serum was used for biochemical analysis of total antioxidant (TAO), reduced glutathione (GSH) and superoxide dismutase (SOD) levels along with the levels of hydrogen peroxide (H2O2) in the RPL and MTP cases using colorimetric assays. The ROS-antioxidants balance in the RPL cases compared to the control cases were then evaluated. Statistical analysis for the cohorts was carried out using SPSS statistical software.

RESULTS: The results of this study show an increased level of H2O2 in the RPL cases (55.56 ± 40.63 nmol) compared to the MTP cases (24.46 ± 9.43 nmol, p=0.231). The TAO levels were also found to be increased in the RPL cases (2.07 ± 0.5 mM) compared to the controls (1.95 ± 0.72 mM, p=0.258). A similar increase was observed in the SOD enzyme activity in the RPL cases (238.55 ± 25.46%) compared to the MTP cases (195.77 ± 66.37%; p=0.289). However, the serum level of GSH was found to be reduced in the RPL cases (0.23 ± 0.14 µg/µl) compared to the controls (0.26 ± 0.111 µg/µl; p=0.189). Additionally, no significant correlations were observed between the serum levels of H2O2 and the antioxidants.
CONCLUSIONS: The increased level of H$_2$O$_2$ despite the high serum levels of total antioxidant and increased SOD activity is indicative of aberrations in the antioxidant capacity of these molecules. These aberrations, combined with the decreased levels of GSH, which is a major antioxidant during pregnancy, may alter the ROS-antioxidant balance leading to a detrimental impact on fetal sustenance resulting in pregnancy loss.

IMPACT STATEMENT: This study confirms the possible role of aberrations in the ROS-antioxidant balance in RPL pathogenesis in the Northeast Indian population. These can be used as therapeutic targets and augmented to normalise the ROS-antioxidant balance required for a healthy pregnancy. This will allow at least a sub-population of the RPL patients to carry a pregnancy to term.

P-164 6:30 AM Monday, October 24, 2022

COMPARATIVE ASSESSMENT OF CYTOGENETIC AND MOLECULAR APPROACHES FOR PRODUCT OF CONCEPTION: A RETROSPECTIVE STUDY OF 726 CASES. Natalia Juliana Nardelli Gonçalves, PhD, Camila Madaschi, BsC, Priscila Paternostro, MsC, Kalina Renata Endo, BsC, Adriano Bonaldi, PhD, Milena A. de Oliveira, PhD, Maria Fernanda Grillo, MD, MSc, MBA, Keitty Benevides Pereira, BsC, Barbara De Bells, BsC, Natacha Pinho Pinho Ribino, BsC, Viviane de Cássia Jesus Da Silva, BsC, Ciro Martinhago, M.D., PH.D., 1Diagnósticos da América S.A., DASA, Brazil, Brazil, Sao Paulo, Sp, Brazil; 2São Paulo, Sp, Brazil; 3Diagnósticos da América S.A., DASA, Brazil, Brazil.

OBJECTIVE: Spontaneous abortions occur approximately in 15 to 20% of pregnancies and chromosomal alterations are responsible for 50 to 70% of the cases. In the past, assessment of genetic abnormalities was limited to karyotype performed on placental or fetal tissue. However, advances in molecular genetic technologies now provide rich genetic information about the causes and risks for pregnancy loss. The main goal was to analyze the molecular and cytogenetic data obtained from miscarriage product, evaluated by four different techniques, to understand the advantages and limitations of each approach and have a conclusive result that assists in the investigation of the couple.

MATERIALS AND METHODS: Retrospective study of 726 cases performed in our Genetic Laboratory, DASA, Brazil. In total, 220 cases were analyzed by G banding karyotype; 331 cases by MLPA (Salsa MLPA P036 MRC Holland), 155 cases by Next Generation Sequencing (Ion ReproSeq Thermo Fisher Scientific) and 20 cases performed with SNP-array technology (Infinium CytoSNP-850K-Illumina). All results came from first-trimester abortion material from patients aged 28 - 53 years old and were statistically evaluated by Fisher’s Exact test (R 4.1.3).

RESULTS: The conclusive results observed among all techniques were 61.36% for karyotype, 96.37% for MLPA, 96.13% for NGS and 100% for SNP-array (p-value: 2.2e-16). Karyotype showed the highest rate of conclusive results (38.64%), mainly related to absence of cell growth in culture, and is the technique that most detected mosaicism and polyplody (12%). Trisomy was the most prevalent aberration (p-value: 0.00197), mainly from chromosomes 15, 16, 21, 22, followed by monosomies of sexual chromosomes (10 - 15%). High rates of maternal contamination were observed for MLPA (63.64%) and NGS (55.77%). Normal results, as expected, were inversely proportional to maternal age (28-35 years: 47.54%, 35-37 years: 43.75%, 38-39 years: 39.58% and 29% for women over 40 years old).

CONCLUSIONS: In summary, the karyotype showed the highest rate of conclusive results and cannot exclude maternal contamination, increasing the chances of false negative results. MLPA showed the highest rate of conclusive results, being an appropriate strategy of better cost benefit, but with some technical limitations. SNP-array has the highest resolution among all chromosomes with a high conclusive rate and is able to exclude maternal contamination. By choosing the best study approach, couples can be appropriately counseled on different reproductive strategies if an aneuploidy is identified, to understand the risk for subsequent pregnancy.

IMPACT STATEMENT: Comparative study to support a paradigm shift for applying molecular approach in routine investigation for abortion material, to expand the capability of genetic diagnosis for chromosomal alterations in recurrent miscarriage affected couples.

P-165 6:30 AM Monday, October 24, 2022

THE ECONOMIC BURDEN OF RECEIVING RECURRENT MISCARRIAGE CARE IN IRELAND: THE PATIENT’S PERSPECTIVE. Caragh Flannery Dr, BA, PhD, Marita Hennessy, PhD, Keelin Odonoghue Prof, PhD FRCOG FRCPI, 1University College Cork, Cork, Ireland; 2CENTRE, Cork, Ireland.

OBJECTIVE: Recurrent miscarriage (RM) can have an emotional, psychological and economic impact. Women who experience RM may require frequent contact with healthcare services resulting in additional costs. This study aimed to characterise the incremental burden of receiving RM care for women experiencing two or more first-trimester miscarriages in terms of work productivity, healthcare utilisation, out-of-pocket cost and health-related quality of life (HRQoL).

MATERIALS AND METHODS: A cross-sectional study was conducted using an anonymous web-based national survey. Women over 18 who had experienced two ≥ first trimester miscarriages in the last ten years and who had received care in Ireland were invited to participate. The survey was purposefully designed, covering sociodemographic information, the RM care pathway and included items from the Stanford presenteeism scales (S-P-6) and HRQoL (SF-12). The survey was distributed online using Qualtrics in September 2021. Analysis was conducted using Stata.

RESULTS: In total, 135 female participants were eligible (79% aged 53-44yrs (n=106), 95% white Irish (n=128). On average, women scored low on the mental component summary (38.7) of the HRQoL, indicating the likelihood of women experiencing depression, with 50% (n=68) below the population norm. 66% (n=47) of women took time off from work for investigations (n=71), 62% (n=38) for receiving results (n=61), 77% (n=75) for early reassurance scans in the next pregnancy (n=97) and 18% (n=24) for attending support services (n=135). Women spent a combined average of 3250 hours off work to attend all RM care appointments, including investigations, receiving results, treatment, and follow-up pregnancy care. 70% (n=95) of women experienced decreased productivity from receiving RM care. 64% (n=87) attended primary care appointments (on average, four additional appointments), and 63% (n=85) attended other appointments such as alternative therapies and private scans, of which 40% (n=34) attended fertility services more than three times. To receive RM care, women travelled a combined 32,109km to attend all RM care appointments, costing on average €20,300 for transport, parking and fuel. Other out-of-pocket expenses included further investigations, scans, and other services such as fertility services, averaging over €250,000 with additional costs for the minding of children/dependents while attending RM care appointments of €1,350.

CONCLUSIONS: Women who receive RM care experience a poorer HRQoL, decreased productivity and experience substantial out-of-pocket costs for travel to RM care appointments and other medical expenses such as additional scans and attending fertility services. Public health policies need to address ways to prevent high patient costs, provide timely diagnosis and treatment, and provide effective interventions to support women with RM.

IMPACT STATEMENT: This study is the first costing study conducted from the patient perspective addressing work productivity, healthcare utilisation, out-of-pocket cost, and health-related quality of life for receiving RM care in Ireland.

P-166 6:30 AM Monday, October 24, 2022

T REGULATORY, TH17, AND TREG/TH17 RATIO, IN PREGNANT WOMEN WITH RECURRENT PREGNANCY LOSSES AND NORMAL PREGNANT WOMEN. Thanh Vinh Luu, D.O., Amy Thees, PhD, Umida Ganieva, PhD, Svetlana Dambaeva, PhD, Kenneth Beaman, Ph.D., Joanne Kwak-Kim, MD, MPH, Rosalind Franklin University Health Clinics, Vernon Hills, IL; 1Clinical Immunology Lab, Department of Microbiology and Immunology, Chicago Medical School; Rosalind Franklin University of Medicine and Science, North Chicago, IL; 2North Chicago, IL; 3Rosalind Franklin University of Medicine and Science, North Chicago, IL; 4Chicago Medical School, Rosalind Franklin University of Medicine and Science, North Chicago, IL, Vernon Hills, IL.
OBJECTIVE: Dysregulated T regulatory cells and T helper (Th)-17 cells have been proposed as possible immune etiologies for recurrent pregnancy losses (RPL) and repeated implantation failures (RIF). In this study, we aim to investigate Th17, Treg cells, and the Treg/Th17 ratios during pregnancy in women with RPL (≥2 prior to 20 weeks) and normal pregnant women.

MATERIALS AND METHODS: A prospective cohort study was performed to investigate Th17, Treg, and Th17/Treg ratios in normal pregnant women (n=220) and women with a history of 2 or more RPL (n=43). Women with RPL (n=43) were composed of 11 women who miscarried (RPL-SAB) and 32 women who had a live born infant (n=32) with personalized immunomodulation treatment.

Peripheral blood samples were collected during pregnancy, CD3+CD4+IL-17+T helper 17 (Th17), CD3+CD4+CD25+CD127-T regulatory (Treg) were measured by flow cytometric analysis and Treg/Th17 ratio was calculated. Th1/Th2 cell ratios and natural killer (NK) cell levels and cytotoxicities were also measured by using flow cytometric analysis.

Statistical analysis was performed by using the student t-test, the one-way ANOVA, a binary logistic regression analysis, and a receiver operating characteristic (ROC) – area under the curve (AUC) analysis as indicated.

RESULTS: In normal pregnant women, Treg cells tend to increase in the mid-second trimester and decrease in the third trimester. However, there were no significant changes in Th17 or Treg cells throughout pregnancy. Again, Treg/Th17 ratios tend to decrease towards the end of gestation but it was not statistically significant.

The RPL-SAB group had significantly lower proportions of Th17 cells (Mean ± SE %) (1.10 ± 0.12 %) and Treg cells (4.48 ± 0.33%) than normal pregnant women (1.54 ± 0.67%, 6.82 ± 0.101 respectively) (P<0.05, P<0.001 respectively). However, there was no difference in the Treg/Th17 Ratio between RPL-SAB group and normal pregnant group. RPL-SAB group tends to have decreased Treg/Th17 ratios.

In women with RPL, the ROC curve analysis of Treg/Th17 ratio in the early pregnancy revealed the AUC was 0.760 (P = 0.054). Similarly, when combining 4 covariates of Treg/Th17 Ratio, %CD56, NK 50:1, and TNFα/IL10 producing Th1/Th2 cell ratios the AUC was 0.856 (P = 0.007), between 4-10 weeks of gestations.

CONCLUSIONS: Our findings suggest that patients with a history of RPL undergoing immune modulation treatment have lower levels of Treg and Th17 when compared to normal controls. However, Th17/Treg cell ratios were the same between women who delivered a liveborn infant and normal pregnant women. Treg/Th17 ratios in the first trimester may be a useful biomarker to differentiate between patients who may experience an SAB. Additionally, combining addition biomarkers may be of clinical relevance in predicting pregnancy success.

IMPACT STATEMENT: With the new emerging data, new biomarkers could be used to determine the outcomes of pregnancy in the field of RPL.

P-168 6:30 AM Monday, October 24, 2022

A NATIONAL SURVEY OF WOMEN AND MEN’S EXPERIENCES OF RECURRENT MISCARRIAGE CARE. Caragh Flannery, Dr Marita Hennessy, BA, PhD, Rebecca Dennedy, PhD, Karen Matvienko-Sikar, PhD, Keelin Odonoghue Prof, PhD FRCOG FRCPI 1University College Cork, Cork, Ireland; 2Infant Research Centre, University College Cork, Cork, Ireland; 3INFANT Centre, Cork, Ireland.

OBJECTIVE: Providing individualised care, respect for women’s opinions, and appropriate clinical information is imperative to those who experience recurrent miscarriage (RM). However, currently, there is no national standard for the management/care of those who experience RM in Ireland. This study aims to explore the experiences of women and men who have received RM care in Ireland.

MATERIALS AND METHODS: A cross-sectional study was conducted using an anonymous web-based national survey. Women and men over 18 who have experienced two ≥ first trimester miscarriages in the last ten years and who have received care in Ireland were invited to participate. The survey

Table 1: Prevalence of Mullerian Anomalies

<table>
<thead>
<tr>
<th>ASRM MAC 2021</th>
<th>Variant</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septate Uterus</td>
<td>Normal/ Arcuate uterus</td>
<td>23 (24.0)</td>
</tr>
<tr>
<td>Bicornuate uterus</td>
<td>Bicornuate uterus</td>
<td>49 (51.0)</td>
</tr>
<tr>
<td>Unicorne uterus</td>
<td>R/L Unicorne uterus</td>
<td>3 (3.13)</td>
</tr>
<tr>
<td>Unicorne uterus</td>
<td>R/L Unicorne uterus with R/L uterine body communicating cavity</td>
<td>9 (9.38)</td>
</tr>
<tr>
<td>R/L Unicorne uterus with R/L associated uterine remnant with functional endometrium</td>
<td>2 (0.08)</td>
<td></td>
</tr>
<tr>
<td>Uterus didelphys</td>
<td>Uterus didelphys</td>
<td>1 (1.04)</td>
</tr>
<tr>
<td>Uterus didelphys with longitudinal vaginal septum</td>
<td>1 (1.04)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>96</td>
</tr>
</tbody>
</table>
P-169 6:30 AM Monday, October 24, 2022

GESTATIONAL SAC DIAMETER IN EARLY PREGNANCY PREDICTS BIRTHWEIGHT AND PREMATURITY
Bruce S. Shapiro, M.D., Ph.D.,1 Kajal Verma, M.D.,2 Melody A. Rasouli, M.D., MBA,3 Forest C. Garner, M.S.,4 Leah A. Kaye, B.A., M.D., M.S.,4 Carrie E. Bedient, M.D.1,4
1Fertility Center of Las Vegas, Las Vegas, NV; 2INFANT Centre, Cork, Ireland; 3University College Cork, Cork, Ireland; 4University of Connecticut Health Center, Las Vegas, NV.

OBJECTIVE: To determine if sonographically observed factors predict birthweight and prematurity.

MATERIALS AND METHODS: This is an IRB-approved retrospective study. The study includes pregnancies following transfer of single vitrified-warmed blastocysts resulting in live birth for which the requisite ultrasound data were available. Gestational sac diameter were measured at 6.5-7 weeks and again at 10 weeks gestation over a 5-year period. Endometria were artificially prepared with exogenous estradiol and progesterone. To preclude any effects of vanished twins, only single-blastocyst transfers resulting in single sacs, single fetal hearts, and singleton deliveries were included. Other available predictors were maternal age, endometrial thickness, day of blastocyst expansion, post-warming blastocyst grade, and infant gender. Multiple linear regression models to predict birthweight were run with and without gestational age at birth included, because it is a potential moderator of other effects. Logistic regression was used to evaluate predictors of premature birth (<37 weeks). P-values less than 0.05 were considered significant.

RESULTS: There were 250 qualifying ultrasounds at 6.5-7 weeks and 238 at 10 weeks. Patients averaged 32.2±5.1 years at oocyte collection. For the 6.5-7 week ultrasounds, the significant predictors of birthweight were infant gender, and gestational sac diameter. For the 10-week ultrasounds, the significant predictors of birthweight were blastocyst expansion grade, infant gender, crown-rump length, and gestational sac diameter. In all cases, a larger sac was associated with greater birthweight. This was also true when gestational age at birth was included in the model. Small sacs appeared to assist their own growth/face gestational age at birth and increased risk of prematurity in the 6.5-7 week ultrasound, but had no significant correlation in the later ultrasounds.

CONCLUSIONS: Sonographic measures of early in utero embryonic growth correlated with birthweight and prematurity. This might be through variation in the quality of early placentation.

IMPACT STATEMENT: It is possible that sonographic measures can give early prediction of perinatal risks following ART pregnancies. Further investigation is needed to determine if this might predict other consequences of abnormal placentation.

SUPPORT: None

P-170 6:30 AM Monday, October 24, 2022

ASSESSING THE COSTS ASSOCIATED WITH THE IMPLEMENTATION OF A BEST PRACTICE MODEL OF CARE FOR RECURRENT MISCARRIAGE CLINICS IN THE REPUBLIC OF IRELAND
Caragh Flannery Dr, BA, PhD,1 Lee-Anne Burke, BA, MA, PhD,2 Keelin Odonoghue Prof, PhD FRCOG FRCP1 1University College Cork, Cork, Ireland; 2INFANT Centre, Cork, Ireland.

OBJECTIVE: Recurrent miscarriage (RM) affects 1%-5% of the reproductive age population. Given increasing calls for dedicated recurrent miscarriage clinics (RMC), decision-makers will require data on the resultant budgetary implications. The aim of this study was to identify the potential costs to the Irish healthcare system of implementing a best practice RMC model of care.

MATERIALS AND METHODS: A ‘best practice’ RMC was developed as part of the RE:CURRENT Project. A micro-costing approach was employed to assess the total cost of the proposed best practice RMC model, including assessing measures of effectiveness of this or similar models of care, this analysis provides a valuable system level. While future studies should explicitly consider the cost-effectiveness of this or similar models of care, this analysis provides a valuable first step in providing a detailed breakdown of the associated costs and budget implications.

IMPACT STATEMENT: At present, current provision in Ireland does not appear to meet the needs of the target patient population and alternative models of care, informed by international best practice, should be designed, piloted, and evaluated. In this and in the wider context of increasing constraints on public finances and healthcare resources specifically, evidence on costs and economic impact should be a key consideration.

E-POSTER ABSTRACT SESSION: 18

P-171 6:30 AM Monday, October 24, 2022

ASSOCIATION OF MIR -149 T>C AND MIR-27AA>G GENE POLYMORPHISMS WITH RECURRENT PREGNANCY LOSS RISK IN GREEK POPULATION
Sofoklis Stavros, MD, Ph.D.,1 Georgia Panagou, MSc,1 Despoina Mavrogianni, PhD, Dr.1 Peter Drakakis, Professor 1Molecular Biology of Reproduction Unit and Recurrent Abortions Unit, Assisted Reproduction Division, Athens, Greece; 2Molecular Biology of Reproduction Unit and Recurrent Abortions Unit- Assisted Reproduction Division-Medical School- National and Kapodistrian University of Athens, 1st OB-GYN Department- Alexandra General Hospital, Athens, Greece; 3Molecular Biology of Reproduction Unit and Recurrent Abortions Unit, Assisted Reproduction Division, Athens, Greece.

OBJECTIVE: Are miR-149 T>C AND miR-27AA>G gene polymorphisms associated with recurrent pregnancy loss risk in Greek population?
MATERIALS AND METHODS: Two hundred women with at least two consecutive spontaneous abortions (RPL) and 200 women as a control group who have completed one pregnancy were included in this study, between September 2010 and September 2021 in Alexandra Maternity Hospital. Controls were selected from women who delivered term babies. Arterial blood was collected from all women and the blood sample was collected from the maternal vein after excluding fetal blood. DNA was extracted, and PCR was performed to identify the miR-149 T>C and miR-27a A>G genotypes. Statistical analysis for RPL group was performed via chi-squared test and the Fisher’s exact test.

RESULTS: 58 women (29%, 1) were homozygous for the wild type allele, miR-27aAA, 90 women (45.2%), were heterozygous, miR-27aAG, while 51 women (25.6%) were revealed homoygous for the miR-27aA-G polymorphism, miR-27a GG. The frequencies of miR-27a GG (OR = 3.283, P-value < 0.001, 95% Confidence Interval [CI] = 1.857 - 5.804) genotype were higher in patients with at least two consecutive spontaneous miscarriages than control group and the difference was statistically significant. In specific, patients with recurrent abortions are 3.2 times statistically significantly more likely to have polymorphism (GG) compared to controls (OR = 3.283, p < 0.001). In the group of patients with recurrent spontaneous miscarriages, 102 women (51.3%) were homozygous for the wild type allele, miR-149TT, 68 women (34.2%) were heterozygous, miR-149CT, while 29 women (14.6%) were revealed homoygous for the miR-149 T>C polymorphism, miR-149 CC. The frequencies of miR-499CC (OR= 0.896, P-value= 0.692, 95% Confidence Interval [CI] = 0.519 - 1.546) genotype were not higher in patients with at least two consecutive spontaneous miscarriages than control group and the difference was not statistically significant.

CONCLUSIONS: Results of the present study may be applied to establish a genetic panel associated with immune response in women with RPL, providing additional information for the pathophysiology of the disease, and a subsequent personalized approach to RPL women.

IMPACT STATEMENT: A statistically significant difference may be established between miR-27aA>G polymorphism and recurrent pregnancy loss (RPL), but not between miR-149 T>C and RPL.

SUPPORT: This Research is co-financed by Greece and the European Union (European Social Fund-ESF) through the Operational Programme «Human Resources Development, Education and Lifelong Learning» in the context of the project “Reinforcement of Postdoctoral Researchers – 2nd Cycle” (MIS-5033021), implemented by the State Scholarships Foundation (IKY).

P-172 6:30 AM Monday, October 24, 2022

FUTURE PREGNANCY OUTCOMES AFTER RECURRENT FIRST-TRIMESTER MISCARRIAGE.

Laura Aoife Linehan, MB Bch BA, MSc,1 Indra Judit San Lazaro Campillo, PhD,1 Marta Hennessy, PhD,1 Caragh Flannery, Dr, BA, PhD,2 Keelin Odonoghue, Prof, PhD FRCOG FRCP1 1University College Cork, Cork University Maternity Hospital, Cork, Ireland; 2National Perinatal Epidemiology Centre, Cork, Ireland; 3University College Cork, Cork, Ireland; 4INFANT Centre, Cork, Ireland.

OBJECTIVE: We undertook a retrospective cohort study to identify subsequent pregnancy outcomes in women with recurrent miscarriage (RM), defined as three or more consecutive first-trimester miscarriages, to assess if maternal characteristics, investigations or treatments were linked to pregnancy outcomes and to measure the overall live birth rate.

MATERIALS AND METHODS: Women attending a consultant-led RM clinic at a tertiary university hospital in Ireland over a 12-year period (2008–2020) with a confirmed diagnosis of primary or secondary first-trimester RM were eligible for inclusion. Women with non-consecutive first-trimester miscarriages or ectopic pregnancy were excluded. Medical history, investigative findings and management were gathered from paper and electronic medical records. Data were analysed using SPSS (V27). Associations between maternal characteristics and outcomes were explored using χ² test, (significance, p < 0.05). Multiple linear regression analysis was performed using a stepwise approach.

RESULTS: 748 women were included; 332 (44%) primary and 416 (56%) secondary RM. The median age was 36 years (range 19-47). 573 women had a subsequent pregnancy (77%); 359 (63%) had a live birth and 208 (36%) had a further pregnancy loss, (189 first-trimester miscarriages, 19 adverse pregnancy outcomes). Women aged 35-39 were more likely to have a live birth than no pregnancy (RR 2.3 (95% CI [1.51,3.50])). Women aged 16-20 were least likely to have a live birth (RR 3.74 (95% CI [1.80,7.79])) or a miscarriage (RR 2.3 (95% CI [1.07,4.96])) than no pregnancy. Smokers were less likely to have a live birth (RR 0.37 (95% CI [0.20, 0.69])) or a miscarriage (RR 0.45 (95% CI [0.22, 0.90])) than no further pregnancy. Couples with an abnormal parental karyotype were less likely to have a miscarriage than no further pregnancy (RR 0.09 (95% CI [0.01,0.79]))

Including successive pregnancies during the study period, the overall live birth rate was 81% (n=466), falling to 44% in women ≥40 years and 54% in women with infertility.

Fetal aneuploidy was the most common investigative finding (78%; n=111). Following disclosure from maternal anti-nuclear antibodies (12%; n=89), abnormal thyroid function tests (8%, n=59), Factor V Leiden gene mutation (5%, n=35) and parental balanced translocation (4%, n=28).

Prescribed pharmacological treatments included high dose folic acid (75%; n=348), aspirin (96%; n=696), progesterone (52%; n=389), tinzaparin (24%); n=175), prednisolone (4%; n=28), metformin (2%; n=12) and hydroxychloroquine (1%; n=7).

CONCLUSIONS: Aneuploidy was the leading causative finding in our cohort; 60% of women had unexplained RM. Alongside supportive care, most women were prescribed folic acid and aspirin in a subsequent pregnancy. Most women (63%) had a live birth. Age, smoking and parental karyotype were associated with future pregnancy or live birth.

IMPACT STATEMENT: Our findings are largely reassuring for women with RM hoping to conceive. However, individual risk factors impact greatly on subsequent pregnancy outcomes, highlighting the importance of tailored counselling, especially for women over 40 and those with infertility.

SUPPORT: LL is PhD scholar funded through the Pregnancy Loss Research Group, Department of Obstetrics and Gynaecology, University College Cork.

MH and CF are Postdoctoral Researcher on a project funded by the Health Research Board Ireland [ILP-HSR-2019-011] and led by KOD, titled: ‘Study of the impact of dedicated recurrent miscarriage clinics in the Republic of Ireland’. The funders had no role in study design, data collection, analysis, decision to publish, or preparation of the manuscript.

P-173 6:30 AM Monday, October 24, 2022

ANRIL (ANTISENSE NON-CODING RNA IN THE INK4 LOCUS) GENE POLYMORPHISM rs4977574 IN WOMEN WITH RECURRENT PREGNANCY LOSS (RPL). Panagiotis Cheroveim, Cheroveim, MD, Despoina Mavrogianni, PhD, Dr, Sofoklis Stavros, MD, Ph.D., Peter Drakakis, Professor Molecular Biology of Reproduction Unit and Recurrent Abortions Unit, Assisted Reproduction Division, Athens, Greece, Greece.

OBJECTIVE: To investigate the potential association of ANRIL gene polymorphism rs4977574 associated with the presence and number of RPL.

MATERIALS AND METHODS: Design: Case-control study involving women with RPL and women following livebirth from a University Hospital.

Patients: Peripheral blood samples were collected from 56 women with RPL (RPL group) and 69 women following livebirth (Control group).

Laboratory techniques: DNA was extracted from peripheral blood utilizing PureLink Genomic DNA Kits. The genomic region containing the polymorphism of interest was amplified by PCR. Finally, results were visualized with agarose electrophoresis and ethidium bromide staining.

Statistics: T-test, analysis of variance, and χ² were used as appropriate. RPL group was further stratified according to number of pregnancy losses (two, three, and four pregnancy losses). Odds ratio (OR) and their respective 95% confidence intervals (CI) for allele A between two and three pregnancy losses was adjusted for maternal age and body mass index (BMI).

RESULTS: Allele A was significantly less prevalent in the RPL group compared to the controls [14 (25%) and 31 (44.9%), for RPL and controls respectively, p = .021]. When analysis was done according to specific genotypes, women in the RPL were more commonly homozygous for allele G (G/G), however results did not reach statistical significance [42 (75.0%) G/G, 11 (19.6%) G/A, and 3 (5.4%) A/A in RPL; 38 (55.1%) G/G, 22 (31.3%) G/A, and 9 (13.0%) A/A in controls; p = .062]. Following stratification with the number of pregnancy losses, 8 (30.8%) women with two pregnancy losses, 6 (23.1%) with three losses and none with four losses had at least one copy of allele A. Of them, 3 (11.5%) with two and none with three or four losses were homozygous (A/ A). After stratification, differences among groups were not significant [p = .078 and .188, for homozygous genotype (A/A) and allele A frequency, respectively]

Finally, adjusted OR for the presence of allele A between two and three pregnancy losses was not significant (adjOR, 95%CI: 0.54, 0.14-2.13, p = .375).

CONCLUSIONS: We found evidence that ANRIL gene rs4977574 polymorphism may be associated with the presence and number of RPL.
VITAL TRAINING IN SYSTEMATIC REVIEW AND META-ANALYSIS IN BIOMEDICAL RESEARCH: RESULTS OF SELF-EVALUATION BY RESEARCHERS.

Rossella Cannarella, MD, PhD; Yumna Yagoob, MD; Ramzan Saleh, MD; Florence Boitrelle, MD, PhD; Damayanthi Durairajanyagam, PhD; Ahmed Harraz, MD; Ashok Agarwal, PhD; Cleveland Clinic, Cleveland, OH; Department of Urology, Lilavati Hospital and Research Centre, Mumbai, India; Sohag University, Sohag, Egypt; ART Center - Andrology - CECOS, France; Department of Physiology, Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh Campus, Sungai Buloh, Malaysia; Mansoura University, Mansoura, Egypt.

OBJECTIVE: Systematic review and meta-analyses (SRMAs) are used to generate evidence-based guidelines. Although the number of SRMAs published in the literature has increased dramatically in the last decade, the training and the experience of the researchers performing SRMAs is usually never explained in the SRMAs’ methodology, which may reasonably represent a source of bias. The objective of this study was to describe in an objective manner the methodology used to train researchers joining a SRMA, in order to offer a model for use in future SRMAs.

MATERIALS AND METHODS: The Global Andrology Forum (GAF) is an international working group comprising experts in the field of andrology. On June 2021, the GAF planned to carry out a series of SRMAs on important topics related to male infertility. Researchers willing to participate underwent a focused online training before being approved to participate in the planned studies. The goals of training were to teach how to perform a search strategy using the Scopus database, evaluate the articles for quality of evidence (QoE) through four different scales [the Cambridge Quality Checklist, the Cochrane Risk of Bias Tool for Randomized Controlled Trials, the Consolidated Standards of Reporting Trials (CONSORT) guidelines, and the Jadad score], and extract the data from studies selected after the Scopus search. A total of 35 researchers were asked to complete 43 multiple choice questions (MCQs) which covered the knowledge in conducting SRMA.

RESULTS: Overall, the after-training scores were significantly higher than the before-training ones. In particular, knowledge of conducting a literature search using Scopus improved from 5.0 (2.5-7.0) to 8.0 (8.0-9.0) (p<0.001), knowledge of using the Cambridge Quality Checklists improved from 4.0 (1.5-7.0) to 8.0 (8.0-9.0) (p<0.001), knowledge of using the Cochrane Risk of Bias Tool for Randomized Controlled Trials improved from 4.0 (2.0-7.0) to 8.0 (7.0-8.5) (p<0.001), knowledge of using CONSORT guidelines improved from 4.0 (2.0-7.0) to 8.0 (7.0-9.0) (p<0.001), knowledge of using the Jadad (Oxford Quality) scale improved from 4.0 (1.0-6.5) to 8.0 (7.0-9.0) (p<0.001), knowledge of the PICO model for conducting a meta-analysis improved from 5.0 (3.0-7.0) to 8.0 (7.0-9.0) (p<0.001), and knowledge of critical reading of scientific articles improved from 7.3±2.1 to 8.8±1.0 (p<0.001).

CONCLUSIONS: Our results indicate that the use of the methodological steps employed in the training for conducting systematic review and meta-analyses can improve the knowledge in search strategy, the QoE analysis of articles, PICO model and on critical interpretation of scientific articles.

IMPACT STATEMENT: We describe, for the first time in literature, the step-by-step training for researchers in a set of skills essential for conducting meta-analysis before approving their participation in a SRMA. An objective description of the methodology used to train researchers to perform high quality SRMAs may improve their overall quality and reliability.

SUPPORT: None

P-174 6:30 AM Monday, October 24, 2022

IMPACT STATEMENT: Our results suggest that ANRIL gene polymorphism might have a role in the development of RPL. Providing additional evidence for the shared pathophysiological mechanisms hypothesis between cardiovascular diseases and RPL. Further research is required to shed light on the underlying mechanism, if one exists.

SUPPORT: None

P-175 6:30 AM Monday, October 24, 2022

GENDER DISPARITY IN LEADERSHIP ROLES: HOW DOES OBSTETRICS & GYNECOLOGY COMPARE TO OTHER SPECIALTIES?

Oliveia Vukcevich, BS; Manpreet Singh, BS; Erica Mitchell, BS; Pamela Sheffer, M.A.; Samar Nahas, MD; Mallory A. Stuparich, MD; Sadikah Behbehani, M.D.; University of California, Riverside, Riverside, CA; Memorial University of Newfoundland, St. John’s, NF, Canada; University of California Riverside, Riverside, CA; University of California, Riverside, School of Medicine, Riverside, CA.

OBJECTIVE: This study aims to explore gender trends in obstetrics and gynecology (OB/GYN) leadership positions compared to other specialties at medical academic institutions in the western region and identify potential contributing factors to existing gender discrepancies.

MATERIALS AND METHODS: Western states were chosen based on classification of western region states defined by the American Medical Association. These states included Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, North Dakota, Oregon, South Dakota, Utah, and Washington. A total of 26 United States allopathic medical schools were identified. Information collected included gender of department chair, number of years post-residency, subspecialty training, number of divisions in the department, and number of physicians in department. Gender identity of the medical school dean was also collected. Medical fields studied included OB/GYN, family medicine, psychiatry, and internal medicine. All information gathered was publicly available.

Chi-square tests of independence were performed to examine differences in the proportion of male and female chairs across the major medical specialties and associations between specialty chair gender and subspecialty training, department size, and division size. An independent samples t-test was conducted to assess differences in years in practice between male and female chairs across specialties.

RESULTS: OB/GYN and family medicine department chairs showed no significant difference in gender proportion (p > .05), whereas psychiatry, surgery and internal medicine had significantly more male chairs compared to female chairs (p = .022, .003, and .004 respectively). There were also significantly more male deans compared to female deans (p = .006). Gender of specialty chair was not associated with subspecialty training, size of department, or number of divisions, and male and female chairs did not differ in terms of years in practice, t(106) = 0.98, p = .328.

CONCLUSIONS: Although there has been increasing representation of women in academic medicine, significant gender discrepancies still exist in leadership positions. The fields of obstetrics and gynecology and family medicine set the precedent for fields to follow having more women in department chair positions compared to internal medicine, surgery, and psychiatry. Our current data show a multitude of factors did not significantly contribute to the gender identity of department chairs, raising the question of why such discrepancies exist. Our future directions include further investigation of this trend across all US allopathic medical schools.

IMPACT STATEMENT: Women continue to be underrepresented in academic medicine leadership with existing gender discrepancies in internal medicine, surgery, and psychiatry department chair and dean positions in western region institutions. Women have equitable representation in leadership positions in obstetrics and gynecology and family medicine. Further research is needed to identify existing trends nationwide.

SUPPORT: None financial support to disclose

P-176 6:30 AM Monday, October 24, 2022

CHALLENGES AND POTENTIAL PRACTICE GAPS FACED BY HEALTHCARE PROFESSIONALS INVESTIGATING MALE INFERTILITY: A PATIENT-INFORMED EDUCATIONAL STUDY IN EIGHT COUNTRIES. Markus S. Kupka, MD PhD; Monica Augustyniak, MPH; Sandro C. Esteves, M.D., Ph.D.; Giovani Coticchio, MD; Anita Fincham, MA; Patrice Lazare, M.Sc.; Sophie Peloquin, M.Sc.PH; Ludwig-Maximilians University, Munich, Germany; 2AXDEV Group Inc., Brossard, QC, Canada; Androfert, Campinas, Brazil; 3Family and Fertility Center, 9baby, Bologna, Italy; 4Fertility Europe, Brussels, Belgium.

OBJECTIVE: To explore the challenges and potential practice gaps that healthcare professionals (HCPs) investigating male infertility face in their work using a patient-informed educational study (PIES).

MATERIALS AND METHODS: A cross-sectional, single-blinded survey was conducted online using electronic questionnaires among self-identified HCPs from eight countries in Europe and the Americas. Participants were asked to rate challenges on a 4-point Likert scale and indicate where they would like to see more focus on education.

RESULTS: A total of 175 participants from eight countries completed the survey. The majority of participants were from the United States (52.6%) and Europe (39.5%). The most common challenges reported by HCPs were related to patient education (85.6%) and access to diagnostic tools (83.6%). Participants also identified the need for more education on the latest treatment options (90.4%) and the importance of patient counseling (91.6%).

CONCLUSIONS: The results from this study highlight the importance of addressing patient education and the need for more focus on access to diagnostic tools. This information can be used to develop targeted educational programs to better support HCPs investigating male infertility.

SUPPORT: None funding support to disclose
OBJECTIVE: This study aimed to inform continuing professional development (CPD) and continuing medical education (CME) activities by identifying challenges, barriers, and practice gaps of healthcare professionals (HCPs) providing fertility care and male and female patients. MATERIALS AND METHODS: Inclusion criteria for this mixed methods study were: being a physician (PHYS) or a laboratory professional (LAB) specialized in fertility care or being a patient (PAT) seeking/receiving care for infertility. Subjects were recruited from online panels and purposively sampled in Brazil, China, France, Germany, Italy, Mexico, Spain, and the UK. In-depth 45-minute semi-structured interviews were conducted (June-August 2021) with PAT, PHYS, and LAB, then transcoded and coded to identify emerging themes. An online quantitative survey was administered (November 2021) to a separate sample of PHYS and LAB then analyzed descriptively and using chi-squared statistical tests.

RESULTS: The perspectives of 248 PHYS (interviews=24, surveys=224), 123 LAB (interviews=24, surveys=99), and 28 PAT (all interviews) were collected. Triangulated results indicated sub-optimal knowledge and skills among HCPs to thoroughly investigate males' infertility. Attitudes, such as “male are rarely the cause of infertility,” were barriers to considering the relevant role of both genders. Over 67% of surveyed PHYS did not select visual disturbance, lubricant usage, and bariatric surgery as potential risks or indicators of male infertility. The theme of insufficient investigation was identified in PAT interviews, especially if perceived as “low-risk” by their HCPs. Variations by country were observed among PHYS surveyed, with sub-optimal skills investigating hypothalamic-pituitary-gonadal dysfunction (x̄=34%, n=22/63; Brazil 44%, n=12/27) and infectious causes of male infertility (x̄=35%, n=77/222; higher gaps in UK 52%, n=13/25, Spain 52%, n=14/27; China 44%, n=17/39). Surveyed LAB (30%) rated skills investigating spermatic defects as sub-optimal. Doubts and misinterpretations about the value of sperm DNA damage testing were found among interviewed HCPs, with perceived complexities in performing this type of diagnosis. An average of 26% (85/323) of survey respondents disagreed or were unsure if “sperm DNA damage testing is a tool that can guide optimal application of assisted reproductive technologies,” with higher reports in Germany (41%, n=15/37) and the UK (49%, n=18/37).

CONCLUSIONS: This study identified gaps in knowledge and skills hindering HCPs’ optimal screening and diagnosis of patients seeking fertility care, especially as it relates to the investigation of male-related factors of infertility. IMPACT STATEMENT: Findings derived from the perspective of both HCPs and patients point out to essential educational needs that should be addressed through tailored interventions, including CME/CPD opportunities, aimed to optimize the care of all patients.

SUPPORT: This project was supported by educational research funds from Merck KGaA, Darmstadt, Germany.

P-177 6:30 AM Monday, October 24, 2022
INFORMATION WANTED: REI FELLOWSHIP WEBSITES DO NOT DELIVER. Emily Allard-Phillips, M.D., 1 Meghan C. H. Ozcan, M.D., 1 Reetam Ganguli, undergraduate, 1 Alexis K. Gadson, M.D., 2 Gary N. Frishman, M.D. 3 University of Florida, Gainesville, FL; 2 Warren Alpert Medical School of Brown University, Division of Reproductive Endocrinology and Infertility, Providence, RI; 3 Brown University Women & Infants Hospital, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Providence, RI.

OBJECTIVE: Reproductive Endocrinology and Infertility (REI) fellowship websites are often the primary information source for prospective fellows. MATERIALS AND METHODS: A cross sectional review was performed of the websites of all ACGME certified REI fellowship programs. A total of 23 criteria across education and recruitment content areas were chosen based on literature with all utilized criteria appearing in 9 or more websites studied in this analysis. A total of 11 criteria were assessed. The website was then scored from a panel of four, with an additional independent review if discordance of more than 15% was noted. All informative points were analyzed using descriptive statistics. Websites total content scores were then compared based on geographic location and program size (1 fellow a year vs >1) using an ANOVA and t-test, respectively. Reviewers also quantified accessibility of information on the website using a 5-point Likert scale.

RESULTS: 49 REI Program websites were reviewed with a mean score of 13.7 of a possible 33 informative points (SD 4.7). Of the 23 areas assessed, on average, 59% of content was available on program websites. There was a significant difference between educational content (56.2%) and recruitment content (50.6%) (P<0.001). On average, 23% (15/64) of REI websites contained comprehensively accessible information (98%), program description (94%), description of application process (92%) and faculty listing (90%)—were present in 90% or more of all websites. Seven criteria, most notably surgical numbers (10%), use of simulation (16%), and commitment to diversity (22%) were absent from at least 50% of all websites. There were no significant differences when comparing by program size or region. The mean accessibility score was 2.9 out of 5.

CONCLUSIONS: There is a lack of consistently accessible, comprehensive information available on REI fellowship websites, independent of geographic location or fellowship size, identifying a universal opportunity for improvement. Increased information transparency could enhance the knowledge of prospective applicants regarding program details and potentially improve the match and compatibility between applicants and programs.

IMPACT STATEMENT: This study reveals a clear opportunity to improve the quality and usefulness of information shared on websites across all REI fellowships. REI fellowships should consider being the thought leader and implementing a standardized approach to both website content and presentation.

P-178 6:30 AM Monday, October 24, 2022
ANALYSIS OF REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY FELLOWS: CHARACTERISTICS FOR CURRENT TRAINEES TO CONSIDER. Zachary Anderson, MD, 1 Erika New, M.D., 2 Blake Evans, D.O. 3 University of Southern California, Los Angeles, CA; 4 University of South Florida, Tampa, FL; 5 S40 Research Pkwy, Oklahoma City, OK.

OBJECTIVE: To identify where current REI fellows trained for residency, and discover any patterns or characteristics of residency programs that lead to successfully matched REI fellows.

MATERIALS AND METHODS: All data was collected from publicly available websites. A current list of Obstetrics and Gynecology (OBGYN) residency and REI fellowship programs was obtained from the Accreditation Council for Graduate Medical Education (ACGME) website (www.acgme.org). Each fellow’s name and fellowship training institution were collected from a match list distributed by the Society for Reproductive Endocrinology and Infertility (SREI) for the graduating classes of 2023, 2024, and 2025. Residence training institution for each fellow was collected using search engines with search phrases that included: The fellow’s name, and combinations of the terms “Dr.”, “OBGYN”, “resident”, “REI”, and “fellow”. Statistical analysis consisted of descriptive statistics for numerical data.

RESULTS: There were 170 fellows identified in the REI fellowship classes of 2023-2025, and residency information was available for 169 fellows. There were 49 REI fellowship programs and 296 OBGYN residency programs identified. 16.5% (49/296) of all OBGYN residency programs also had an REI fellowship program. It was found that 63.9% (108/169) of REI fellows completed residency at an institution with an REI fellowship program, and 33.3% (36/108) of this group remained at the same institution for fellowship. The remaining 36.1% (61/169) of fellows trained at a residency institution not associated with an REI fellowship. Interestingly, many of these residents still came from the same institutions. 25 of the 61 residents in this group trained at the same 10 residency programs.

CONCLUSIONS: This study explores one variable consistently cited as important in matching competitiveness—where an applicant trained for residency. The majority of REI fellows train at residency programs with REI fellowships. This descriptive analysis provides a complete profile for one characteristic of REI fellows graduating from 2023-2025. This study may help medical students interested in REI select a residency training program.

IMPACT STATEMENT: Currently, the majority of fellows attended residency at a program affiliated with a REI fellowship. It is important to recruit and support applicants from OBGYN residencies without a fellowship.

P-179 6:30 AM Monday, October 24, 2022
DO GENDER DIFFERENCES EXIST IN LETTERS OF RECOMMENDATION FOR REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY FELLOWSHIP? Katherine M. Bolten, B.S., 1 Oluwateniola Brown, M.D. 2 Allison S. Komorowski, M.D., 1 Eve C. Feinberg, M.D., 2 Mary Kwasny, ScD 1 Chicago, IL; 2 Northwestern University, Chicago, IL; 3 Northwestern University.

OBJECTIVE: To determine if gender differences exist in letters of recommendation for REI fellowship for current trainees.

MATERIALS AND METHODS: An online survey was designed to collect letters of recommendation. A letter of recommendation was defined as any written material used to evaluate a candidate for fellowship consideration. The survey asked participants to rank order the importance of various characteristics in a letter of recommendation. These characteristics were ranked by 150 REI fellowship programs. SAVE statistics were then calculated.

RESULTS: 130 letters of recommendation were collected from REI fellowship programs. The most common characteristic was technical ability followed by practicing the specialty, knowledge of the candidate, and volume of patients seen. The SAVE statistic was 64% for technical ability, 58% for practicing the specialty, 46% for knowledge of the candidate, and 41% for volume of patients seen. The SAVE statistic was calculated to determine if gender differences exist in the importance of these characteristics.

CONCLUSIONS: Gender differences were not found in the importance of characteristics in letters of recommendation for REI fellowship. This may suggest that gender does not play a role in the evaluation of a candidate for REI fellowship.

IMPACT STATEMENT: This study reveals that gender differences do not exist in the evaluation of a candidate for REI fellowship. This information can help medical students and residents select a residency training program that aligns with their career goals.
OBJECTIVE: To determine if gender differences exist in letters of recommendation (LOR) for Reproductive Endocrinology and Infertility (REI) fellowship.

MATERIALS AND METHODS: All REI fellowship applicants’ LOR submitted in 2021 to a single institution were linguistically analyzed and qualitatively coded. Demographic information of both applicant and letter writer was collected and letters were de-identified by removal of names and pronouns of applicant and letter writer. Linguistic Inquiry and Word Count (LIWC), a validated computerized text analysis software, was used to explore the presence of 4 summary variables and 20 word categories. Multivariable analysis compared the LOR linguistic characteristics by gender of applicant and author. Dedoose was used for qualitative analysis to compare the frequency of code themes in LOR by applicant gender. Investigators independently coded letters and then met to reconcile codes with a third party if agreement could not be reached. Conducting a qualitative analysis in parallel to the linguistic text analysis allowed for further exploration of themes conveyed that were not evaluated in the text analysis. The mixed-method design was planned a priori. Interrater reliability was measured using Cohen’s kappa coefficient.

RESULTS: There were 272 letters from 72 applicants, 54 (76%) of which were women and 17 (24%) were men. One applicant was excluded because gender information was not specified and 269 letters were included in the LIWC and qualitative coding analysis. One hundred ten letters (41%) were written by women, and 159 (59%) by men. LOR written for men had higher mean word count than those written for women (537(27) vs 474 (10), p<0.04). LIWC showed that there were more risk words used to describe men applicants (p=0.01). When comparing word categories by applicant gender, women letter writers more frequently used communal (relationship-oriented), affect, and home word categories while men writers more frequently used affiliation-related words.

The most common themes identified on qualitative analysis were ability, research achievement, and leadership. LOR for males more commonly included: ability, rapport with patients, leadership, and altruism, while women applicants’ LOR more frequently mentioned grindstone and research achievement. Male applicants more commonly had strong endorsements while women had more doubt raisers. Cohen’s kappa coefficients ranged from 0.69 to 0.80, indicating good to excellent agreement.

CONCLUSIONS: Gender differences exist among both letter writers and applicants. Qualitative analysis revealed that women applicants were more likely to be described by their work ethic and research participation while men were more likely to be described by their ability and leadership.

IMPACT STATEMENT: Gender differences exist in letters of recommendation for Reproductive Endocrinology and Infertility fellowship applicants. Awareness of bias and mitigation strategies should be implemented to improve gender equity.

TABLE 1.

<table>
<thead>
<tr>
<th>Subscale of MBI-HSS</th>
<th>Score Before Pandemic</th>
<th>Burnout Level</th>
<th>Score After Pandemic</th>
<th>Burnout Level</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional Exhaustion</td>
<td>24.11</td>
<td>Moderate</td>
<td>33.36</td>
<td>High</td>
<td>.003</td>
</tr>
<tr>
<td>Depersonalization</td>
<td>13.36</td>
<td>High</td>
<td>17.38</td>
<td>High</td>
<td>.09</td>
</tr>
<tr>
<td>Personal achievement</td>
<td>30.79</td>
<td>High</td>
<td>27.55</td>
<td>High</td>
<td>.045</td>
</tr>
</tbody>
</table>

IMPACT STATEMENT: Gender differences exist in letters of recommendation for Reproductive Endocrinology and Infertility fellowship applicants. Awareness of bias and mitigation strategies should be implemented to improve gender equity.

OBJECTIVE: To evaluate the effect of Coronavirus (COVID-19) pandemic on burnout in resident and fellows working at a large academic institution.

MATERIALS AND METHODS: An anonymous, online survey was distributed to residents and fellows between March 16th, 2021 and April 13th, 2022 at a large academic center via a RedCap link. The survey analyzed physician demographics and burnout before and after the COVID-19 pandemic. Burnout was assessed using the Maslach burnout inventory Human Services Survey for Health Personnel (MBI-HSS). The MBI-HSS scale is comprised of 22-items consisting of three sub-scales: emotional exhaustion, depersonalization and personal accomplishment. All items were scored on a seven-point scale, ranging from 0 (never) to 6 (every day). Data analyses were performed using SPSS version 21.0. A p value <0.05 was considered to be statistically significant.

RESULTS: Of the 70 participants (response rate of 7%), median age was 29.9 years and most identified as white (58%) and female (70%). 32% (n=23) had previously been diagnosed with and treated for depression or anxiety. In this study, 25 participants (35%) showed high burnout before Covid and 41 participants (58%) showed high burnout across all sub-scales after Covid. A significant difference was shown on MBI-HSS subscales of emotional exhaustion and personal achievement among trainees before and after the start of the pandemic, indicating worsening burnout after the start of COVID-19 (Table 1). Previous diagnosis of depression and number of years in training were associated with higher levels of burnout.

CONCLUSIONS: Studies evaluating the psychological impact of pandemics on healthcare workers (HCWs) have reported long-lasting anxiety and depression. Burnout has been associated with increased risk of psychological distress and patient safety in HCWs. Our findings indicate worsening burnout among trainees after the start of the COVID-19 pandemic. Understanding the mental health impact of COVID-19 on HCWs is important to formulate preventive strategies for caregivers’ mental health, which could consequently lead to improved well-being for trainees and better care for patients.

IMPLICATION STATEMENT: There is ongoing need to consider and better prioritize the mental health needs of health care trainees during pandemics/epidemics; this will help to ensure that they can continue to provide high quality care to patients.

SUPPORT: None
OBJECTIVE: Patients with 5 or fewer follicles during IVF face a difficult choice: should they cancel the cycle or proceed to retrieval? Limited data exist to guide this decision. This study evaluates LBRs for retrievals with ≤5 follicles at trigger.

MATERIALS AND METHODS: This retrospective cohort study from an academic fertility center reviewed all IVF cycles yielding ≤10 oocytes from 2016-2020. Cycles were included if ≤5 follicles measuring ≥14 mm were verified at trigger. The primary outcome was rate of ongoing pregnancy or live birth per retrieval (LBR) after fresh or frozen transfer. Secondary outcomes were number of oocytes, mature oocytes (M2s), 2 pronuclear zygotes (2PNs), blastocysts for transfer or biopsy and euploid blastocysts (if preimplantation genetic testing for aneuploidy (PGT) was used). Statistics included Chi-squared, Fisher’s exact and Kruskal Wallis tests (p<0.05 significant).

RESULTS: 1502 cycles (900 with PGT) from 972 patients were included. Median age was 40 years (range: 26-48). See table for outcomes. Mean oocytes, M2s, 2PNs, blastocysts and euploids differed by follicle number (FN) (p<0.001). Across all ages, there were differences in LBR associated with FN (p<0.001). For patients <35y, LBR did not differ by FN. In the 35-37y group, LBR with 2, 3 or 4 follicles was lower than LBR with 5 (p<0.01). In the 38-40y group, LBR with 3 follicles was lower than LBR with 4 or 5 (p<0.05). In the 41-42y group, LBR with 2 or 3 follicles was lower than LBR with 5 (p<0.01). In the 42+y group, LBR with 4 follicles was lower than LBR with 5 (p<0.05). There were no other differences in LBR by FN.

IMPACT STATEMENT: Our results can help patients with ≤5 follicles as they weigh the emotional, physical and financial costs of retrieval.

OBJECTIVE: To assess infertility knowledge, mainly on sexually transmitted infections (STIs) and their impact on fertility, among the downtown Detroit African American population seen in a general obstetrics & gynecology (OB/GYN) clinic (not involving any fertility clinics). This is a community that has been disproportionately impacted by Gonorrhea/Chlamydia (G/C), pelvic inflammatory disease, ectopic pregnancies, and tubal factor infertility.

MATERIALS AND METHODS: Participants, after being roomed to see their health care providers, were given anonymous questionnaires with information on the study attached. It was highlighted that their participation was completely voluntary. The participation rate was 97% with only 5 out of 165 patients not interested in participating. The patients were asked to pick true, false or “don’t know” for the 13 statements obtained from the previously applied and field-tested International Fertility Decision Making Study. In the second section, they were asked to self-report their age, height, weight, past medical, surgical & OB/GYN history (including any history of STIs), family history, allergies, medications as well as tobacco, marijuana, and alcohol use. The data obtained was analyzed on SPSS (frequencies, descriptive statistics, and binomial logistic regression).

RESULTS: The mean correct fertility knowledge score for the 160 patients was 35.0%, significantly lower than the average score noted on the original study that designed the questionnaire, 56.9%. Only 41.3% of the participants correctly identified the item testing the knowledge of the relationship between STIs and fertility, while 55% of the same sample population self-reported having had either Gonorrhea and/or Chlamydia, and 41% of them self-reported having had another STI including but not limited to Trichomonas, genital Herpes, and Syphilis. 70% self-reported having had at least either G/C, or another STI. Direct logistic regression was performed to assess the impact of a set of predictor variables on the odds that respondents would correctly identify the statement on STIs and fertility. The model contained the following independent variables: age, parity, number of 1st trimester miscarriages, number of ectopic pregnancies, G/C &/or other STI history and total fertility knowledge score. The full model containing all predictors was statistically significant, χ² (6, N=156) = 44.602, p < 0.001. The model as a whole correctly classified 71.2% of the cases. Only the total fertility score of an individual had a unique statistical contribution to the model.

CONCLUSIONS: The population tested has a limited level of knowledge pertaining to infertility and more importantly, pertaining to the effect of the highly prevalent STIs within the community.

IMPACT STATEMENT: There is no difference in the knowledge of the group of individuals who have had Gonorrhea, Chlamydia &/or another STI, highlighting not only the need for education to the community, but also the need for teaching provided by the healthcare workers to individuals affected by these STIs.

REFERENCES:


<table>
<thead>
<tr>
<th>FN 1 follicle</th>
<th>Mean M2s (SD)</th>
<th>Mean 2PNs (SD)</th>
<th>Mean blastocysts (SD)</th>
<th>Mean euploids (SD)</th>
<th>LBR: age &lt;35y</th>
<th>LBR: age 35-37y</th>
<th>LBR: age 38-40y</th>
<th>LBR: age 41-42y</th>
<th>LBR: age &gt;42y</th>
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<tbody>
<tr>
<td>1.3 (1.1)</td>
<td>1.1 (1.1)</td>
<td>0.5 (1.0)</td>
<td>0.1 (0.6)</td>
<td></td>
<td>20% (1/5)</td>
<td>14% (1/7)</td>
<td>0% (0/8)</td>
<td>0% (0/20)</td>
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<tr>
<td>2.2 (1.5)</td>
<td>1.6 (1.2)</td>
<td>0.8 (0.9)</td>
<td>0.2 (0.4)</td>
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<td>24% (4/17)</td>
<td>7% (2/31)</td>
<td>19% (9/51)</td>
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<td>3.4 (1.7)</td>
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<td>1.3 (1.1)</td>
<td>0.2 (0.5)</td>
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<td>25% (7/28)</td>
<td>18% (9/51)</td>
<td>12% (9/77)</td>
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<td>3.4 (1.7)</td>
<td>1.8 (1.4)</td>
<td>0.3 (0.7)</td>
<td></td>
<td>37% (19/5)</td>
<td>22% (17/78)</td>
<td>25% (32/127)</td>
<td>25% (32/127)</td>
<td>25% (32/127)</td>
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<tr>
<td>5.1 (2.0)</td>
<td>3.7 (1.8)</td>
<td>1.9 (1.4)</td>
<td>0.5 (0.8)</td>
<td></td>
<td>44% (24/55)</td>
<td>41% (36/87)</td>
<td>28% (40/141)</td>
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</tbody>
</table>

SD = standard deviation
OBJECTIVE: To analyze whether there was a difference in search queries regarding the COVID-19 vaccine and male versus female infertility.

MATERIALS AND METHODS: Google Trends was queried using the terms “COVID-19 vaccine fertility”, “COVID-19 vaccine male infertility”, “COVID-19 vaccine female infertility” from 2/2020 – 12/2021. The search volume index graph for the United States was recorded along with the regional distribution of searches. Each query was then compared and analyzed to assess changes in the interest of these search terms over time.

RESULTS: Following the Emergency Use Authorization (EUA) of the COVID-19 vaccine in December 2020, there was a 75% increase in google searches for COVID-19 vaccine effect on fertility. There was an initial 80% increase in the number of searches regarding the vaccine and female infertility compared to a 50% increase in male infertility. There were an additional 2 spikes in April 2021 with an 80% male and 75% female infertility and in August 2021 with close to a 95% increase in female infertility searches and 90% for male infertility.

The Delta variant (August 2021) and Omicron variant (December 2021) surge increased searches in both male and female infertility. The region with the highest number of general vaccine fertility related searches over this study’s time period was the Northeast, with most searches in the states of Pennsylvania, New York and New Jersey.

CONCLUSIONS: There was an overall increase in general COVID-19 vaccine related queries regarding infertility with a slightly higher number of searches for its effect on female (80-95%) compared to male (50-90%) infertility during both variant surges. COVID surges correlated with an increase in both male and female infertility searches. This study highlights the general public concern regarding the COVID-19 vaccine and its effect on fertility. Future research should explore reasons behind these trends including dissemination of public information and landmark study publications.

IMPACT STATEMENT: There was an overall increase in general COVID-19 vaccine related queries regarding its effect on fertility with a higher number of searches for its effect on female compared to male infertility.

Table 1. Fertility knowledge as assessed by modified FIT-KS.

<table>
<thead>
<tr>
<th>FIT-KS Question Topic</th>
<th>Correctly Answered (N=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecundability 30yo</td>
<td>33 (44.6%)</td>
</tr>
<tr>
<td>Fecundability 40yo</td>
<td>43 (58.1%)</td>
</tr>
<tr>
<td>Miscarriage Rate</td>
<td>39 (53.4%)</td>
</tr>
<tr>
<td>IVF pregnancy rate 35yo</td>
<td>30 (40.5%)</td>
</tr>
<tr>
<td>IVF pregnancy rate &gt;45yo</td>
<td>36 (48.6%)</td>
</tr>
<tr>
<td>IVF live birth rate &lt;37yo</td>
<td>8 (10.8%)</td>
</tr>
</tbody>
</table>

OBJECTIVE: OBGYN residents have historically underperformed in Reproductive Endocrinology and Infertility (REI) subject matter on CREOG In-Training Examinations which can be attributed to a lack of time or education on their REI rotation. We seek to determine if utilizing a combination of ASRM computer learning modules and interactive lectures improves confidence in REI topics.

MATERIALS AND METHODS: Participants in the study included University of Colorado OBGYN residents completing their REI rotation. ASRM modules were selected based on the learning objectives for the course. Two interactive lectures related to infertility and the menstrual cycle were given to the residents during their rotation. Using a 5-point Likert scale, an 11 question survey was distributed to the residents at the start of the rotation and again at the end of the rotation assessing their confidence related to REI topics. Statistical analysis was performed using Fisher’s Exact Test for count data.

RESULTS: A total of 7 residents completed the pre-rotation survey and 5 residents completed the post-rotation survey. There was improvement in confidence levels in all topics from pre-rotation to post-rotation, and we noted an improvement from 0% confidence pre-rotation to 80% or more confidence in post-rotation in the following topics: knowledge of REI, interpreting test results of female infertility, best candidates for ovulation induction (OI), and understanding which patients are not candidates for OI. The ASRM modules residents felt were most beneficial included work up and testing of female infertility and PCOS.

CONCLUSIONS: Implementing a formal curriculum including interactive lectures and ASRM modules increased OBGYN residents’ confidence in REI topics and experience during their REI rotation.

IMPACT STATEMENT: We describe a curriculum that can be implemented in resident REI rotations that improves confidence and experience in REI.
95% confidence interval 2.0–4.7), class III (BMI 2.0, 1.2–3.2), 10–20% (3.0, 1.8–5.2), and 12.2), weight gain (compared to weight loss or maintenance) of 1–10%

P-186 6:30 AM Monday, October 24, 2022
RISK FACTORS FOR INCIDENT POLYCYSTIC OVARY SYNDROME (PCOS) DIAGNOSIS. Jacob Christ, MD,1 Onchee Yu, MS,2 Renate Schulze-Rath, MD, MSc,3 Jennifer Covey, BS,2 Erika Holden, BA,1 Jan Hilpert, MD,1 Elizabeth Micks, MD MPH, Susan D. Reed, MD, MPH, MS1 University of Washington, Seattle, WA;1 Kaiser Permanente Washington, Seattle, WA;1 Bayer AG, Berlin, Germany.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, yet it is unclear who are at greatest risk of developing this syndrome. Using a large population-based cohort, we sought to identify risk factors for incident PCOS diagnosis.

MATERIALS AND METHODS: A matched case-control analysis was completed utilizing patients enrolled in Kaiser Permanente Washington from 2006 to 2019. Patients were eligible for inclusion if they identified as female, were aged 16–40 years and had at least 3 years of enrollment with at least one healthcare encounter during that time. Individuals were excluded if they had a history of oophorectomy, hysterectomy or a PCOS diagnosis prior to study entry. PCOS cases were identified using International Classification of Diseases (ICD) diagnosis codes (ICD-9 256.4 or ICD-10 E28.2). For each incident case, 5 individuals without a PCOS diagnosis were matched based on birth year and enrollment status. PCOS diagnosis date was the assigned index date for the matched set. Potential risk factors reported in the 3 years prior to index date included: parity, obesity, metabolic syndrome, family history of PCOS, prediabetes, type 1 and 2 diabetes, weight gain, valproate use, premature menarche, and race (included as a marker of social determinants of health). Differences between cases and non-cases in each factor were evaluated using chi-squared and t tests. Multivariable conditional logistic regression was used to identify significant risk factors for incident PCOS diagnosis.

RESULTS: From 2006 to 2019, 2,491 incident PCOS cases were identified and matched to 12,455 non-PCOS females. Median age of PCOS cases was 29 years (standard deviation 6.8). PCOS cases, compared to non-PCOS, were more frequently nulliparous (69.6% vs 62.1%) and more likely to have obesity (53.8% vs 20.7%), metabolic syndrome (14.5% vs 4.3%), a family history of PCOS (8.5% vs 0.5%), prediabetes, type 1 and 2 diabetes, weight gain, valproate use, premature menarche, and race (included as a marker of social determinants of health). Differences between cases and non-cases in each factor were evaluated using chi-squared and t tests. Multivariable conditional logistic regression was used to identify significant risk factors for incident PCOS diagnosis.

P-187 6:30 AM Monday, October 24, 2022
LONGITUDINAL FOLLOW UP OF PATIENTS DIAGNOSED WITH COVID-19 DEMONSTRATES NO DECREASE IN OVARIAN RESERVE AS DEMONSTRATED BY SERUM ANTI-MULLERIAN HORMONE (AMH) AT 3 AND 6 MONTHS: A PILOT STUDY. Kathryn D. Coyne, MD,1 Jerry Adam Tribout, Jr., BS,2 Heather Tribout, BS, CCRP, Rebecca Flyckt, MD, Rachel S. Weinerman, MD1 University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH;1 University Hospitals, Cleveland, OH;2 Cleveland Clinic Foundation, Cleveland, OH.

OBJECTIVE: To assess the impact of COVID-19 infection on ovarian reserve as measured by serum AMH in reproductive age females at 3 and 6 months post diagnosis of COVID-19 infection.

MATERIALS AND METHODS: An institutional COVID-19 biorepository was used to identify female patients between the age of 18 and 41 years with serum samples collected at time of COVID-19 diagnosis, 3 months post diagnosis, and/or 6 months post diagnosis. After IRB approval, serum samples were analyzed for AMH level at each time point. A power analysis demonstrated a sample size of 22 unique participants provides 80% power to detect a 0.85 ng/mL difference in AMH level, with an alpha of 0.05. The paired Wilcoxon signed rank test was used to determine significant difference in serum AMH levels over two time points and the Friedman test was used to determine significant difference in serum AMH levels over three time points.

RESULTS: 22 unique participants had serum samples over at least two separate time points, including either time of diagnosis (0-13 days post diagnosis), 3 months (84-111 days) post diagnosis, and/or 6 months (180-190 days) post diagnosis. Mean age was 32.67±7.0 years and mean BMI was 32.65±9.1 kg/m². The majority of participants were Caucasian (68.2%) or African American (31.8%). One participant was Hispanic (4.5%) and the remainder were Non-Hispanic (95.45%). 50% of participants had received at least one dose of COVID-19 vaccine by the time of diagnosis, 45.45% had history of prior OCP use.

CONCLUSIONS: Obesity, weight gain and metabolic dysfunction are significant risk factors for incident PCOS diagnosis. The degree of obesity and percentage weight gain in the 3 years preceding diagnosis appear to be directly associated with the likelihood of a new diagnosis of PCOS.
ECLIPSE prognosis. (AMH less than 1 ng/mL), with the ultimate goal of improving the retrieved oocytes. These results lay the groundwork for future studies of AMH (0.50 – 0.99 ng/ml) presented a significantly higher number of oocytes obtained based on electrochemiluminescence (ECL) technology and represents one of the most robust diagnostic methods for measuring this hormone. ECLIPSE® AMH assay could allow the analysis of the relationship between the number of oocytes obtained in a follicular puncture after controlled ovarian stimulation (COS) with AMH levels, when they are lower than 1 ng/ml, a value below which the ovarian response could not be predicted with sufficient confidence. We aimed to establish the diagnostic sensitivity of the ECLIPSE® AMH method when the hormone level is less than 1 ng/ml in relation to the number of oocytes obtained in follicular punctures. Specifically, determine if there are differences in the number of oocytes obtained depending on the concentration of AMH in the sample: less than 0.49 ng/ml and between 0.50 – 0.99 ng/ml

MATERIALS AND METHODS: 1,452 patients who underwent COS for ICSI at Nascentis were studied between 2017 and 2019. All patients with AMH lower than 1 ng/ml were selected. AMH was measured in serum within 6 months prior to COS. In all cases, the diagnostic methodology was by ECL in the ECLIPSE ROCHE auto-analyzer. This methodology has a detection limit of 0.10 ng/ml (0.071 pmol/L) and repeatability 1 - 2.6 % CV (0.33 – 91.1 pmol/L: 0.046 - 20.8 ng/mL). The results of the follicular punctures (Number of oocytes obtained) of two different groups were analyzed based on the concentration of AMH obtained in the samples: A: less than 0.49 ng/ml and B: 0.50 – 0.99 ng/mL

RESULTS: 351 blood samples were analyzed. Group A had a mean AMH concentration of 0.30 ng/ml, while group B showed a mean of 0.76 ng/ml. When the number of oocytes recovered in the follicular punctures was analyzed, a significant difference was observed. Specifically, group A obtained a mean of 2.07 oocytes, while group B obtained 3.31 oocytes (W=19.082 p<0.0001).

CONCLUSIONS: The use of the ECLIPSE®AMH method (ROCHE) allowed us to find significant differences in the number of oocytes obtained post- follicular puncture based on the AMH values, specifically when these were less than 1 ng/ml. The group with the highest concentration of AMH (0.50 – 0.99 ng/ml) presented a significantly higher number of retrieved oocytes. These results lay the groundwork for future studies to assess the predictive value of this technique in poor responder patients (AMH less than 1 ng/mL), with the ultimate goal of improving the EOC prognosis.

IMPACT STATEMENT: It is possible that AMH values less than 1 ng/ml can predict the ovarian response after follicular puncture, if they are analyzed with the appropriate methodology.

P-189 6:30 AM Monday, October 24, 2022

USE OF ELECTROCHEMILUMINESCENCE METHODS TO EVALUATE THE RELATIONSHIP BETWEEN OVARIAN RESPONSE AND ANTI-MULLERIAN HORMONE (AMH) LEVELS WHEN THEY ARE LOWER THAN 1 NG/ML. Karina Genesio Ceratto, M.Sc., Marcela Cullere, PhD, Ivana Capitanelli, M.Sc, Cesar Sanchez Sarmiento, PhD NASCENTIS. ESPECIALISTAS EN FERTILIDAD Y GENETICA REPRODUCTIVA, Argentina.

OBJECTIVE: The evolution of biochemical methods to measure AMH allowed to obtain increasingly precise and reliable values of this marker of ovarian reserve. The Elecsys® AMH assay is an ELISA-type immunoassay based on electrochemiluminescence (ECL) technology and represents one of the most robust diagnostic methods for measuring this hormone. Elecsys® AMH assay could allow the analysis of the relationship between the number of oocytes obtained in a follicular puncture after controlled ovarian stimulation (COS) with AMH levels, when they are lower than 1 ng/ml, a value below which the ovarian response could not be predicted with sufficient confidence. We aimed to establish the diagnostic sensitivity of the Elecsys® AMH method when the hormone level is less than 1 ng/ml in relation to the number of oocytes obtained in follicular punctures. Specifically, determine if there are differences in the number of oocytes obtained depending on the concentration of AMH in the sample: less than 0.49 ng/ml and between 0.50 – 0.99 ng/mL

MATERIALS AND METHODS: 1,452 patients who underwent COS for ICSI at Nascentis were studied between 2017 and 2019. All patients with AMH lower than 1 ng/ml were selected. AMH was measured in serum within 6 months prior to COS. In all cases, the diagnostic methodology was by ECL in the ECLIPSE ROCHE auto-analyzer. This methodology has a detection limit of 0.10 ng/ml (0.071 pmol/L) and repeatability 1 - 2.6 % CV (0.33 – 91.1 pmol/L: 0.046 - 20.8 ng/mL). The results of the follicular punctures (Number of oocytes obtained) of two different groups were analyzed based on the concentration of AMH obtained in the samples: A: less than 0.49 ng/ml and B: 0.50 – 0.99 ng/mL

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CONCLUSIONS: The use of the Elecsys®AMH method (ROCHE) allowed us to find significant differences in the number of oocytes obtained post- follicular puncture based on the AMH values, specifically when these were less than 1 ng/ml. The group with the highest concentration of AMH (0.50 – 0.99 ng/ml) presented a significantly higher number of retrieved oocytes. These results lay the groundwork for future studies to assess the predictive value of this technique in poor responder patients (AMH less than 1 ng/mL), with the ultimate goal of improving the EOC prognosis.

IMPACT STATEMENT: It is possible that AMH values less than 1 ng/ml can predict the ovarian response after follicular puncture, if they are analyzed with the appropriate methodology.

P-189 6:30 AM Monday, October 24, 2022

PREVALENCE OF DIGENIC DISEASE IN PATIENTS DIAGNOSED WITH IDIOPATHIC HYPOGONADOTROPIC HYPOGONADISM/KALLMANN SYNDROME. Alexandra Poch, M.D.,1 Michael P. Dougherty, M.D.2 Robert A. Roman, MD,3 Lynn Chorich, B.S. M.S.4 Zoe Hawkins, B.S.5 Lawrence C. Layman, M.D.1 1Augusta, GA; 2Augusta University; 3Medical College of Georgia at Augusta University, Augusta, GA; 4Warrenville, SC; 5Medical College of Georgia at Augusta University.

OBJECTIVE: To determine the prevalence of digenetic disease in patients diagnosed with idiopathic hypogonadotropic hypogonadism (IHH)/Kallmann Syndrome (KS).

MATERIALS AND METHODS: Whole exome sequencing (WES) of 158 patients with IHH/KS at Yale underwent bioinformatics analysis and were filtered for 44 known genes associated with IHH/KS. The resulting variants were filtered by pathogenicity determined by ClinVar to identify 33 patients with 18 unique variants in 9 genes. Primers were designed by primer3 to confirm these variants using Sanger Sequencing. The pathogenicity of the candidate digenic variants of these 33 probands was obtained using the Varsome database. Prevalence was then calculated based upon these results.

RESULTS: WES of the 158 patients with IHH/KS resulted in over 370,000 variants. These variants were filtered for the 44 known genes associated with IHH/KS as recognized by OMIM. These variants were further filtered to identify those categorized as pathogenic based upon the ClinVar database. This resulted in 33 patients with 18 unique variants in 9 unique genes (ANOS1, CHD7, DUSP6, FGFR1, GNRHR, PROKR2, SOX10, SPRY4, TACR3). Gold standard Sanger sequencing confirmed 17 of the 18 variants in 31 of the 33 patients. Of the 33 patients, 27 patients were found to have an additional 36 variants total in genes associated with IHH/KS but not previously identified as pathogenic by ClinVar. Using the Varsome database, only one of the 36 variants was found to be pathogenic (TACR3). Three variants were found to be likely pathogenic (DMXL2, two variants of FGFR1). The remaining variants (32) were benign or variants of uncertain significance. Four patients did not have any additional variants identified. Of note, one patient with a variant in ANOS1 (X linked recessive) was also found to have a heterozygous pathogenic variant in TACR3 (autosomal recessive). Two patients were each found to have two GNRHR variants (autosomal recessive), suggesting possible compound heterozygosity.

CONCLUSIONS: Digenic inheritance occurs when variants in two different genes manifests a phenotype but variants in only one of the genes may or may not manifest the phenotype. The phenotype is often more severe when both genes are affected. Of the 158 patients with IHH/KS sequenced, 35 patients had a pathogenic variant in a gene associated with IHH/KS. Of these 33, 29 patients had at least one additional variant in a gene associated with IHH/KS. Only 4 of those 29 patients (2.5% overall) had the additional variant identified as likely pathogenic or pathogenic by Varsome. Digenicity is difficult to prove and its true prevalence is unknown. However, based upon our results, we suggest a possible prevalence of 2.5% in genes associated with IHH/KS.

IMPACT STATEMENT: The prevalence of digenetic hypogonadotropic hypogonadism/Kallmann Syndrome is unknown and difficult to prove. These results suggest a possible digenetic prevalence of 2.5% in genes known to be associated with IHH/KS. Further family studies and mouse models are needed to confirm findings.

REFERENCES

THE CLINICAL CORRELATION BETWEEN POLYCYSTIC OVARY SYNDROME (PCOS) AND PITUITARY ADENOMA. Sang Il. Kim, MD St. Vincent’s Hospital. The Catholic University of Korea, Suwon, Korea, Republic of (South).

OBJECTIVE: Hyperprolactinemia and polycystic ovary syndrome (PCOS) are on the list of the most frequent causes of female infertility. A pituitary adenoma is one of the most common brain tumors that cause infertility. In the neurological field, pituitary adenoma with PCOS is not common. However, many neurosurgeons often experience these patients who are referred from obstetrics and gynecology (OBGY). Because most of the patients are young and reproductive women, neurosurgery alone is difficult to establish a treatment plan. In this study, we investigate the incidence of pituitary adenoma combined with PCOS, cut-off prolactin (PRL) level to detect pituitary adenoma and treatment strategy.

MATERIALS AND METHODS: Medical records from November 2009 to March 2020 were reviewed in our institute, retrospectively. Total of 658 patients was enrolled. According to initial serum PRL level, patients were divided in 5 groups: A (0–25 ng/mL); B (25–50 ng/mL); C (50–75 ng/mL); D (75–100 ng/mL); E (≥100 ng/mL). We investigated the frequency of sella MRI and the incidence of pituitary adenomas as each group. Receiver operating characteristic (ROC) curve analysis was performed to determine a cut-off value of serum PRL level that could predict pituitary adenoma in hyperprolactinemic PCOS patients.

RESULTS: Of 658 patients diagnosed PCOS, sella MRI was performed in 19 (2.9%, 19/658) patients. Finally, a total of 14 (2.2%, 14/658) patients with pituitary adenoma were identified. The mean value of serum prolactin level of these patients was 79.2 ± 61.8 (range, 20.8–211.9) ng/mL. The mean age and follow up period were 26.1 ± 6.2 (range, 17–38) years and 29.1 ± 26.9 (range, 3–84) months, respectively. In group A to C, the 11 patients who underwent sella MRI, 6 had pituitary adenoma (54.5%, 6/11). On the other hand, in Group D to E, of the 8 patients who underwent sella MRI, all of them had pituitary adenoma (100%, 8/8). One patient in group A had a PRL of 26.67 ng/dL and underwent surgery (transsphenoidal approach) because of mass size was 2.9 × 3 × 1.9 cm and there was visual field defect with optic chiasm compression. The remaining patients were treated with bromocriptine or cabergoline and followed-up with OBGY department. Most of all (77%, 11/14) showed a favorable outcome (normalization of PRL). Patients who underwent sella MRI to detect pituitary adenoma in PCOS are calculated through self-reported height and weight at enrollment. Chi-square test was used to examine differences of disease prevalence by PCOS.

CONCLUSIONS: Our preliminary analyses showed that in comparison to patients without PCOS, patients with PCOS were more likely to have a family history of PCOS and increased risk of cardiometabolic diseases. We also identified that risk for other cardiovascular conditions is elevated among women with PCOS. Limitations include small sample sizes for some cardiovascular diseases, limiting our ability to determine accurate differences in prevalence among those with and without PCOS. Additionally, the cross-sectional evaluation limits causal inference.

IMPACT STATEMENT: Comparable to other studies, we showed an increased risk of cardiometabolic conditions in women with PCOS compared to those without. We demonstrated an increased risk of other cardiovascular conditions.

E-POSTER ABSTRACT SESSION: 20

P-190 6:30 AM Monday, October 24, 2022

UTILITY OF INSULIN CURVE CHALLENGE TESTING IN INITIAL WORKUP OF PCOS. Lauren Gray, MD, Elizabeth Kravitiz, MD, Morgan A. Fan, BA, Patricia Dillawn, BS, Amy K. Schutt, MD, MSCI, Elizabeth Kravitz, MD, Morgan A. Farr, BA, Amy K. Schutt, MD, MSCI. 1Houston, TX, 2Baylor College of Medicine, Houston, TX.

OBJECTIVE: To investigate and compare the utility of insulin curve testing versus other forms of clinical lab tests, such as the Oral Glucose Tolerance Testing (OGTT) and standard HOMA-IR, in identifying hyperinsulinemia in Polycystic Ovarian Syndrome (PCOS) patients.

MATERIALS AND METHODS: This study is a retrospective chart review from January 2018 to December 2020 of all women at least 18 years of age, presenting to the Texas Children’s Women’s Pavilion Family Fertility Center (FFC). All women with a diagnosis of PCOS by the Rotterdam Consensus Criteria 2003 were included. Patients who did not have a fasting glucose value from their initial clinic visits were excluded. A total of 290 women were included. Insulin curve testing was performed by providing patients with an oral solution of 75 grams of glucose, and measuring insulin values at fasting, one-hour, two-hour, and three-hour. A cutoff value of 2.0 was used for HOMA-IR.

RESULTS: 42.5% (123/289) of those who passed the OGTT challenge, failed the insulin curve challenge. 28.0% (123/437) of those who failed the insulin challenge, passed the BG challenge. Of those with a normal Hgb A1c, 10.8% failed the OGTT while 46.7% failed the Insulin Curve challenge. When using Rotterdam criteria as determining true presence of disease, the insulin curve challenge has a greater sensitivity compared to the OGTT (0.51 vs 0.15) and HOMA-IR (0.79 vs 0.41).

CONCLUSIONS: Early detection of insulin resistance (IR) in PCOS is vital, as hyperinsulinemia increases risk of developing hyperandrogenism and overt Type II Diabetes Mellitus (T2DM). For pregnant women, diabetes increases risk of perinatal morbidity and mortality, as well as detrimental long-term outcomes if not well-controlled.
A large proportion of those who passed the OGTT challenge, failed the insulin curve challenge. This means that many of those with early stage or subclinical IR may be missed by OGTT alone. Further, when examining those with a normal Hgb A1c, a much larger percentage had abnormal insulin curve testing than abnormal OGTT. This further illustrates the utility that insulin curve testing has in detecting IR earlier, compared to OGTT and Hgb A1c.

Currently, the gold standard for detection of insulin resistance is the two-hour OGTT. In our study, we compared the gold standard OGTT and the increasingly-popular HOMA-IR to the insulin curve challenge testing. Our data shows that the insulin challenge demonstrates a much higher sensitivity in detecting insulin resistance, when compared to either test. Thus, using the insulin challenge can help reduce under-diagnosis of insulin resistance in PCOS, especially in early stages of disease.

IMPACT STATEMENT: Insulin curve testing is clinically underutilized to capture those developing insulin resistance, who have yet to receive a diagnosis of PCOS. In order to prevent overlooking patients with insulin resistance, the insulin challenge should be considered as an initial lab test.

Earlier detection of IR allows for quicker initiation of drug therapies, leading to a reduction in the number of those who proceed to develop overt T2DM and eventual long-term health consequences.

SUPPORT: None
REFERENCES: None

P-193 6:30 AM Monday, October 24, 2022
ART OUTCOMES IN LEAN COMPARED TO OBESE PHENOTYPES OF POLYCYSTIC OVARIAN SYNDROME. Yuval Fouks, MD, 1 Denny Sakkas, PhD, 2 Alan S. Penzias, M.D., 3 Werner Neuhausser, M.D., PH.D., 4 David A. Ryley, M.D., 5 Denis A. Vaughan, M.D. 4 1Boston IVF-Eugin Group, Waltham MA 02451, U.S.A., Brookline, MA; 2Boston IVF - The Eugin Group, Waltham, MA; 3Boston IVF-The Eugin Group/Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA; 4Boston IVF, Waltham, MA; 5Boston IVF-The Eugin Group/Beth Israel Deaconess Medical Center/Harvard Medical School, Boston.

OBJECTIVE: To investigate differences in reproductive outcomes among patients with lean compared to obese PCOS phenotypes undergoing IVF.

MATERIALS AND METHODS: A retrospective cohort study was performed of patients with PCOS who underwent IVF in a single, US academically-affiliated infertility center between December 2014 and July 2020. A diagnosis of PCOS was assigned by the physician of record endocrinology charts and Rotterdam criteria. Patients were designated as lean (≤25) or obese (≥25) PCOS phenotype based on BMI (kg/m²) at cycle start. A baseline clinical and endocrinologic laboratory panel, cycle characteristics, and reproductive outcomes were analyzed. A multivariate logistic regression analyses and Kaplan–Meier curve for cumulative live birth rates was used to assess CLBR in the two phenotypes. Regression models were adjusted for age at stimulation cycle start, gravidity, parity, mode of fertilization and total dose of gonadotropins.

RESULTS: 1395 patients who underwent 2348 IVF cycles were included. The mean (SD) BMI was 22.7(2.4) in the lean and 33.79(6.0) in the obese group p <0.001. Reproductive outcomes are shown in Table 1. The mean (SD) number of oocytes retrieved and fertilized oocytes was significantly higher in the lean group (18.9(10.4) vs 16, 8(9.9), p <0.001), and 11.0 (7.6) vs 9.5(6.3), p <0.001, respectively. Blastulation and aneuploidy rates were not significantly different.

Although the pre-cycle endocrinologic panel differed significantly between phenotypes, multivariate regression analysis indicated that after adjustment for relevant confounders, PCOS phenotype was an independent predictor of CLBR. The incidence of adverse outcomes was comparable between different phenotypes of PCOS (OHSS associated cycle cancelation lean 1.6% vs obese 2.8%, p=0.2).

CONCLUSIONS: Lean PCOS phenotype is associated with a significantly higher CLBR compared to their obese counterparts. The number of freeze all cycles was higher among lean PCOS patients. These points can assist with individual patient counseling.

IMPACT STATEMENT: Compared to obese phenotypes, lean patients with PCOS are more likely to overrespond during ovarian stimulation, but ultimately have higher cumulative live birth rates after IVF. This study assists with PCOS patient counseling regarding treatment prognosis.

Table: Reproductive outcomes of PCOS phenotypes

<table>
<thead>
<tr>
<th></th>
<th>Lean (n=425)</th>
<th>Obese (n=971)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freeze all cycles % (n)</td>
<td>66% (282)</td>
<td>43% (425)</td>
<td>0.00</td>
</tr>
<tr>
<td>Blastulation rate</td>
<td>0.7 ±0.3</td>
<td>0.7 ±0.3</td>
<td>0.65</td>
</tr>
<tr>
<td>Aneuploid rate*</td>
<td>43.5 ±0.3</td>
<td>43.8 ±0.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Mean number of embryo transferred</td>
<td>1.1 ±0.8</td>
<td>1.2 ±0.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Live Birth per cycle n(%)</td>
<td>47.3% (125)</td>
<td>42.2% (594)</td>
<td>0.00</td>
</tr>
<tr>
<td>CLBR in freeze all cycles % (n)</td>
<td>53% (112)</td>
<td>45% (175)</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Data presented as mean and ±SD. *PGT cycles lean (28.5%) and obese (20.5%)
TRANSGENERATIONAL EFFECTS OF PRENATAL ANDROGEN EXPOSURE IN A LEAN POLYCYSTIC OVARY SYNDROME MOUSE MODEL. Janet Bruno-Gaston, M.D., 1,2 Alexandra Gannon, M.D., 1 Vipin A. Vidyadharan, PhD, 3 Amy K. Schutt, MD, MSCi, 2 William Gibbons, MD, 3 Chellakkonda Selvanesan Bless, BSC, 4 M.PHIL, M.SC, PHD. 1 Baylor College of Medicine, Houston, TX; 2 Houston, TX; 3 Baylor College of Medicine, Dept of Obstetrics & Gynecology, Houston, TX.

OBJECTIVE: Evaluate the intergenerational and transgenerational impact of prenatal androgen exposure on reproductive and metabolic phenotypes in a lean polycystic ovary syndrome (PCOS) mouse model.

MATERIALS AND METHODS: Pregnant dams (F0 generation) were given dihydrotestosterone or vehicle (sesame oil) on days 16.5, 17.5 and 18.5 gestation. Females of F1 generation developed PCOS with a lean phenotype. Females from F1 and F2 generations were bred with untreated males to yield the F2 and F3 generations respectively with no further androgen exposure during gestation. Estrus cycle analysis, BMI calculations and glucose tolerance test (GTT) were performed at 6-8 weeks for all three generations. A subset of mice from the F1 and F2 generations were superovulated and their oocytes were retrieved to assess for oxidative stress and mitochondrial function using JC-1 dye. Statistical analysis of data was done using student’s t-test, chi square and analysis of variance (ANOVA).

RESULTS: There was no difference in BMI, fasting glucose, or insulin levels between PCOS and control mice across all three generations. Lean PCOS mice demonstrated glucose intolerance with an increase in glucose area under the curve (AUC) at 15 and 30 minutes GTT across all offspring generations. Estrus cycle analysis showed a significant increase in the percentage of time spent in diestrus and cycle irregularity in the F1 generation. There was no difference in mean cycle length across all generations and a trend towards increased cycle irregularity and percentage of time spent in diestrus in lean PCOS mice in the F2 and F3 generations. Analysis of oocytes showed an increasing trend towards higher oxidative stress in the lean PCOS oocytes; further, there was a decrease in the red to green ratio in JC-1 dye indicating compromised mitochondrial membrane potential in the F1 and F2 generations.

CONCLUSIONS: Prenatal androgen exposure results in metabolic and reproductive dysfunction and mitochondrial abnormalities precede the reproductive phenotype. Further, oocytes from F1 and F2 mice demonstrated androgen-induced mitochondrial dysfunction with increased oxidative stress and compromised mitochondrial membrane potential indicating transmission across multiple generations.

IMPACT STATEMENT: Developmental programming can predispose offspring to adult disease patterns and increase susceptibility for ensuing generations Physiologic adaptations following androgen exposure during critical developmental windows alters metabolic and reproductive phenotypes in a lean PCOS mouse model with intergenerational effects on oocyte mitochondrial function. Adaptations in germ line cells could provide a mechanism through which this phenotype is perpetuated.

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P-196 6:30 AM Monday, October 24, 2022

PREVALENCE, INCIDENCE AND TRENDS IN POLYCYSTIC OVARY SYNDROME (PCOS) DIAGNOSIS. Onchee Yu, MS, 1 Jacob Christ, MD, 2 Elizabeth Micks, MD MPH, 1 Renate Schulze-Rath, MD, MSCi, 3 Jan Hilpert, MD, 3 Jennifer Covey, BS, 1 Erika Holden, BA, 3 Susan D. Reed, MD, MPH, MS, 1Kaiser Permanente Washington, Seattle, WA; 2University of Washington, Seattle, WA; 3Bayer AG, Berlin, Germany.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, yet incidence and prevalence rates are poorly defined and vary widely. In a population-based US study, we estimated PCOS incidence and prevalence over time, and by age and race.

MATERIALS AND METHODS: A retrospective cohort study of patients enrolled in Kaiser Permanente Washington in 2006-2019 was conducted. All members identified as female, aged 16-40 years with at least 3 years enrollment and at least one healthcare encounter during that time were eligible for inclusion. Individuals were excluded if they had a history of oophorectomy or hysterectomy. PCOS cases were identified using International Classification of Diseases (ICD) diagnosis codes (ICD-9 256.4 or ICD-10 E28.2). Those with a PCOS diagnosis prior to study entry were excluded from incidence rate estimation. Incidence rates were age-adjusted by direct standardization to the 2010 US census data. Secular trends in incidence overall, by age and by race were assessed using Poisson regression. Prevalent cases were defined as patients with a PCOS diagnosis anytime in or prior to 2019. Chart review was performed to validate incident cases identified by ICD codes using Rotterdam 2003 criteria.

RESULTS: Among 351,171 eligible patients who contributed 586,470 person-years, 2,491 incident PCOS cases were identified. Mean age at diagnosis was 26.9 (SD 6.8) years and mean BMI was 34.8 (SD 9.1) kg/m2. Overall all incidence rates were similar over time between 40.3 and 50.5 per 10,000 person-years. However, diagnosis rates increased over time in individuals ages 16-20 years from 31.0 to 51.9 per 10,000 person-years (p = 0.01) and decreased among those ages 26-30 years from 82.8 to 45.0 per 10,000 person-years (p = 0.02). Compared to other race groups, Hispanic individuals appeared to have higher PCOS incidence rates but the differences were not statistically significant. A small decreasing temporal trend in incidence rates was only observed among White individuals (p = 0.01). Among the 58,241 patients who contributed person-time in 2019, 3,036 (5.2%) had a PCOS ICD diagnosis code. Chart review of 700 incident cases diagnosed in 2011-2019 classified 60% as probable or definite incident, 14% as possible incident and 17% as prevalent PCOS.

CONCLUSIONS: Among a cohort of non-selected women in the US, not relying on patient self-report, we observed fairly constant rates of incident PCOS diagnoses over time (although estimates were conflated by prevalent cases). PCOS prevalence (5.2%) based on ICD codes was higher than prior published US nation-wide estimates (2.9%) [1]. Incident diagnoses increased through time in younger age groups and decreased in older age groups. Race did not appear to have a major impact on temporal rates.

IMPACT STATEMENT: In recent years, PCOS diagnosis rates have increased among younger individuals. This may be related to shifting practice patterns with greater awareness among practitioners of the impact of PCOS on long term health outcomes or improved prevention efforts. Increasing obesity rates may also be a factor driving the earlier ages at diagnosis.

SUPPORT: This project was supported by grant funding from Bayer AG.

REFERENCES:


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P-197 6:30 AM Monday, October 24, 2022

UTILITY OF INSULIN CURVE CHALLENGE TESTING AND TESTOSTERONE AS INITIAL LABWORK FOR PCOS WORK UP. Lauren Gray, MD, Elizabeth Kravitz, MD, Patricia Dillawn, BS, Morgan A. Farr, BA, Amy K. Schutt, MD, MSCi Baylor College of Medicine, Houston, TX.

OBJECTIVE: To assess the utility of the insulin curve challenge versus testosterone testing in detecting early development of insulin resistance

MATERIALS AND METHODS: This study is a retrospective chart review from January 2018 to December 2020 of all women at least 18 years of age, presenting to the Texas Children’s Women’s Pavilion Family Fertility Center (FFC). All women with a diagnosis of Polycystic Ovarian Syndrome (PCOS) by the Rotterdam Consensus Criteria 2003 were included. Patients who did not have a fasting glucose value, nor Total Testosterone value, from their initial clinic visits were excluded. A total of 290 women were included. A cut off value of 2.0 was used for Homeostatic Model Assessment for Insulin Resistance (HOMA-IR).

RESULTS: Neither Testosterone and HgbA1c (r=0.12, r2 = 0.015), nor testosterone and HOMA-IR (r2 =0.0004) are significantly correlated. When comparing those with PCOS to those without PCOS (as defined by Rotterdam criteria), there was a significant difference in mean testosterone values (39.67 ± 19.53 vs 13.61, p-value = 0.012), nor testosterone and HOMA-IR (r2 =0.0004) are significantly correlated. When comparing those who failed the insulin challenge to those who passed. This means that the insulin curve challenge may be largely superior in detecting insulin resistance and early development of subsequent hyperandrogenism in patients developing PCOS.

CONCLUSIONS: Among a cohort of non-selected women in the US, not relying on patient self-report, we observed fairly constant rates of incident PCOS diagnoses over time (although estimates were conflated by prevalent cases). PCOS prevalence (5.2%) based on ICD codes was higher than prior published US nation-wide estimates (2.9%) [1]. Incident diagnoses increased through time in younger age groups and decreased in older age groups. Race did not appear to have a major impact on temporal rates.

IMPACT STATEMENT: In recent years, PCOS diagnosis rates have increased among younger individuals. This may be related to shifting practice patterns with greater awareness among practitioners of the impact of PCOS on long term health outcomes or improved prevention efforts. Increasing obesity rates may also be a factor driving the earlier ages at diagnosis.

SUPPORT: This project was supported by grant funding from Bayer AG.

REFERENCES:

The findings in this study further support the pathophysiology behind development of PCOS. Hyperandrogenemia is a primary biochemical marker of PCOS. Insulin resistance in PCOS has been posited as the mechanistic precursor to hyperandrogenemia, as insulin binds to insulin receptors and IGF-1 receptors in the ovary leading to dysregulated androgen secretion from ovarian theca cells. IMPACT STATEMENT: These findings support the incorporation of the insulin curve challenge into the diagnostic workup of PCOS in order to detect patients earlier in their disease progression. Detecting insulin resistance earlier in patients with PCOS would allow for more timely medication initiation and thus tighter glycemic control that could prevent them from progressing to a more overt metabolic syndrome.

P-199 6:30 AM Monday, October 24, 2022
THE EFFECT OF CLOMIPHENE, METFORMIN, OR BOTH ON ANTI-MULLERIAN HORMONE (AMH) LEVELS: A NEW LOOK AT THE PREGNANCY IN POLYCYSTIC OVARIAN SYNDROME Trial (PPCOS I). Lydia Hughes, MD, Allison S. Komorowski, MD, David A. Aaby, MS, Protusha Sarkar, BA, Bhanu Kalra, PhD, Ajay Kumar, PhD, Richard S. Legro, M.D., Christina E. Boots, MD, MSCF, Northwestern University Feinberg School of Medicine, Chicago, IL; Northwestern University, Chicago, IL; Northwestern Feinberg School of Medicine, Chicago, IL; Ansh Labs, Webster, TX; Penn State College of Medicine, Hershey, PA; Northwestern University.

OBJECTIVE: To examine serum AMH levels in infertile women with polycystic ovarian syndrome (PCOS) before and after treatment with metformin, clomiphene citrate, or both.

MATERIALS AND METHODS: Cryopreserved serum samples were obtained from the PPCOS I. This study was a multi-institutional, randomized control trial of 626 infertile women with PCOS treated with clomiphene citrate plus placebo, extended-release metformin plus placebo, or a combination of metformin and clomiphene. Fasting serum was collected before and at study completion (confirmation of a pregnancy or up to 6 treatment cycles). AMH level was measured using an enzyme-linked immunosorbent assay (AMCHECK ELISA, AL-196, Ansh Labs LLC) and delta (Δ) AMH was calculated. A linear regression model was used to adjust for treatment duration and patient co-variants.

RESULTS: A total of 610 serum samples from 305 patients were obtained from PPCOS I (N = 113 clomiphene group, N = 79 metformin group, N = 113 combined group). There was no significant difference between groups by age, body mass index (BMI), race, bilateral ovarian volume, hirsutism score, fasting total testosterone, free androgen index, maximum follicular count, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) score, or treatment time. There was also no difference in baseline AMH between groups, but there was a significant decline in AMH following clomiphene (Δ = -2.1, P < 0.001) and combined clomiphene and metformin (Δ = -2.9, P < 0.001). However, there was no change in AMH in the metformin alone group, Δ = 0.0 (P = 0.7). Linear regression models revealed that the rate of change in AMH was dependent on the type of treatment (P < 0.001). The relationship between baseline AMH and treatment group remained significant after controlling for multiple patient covariates.

CONCLUSIONS: AMH significantly declined following ovulation induction with clomiphene and combined clomiphene and metformin in patients with PCOS. There was no effect of metformin alone on AMH levels.

IMPACT STATEMENT: While elevated AMH levels are associated with PCOS, little is known about the effect of ovulation induction on AMH. Understanding the influence of ovulation induction therapy on the fluidity of AMH levels may help providers predict treatment response in PCOS patients and better understand the pathophysiology of AMH levels as anovulatory women become ovulatory.

SUPPORT: Northwestern University Department of OBGYN Biostatistical Support Grant.

REFERENCES: none

P-201 6:30 AM Monday, October 24, 2022
THE ROLE OF CIRCULATING miRNAs IN MECHANISM OF ACTION AND PREDICTION FOR THE THERAPEUTIC RESPONSES OF METFORMIN IN POLYCYSTIC OVARIAN SYNDROME. Chu-Chun Huang, MD, Mei-Jou Chen, MD, PhD, Department of Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan; Department of Obstetrics and Gynecology, National Taiwan University Hospital National Taiwan University University Livia Shangyu Wan Scholar, Taiwan, Taipei, Taiwan.

OBJECTIVE: To study whether and how miRNAs were involved in the mechanism of action of metformin treatment for PCOS, and whether circulating miRNAs can be applied to predict the therapeutic responses of metformin.

MATERIALS AND METHODS: This is a case-control study at tertiary university hospital. Totally 75 PCOS patients with chronic anovulation and 20 non-PCOS controls were enrolled. All PCOS patients received metformin treatment for 6 months. Thirty-seven PCOS patients resumed ovulation after metformin treatment and were assigned as MET-OV group, while 38 patients remained anovulatory after metformin treatment and were assigned as MET-AO group. Pre-treatment and post-treatment plasma levels of fourteen miRNAs which were selected by literature review and were related to PCOS, insulin resistance, steroidogenesis were quantified with rtPCR (miR-21, miR-93, miR-132, miR-193b, miR-221, miR-222, miR-223, miR-27a, miR-125b, miR-208b, miR-212, miR-320a, miR-429, miR-483). Pre-treatment and post-treatment anthropometric data, hormonal and metabolic profiles were also measured. Predictive modeling based on miRNA levels was conducted to predict the recovery of ovulation after metformin treatment.

RESULTS: There was no significant difference among all the baseline hormonal and metabolic profiles between the MET-OV and MET-AO groups. However, significantly higher expressed miR-27a, miR-93 and miR-222 were shown in MET-OV group than the MET-AO group (P = 0.038, 0.03, 0.012) and the control group (P = 0.0001, 0.0003, 0.0272). After six-month metformin treatment, the level of insulin, homeostatic model assessment for insulin resistance, luteinizing hormone and six circulating miRNAs were significantly declined in MET-OV group (P = 0.0035, 0.0004, < 0.0001, 0.0004, < 0.0001, < 0.0001), while remained unchanged in MET-AO group. The area under curve, sensitivity and specificity of adjusted prediction model based on miRNA levels and clinical parameters (age, BMI, menstrual interval, the presence of hyperandrogenism) using logistic regression analysis was 0.807, 0.892, 0.632, respectively.

CONCLUSIONS: The present study demonstrated differentially expressed baseline plasma miRNAs levels between the MET-OV and MET-AO group, which could be applied to predict the therapeutic responses of metformin. And there was also significant difference among the chronologic changes of several circulating miRNAs between the MET-OV and MET-AO group, suggesting that these aberrantly overexpressed miRNAs might be involved in the pathophysiology of chronic anovulation in PCOS and their downregulation might participate in the underlying mechanisms of metformin treatment.

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<table>
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</table>

Values in mean ± SD

E-POSTER ABSTRACT SESSION: 21
OBJECTIVE: Our study suggested that these miRNAs which were related to insulin signaling pathways were involved in the pathophysiology of PCOS and the mechanism of action of metformin therapy. The baseline levels of these circular miRNAs could be applied to predict the therapeutic responses of metformin treatment. 

SUPPORT: This study was supported by grants MOST 109-2628-B-002-030-(C.C. Huang), and MOST 108-2314-B-002-146-MY3 (S.U. Chen) from the Ministry of Science and Technology of Taiwan and the National Taiwan University Hospital (110-004994).

P-203 6:30 AM Monday, October 24, 2022

IMPACT OF TSH LEVELS ON IN VITRO FERTILIZATION OUTCOMES IN EUTHYROID INFERTILE WOMEN. Viviane Rosado Rosado Negreiros D’Assunção, MD PhD,1 Caio Barbosa, MD, PhD,2 Luí Eduardo Negreiros Negreiros D’Assunção, MD,3 Denise Christofolini, M.SC., PHD,1 Ricardo Medeiros Negreiros, MD,3 Renato Oliveira, M.D, Bi ana Bianco, PHD,3 1Faculdade de Medicina do ABC, Brazil; 2Instituto Ideia Fertil de Saúde Reproductiva, Santo André, Brazil; 3Federal University of Paraíba, Brazil; 4fundação, Santo Andre, Sp, Brazil; 5Faculdade de Medicina do ABC, Sao Paulo, Brazil.

OBJECTIVE: International guidelines recommend TSH values <2.5 mIU/L in women trying to conceive since values above this level are related to a higher frequency of adverse reproductive outcomes. However, studies have produced conflicting results regarding the impact of TSH levels on reproductive outcomes, especially pregnancy rates. Therefore, we performed a retrospective study aiming to evaluate whether TSH values correlate with different gestational outcomes in euthyroid infertile women without autoimmune diseases undergoing in vitro fertilization (IVF) treatment.

MATERIALS AND METHODS: A retrospective cohort study was conducted comprising 256 women who underwent IVF treatment, aged ≤40 years, FSH ≤12.0 IU/L, both ovaries present without morphological abnormalities, and no history of endocrine diseases. The participants were divided into two groups: TSH 0.5-2.49 mIU/L (n=211) and TSH 2.5-4.5 mIU/L (n=45). The Mann–Whitney U test or the chi-square test was used to analyse the difference between groups regarding hormone levels and reproductive outcomes. A logistic regression was performed to verify possible associations among the primary and secondary outcomes with categorical variables.

RESULTS: Age, BMI, hormonal profile and IVF outcomes were not different between groups, neither gestational outcomes (p=0.982). Also, no difference was observed when the TSH levels were compared between patients with positive or negative gestational outcomes (p=0.27). Women who presented clinical pregnancy showed statically greater AFC (p<0.001), oocytes retrieved (p=0.032), MII (p=0.012) and total embryos (p=0.004), besides being a slightly younger than women who did not achieve clinical pregnancy (p=0.013). So, we stratify the women according to the age into women aged ≤35 years (n=154) and women aged >35 years (n=102). As expected, women aged ≤35 years presented statistically greater AFC (p<0.001), oocytes retrieved (p=0.029), MII (p=0.015), embryos (p=0.002); clinical pregnancy rate (p=0.019), and live births (p=0.041). The Spearman’s correlation test for serum TSH levels of euthyroid women and variables of interest associated to clinical pregnancy showed no statistically significant correlations.

CONCLUSIONS: TSH levels within the normal range did not affect pregnancy and live-birth rates in women who underwent IVF treatment.

IMPACT STATEMENT: It should be noted that despite international recommendations to maintain TSH levels <2.5 mIU/L in women with hypothyroidism, the results presented do not support encouraging treatment with Levothyroxine Sodium with the aim to lower the TSH range between 2.5 and 4.0 mIU/L to a target <2.5 mIU/L.

SUPPORT: None.

P-204 6:30 AM Monday, October 24, 2022

ASSESSING THE UTILITY OF SIMULTANEOUS CO-TESTING APPROACH WITH THYROID STIMULATING HORMONE (TSH) AND THYROID PEROXIDASE (TPO) ANTIBODY TESTING IN INFERTILE WOMEN. Alexandra Bader, MD,1 Navin N. Maredia, MD,2 Amanda Kohlmeyer, M.D.1, Stephanie K. Dahl, MD,3 April E. Batcheller, MD,3 Brent Hanson, MD2 1University of Minnesota, Minneapolis, MN; 2CCRM Fertility of Minneapolis, Edina, MN; 3CCRM Fertility of Minneapolis, Edina.

OBJECTIVE: Thyroid stimulating hormone (TSH) levels >2.5 mIU/L in the presence of thyroid peroxidase (TPO) antibodies have been associated with adverse pregnancy outcomes but treatment with levothyroxine has been shown to improve outcomes. Many fertility centers initiate treatment when TSH is >2.5 without evaluating TPO antibodies though benefits are unclear when TPO antibodies are negative. By forgoing TPO antibody testing, patients with elevated TSH but negative TPO antibodies are not identified. Therefore, we sought to identify the number of patients needing to undergo co-testing (NNT) with TSH and TPO antibodies to identify 1 patient with TSH >2.5 and negative TPO antibodies. A second objective was to characterize the relationship between TSH, TPO antibodies, and several demographic/gynecologic factors.

MATERIALS AND METHODS: A retrospective cohort study was performed at a university-affiliated fertility practice. Patients undergoing initial fertility evaluation between January and March 2022 were included. All patients had TSH and TPO antibodies drawn. NNT was calculated to identify 1 patient with TSH >2.5 and negative TPO antibodies. Logistic regression analyses were performed to characterize the relationship between TSH, TPO antibodies, and the following: age, race, anti-mullerian hormone (AMH) level, menstrual cycle regularity, miscarriage history, and infertility diagnosis.

RESULTS: 157 patients were evaluated (mean age 35.0±4.9). Mean TSH was 2.23, with 67.5% having a TSH >2.5 and 32.5% having a TSH >2.5. TPO antibody status was negative in 84.1% and positive in 15.9% of patients. The NNT to identify 1 patient with TSH >2.5 and negative TPO antibodies was 5 patients.

Logistic regression analyses compared patients with TSH ≤2.5 to those with TSH >2.5, respectively. No statistically significant differences were noted in age (34.7±4.8 vs. 35.6±5.0), race (68.9% white & 31.1% non-white vs. 64.7% white & 35.3% non-white), AMH level (3.4±3.4 vs. 2.8±2.8 ng/mL), percent of patients with irregular menses (27.4% vs. 21.6%), history of prior miscarriage (32.1% vs. 35.3%), or infertility diagnosis.

Similarly, comparing patients with negative TPO antibodies to those with positive TPO antibodies, respectively, no statistically significant differences were noted in age (34.5±4.7 vs. 37.4±5.3), race (65.9% white & 34.1% non-white vs. 76.0% white & 24.0% non-white), AMH level (3.3±2.4 vs. 2.5±2.3 ng/mL), percent of patients with irregular menses (25.8% vs. 24.0%), history of prior miscarriage (31.1% vs. 44.0%), or infertility diagnosis.

CONCLUSIONS: Patients with TSH >2.5 and negative TPO antibodies were frequently identified when a co-testing approach was applied, highlighted by the low NNT. In this population of infertile patients with no history of thyroid disease, levels of TSH and TPO antibody status were not associated with any of the demographic or gynecologic factors evaluated.

IMPACT STATEMENT: Obstetrical outcomes and levothyroxine treatment practices should be clarified for patients with TSH >2.5 and negative TPO antibodies since this subgroup is commonly encountered.
REMOTE MONITORING OF CYCLE TRENDS IN PATIENTS OF ADVANCED MATERNAL AGE - AN OPPORTUNITY TO STREAMLINE ACCESS TO IVF
Neha Kumar Sc.M., Aparna Divaraniya, PhD, Serena H. Chen, M.D., Oova Inc, New York, NY; Division of Reproductive Medicine, IRMS at St Barnabas, Livingston, NJ.

OBJECTIVE: Advanced maternal age (AMA) is associated with a decline in both ovarian reserve and oocyte competence. Yet, the proportion of individuals delaying childbearing until the 3rd-early 4th decade of life has greatly increased. In AMA patients, an infertility work-up is recommended after 6 months of regular unprotected intercourse. We looked to compare quantitative hormone data and cycle trends among AMA and non-AMA patients to inform fertility management.

MATERIALS AND METHODS: A total of 1,782 women were included in this study, and were grouped into two age-based cohorts: 34 years or older (829, 46.5%) and <34 years (953, 53.5%). All participants were users of the Oova platform, which collects patient demographic information, self-reported clinical information, and daily quantitative measurements for both luteinizing hormone (LH) and progesterone. Hormone levels were measured using an at-home urine-based lateral flow quantitative and multiplexed immunoassay (“test strip”) in combination with AI-enabled image processing via a smartphone camera. Cycle information was compiled for all users, including number of cycles tracked, cycle length, and average number of measurements obtained per cycle. Hormone data was used to classify cycles as ovulatory or anovulatory. Demographic, clinical, cycle, and hormone information was compared between the two age-based cohorts.

RESULTS: Results demonstrate that more cycles and more measurements per cycle were tracked with increasing age. Among women who were 34 years or older, 7.23% of cycles were classified as anovulatory; among women who were <34 years, 4.46% cycles were classified as anovulatory. The difference observed was statistically significant, with an odds ratio of 2.4. No other significant differences were identified between the two age-based cohorts.

CONCLUSIONS: The results from this study highlight the need to accurately monitor patients of advanced maternal age for ovulation confirmation. Earlier identification of patients who have anovulatory cycles can enable faster access to fertility treatment and care. The results additionally show that with increasing age, women are more engaged in tracking cycle data, particularly with a remote lab-quality diagnostics system like Oova.

IMPACT STATEMENT: Remote diagnostic tools can potentially lower barriers to care by providing more detailed data as well as greater efficiency and satisfaction for both patient and provider. Clinicians can use this data to inform management beyond historical guidelines. Here, we show that by proactively monitoring fertility hormone levels in AMA patients, we can identify patients who are experiencing anovulatory cycles and expedite access to fertility treatment.

FERTILITY BENEFITS FOR RESIDENTS: PUBLICLY AVAILABLE INFORMATION AT THE TOP 50 US MEDICAL SCHOOLS
Melody A. Rasouli, MD, MBA, Francesca Barrett, MD MBA, Morgan S. Levy, BS, Ashley S. Kim, MD, Maya Roymtan, BS, Nicole Cumbo, BS, Hina Talib, MD, Erica C. Kaye, MD University of Nevada, Las Vegas, Las Vegas, NV; New York University School of Medicine, New York, NY; Boynton Beach, FL; University of Oklahoma, Oklahoma City, OK; Loyola University, Chicago, IL; Pennsylvania State Hershey, PA; Montefiore, Bronx, NY; St. Jude, Memphis, TN.

OBJECTIVE: Infertility affects one in four physicians, yet current availability of fertility benefits within ACGME-accredited residency programs in the United States (US) is unknown. In particular, 29% of residents experience infertility, and 63% feel low or no support from their residency program regarding fertility care (Aghajanova et al., 2017). Our objective was to examine the publicly available fertility benefits information for prospective residents.

MATERIALS AND METHODS: The top 50 medical schools in the US were identified using US World News and Report rankings. Websites of their associated graduate medical education (GME) websites were queried for details surrounding fertility benefits. Two investigators collected data from GME and publicly available institutional websites. The primary outcome was fertility coverage, and rates are reported as percentages.

RESULTS: Within the top 50 medical schools, geographic distribution included 30% Northeast, 24% Midwest, 24% in the South, and 22% in the West. 66% of institutional websites included publicly available medical benefits, 40% included any mention of fertility benefits, and 32% had no forwarding-facing information on fertility or medical benefits. Fertility benefit coverage included infertility diagnostic work up (40%), intrauterine insemination (32%), prescription coverage (12%) and in-vitro fertilization (IVF, 30%). No information on coverage for third party reproduction or LGBT family building was available on public websites. Most programs with fertility benefits were in the South (40%) or Midwest (30%). Even among programs that offered fertility benefits, information was not readily available for many, and the insurance benefits summaries were not directly linked on the GME website.

CONCLUSIONS: Only 40% of GME websites at institutions affiliated with the top 50 US medical schools share publicly available information on fertility benefits. Even among programs with coverage for IVF, none discuss fertility benefits as a highlighted benefit on the GME website. Instead, information can be found on insurance benefits summaries on outside websites. For institutions that cover IVF, most require residents to be treated at the institution, a practical solution to lowering overall cost and increasing access. To support the reproductive autonomy of physicians in training, it is critical to ensure access to information on coverage of fertility care. Given the prevalence of infertility among physicians and the impact of medical training on family planning goals, more programs should consider offering coverage for fertility care. Additionally, improved clarity surrounding availability of fertility benefits is needed for prospective residents.

IMPACT STATEMENT: Forty percent of the top institutions have publicly available information about covering fertility benefits. There is a paucity of information available to applicants of residency programs about fertility coverage, and increasing access to fertility coverage and transparency on benefits offered is a key step in increasing resident physician reproductive autonomy.

REFERENCES:
enrollment. The average age of non-Hispanic Black (37y) and Hispanic patients (36y) was higher than that of non-Hispanic White (35y) and Asian patients (34y). Only 6% (9) of patients with initial BMI ≥40 kg/m² achieved any weight loss within 6 months of presentation, of which 11% (1) was non-Hispanic Black, 11% (1) was Asian, and 78% (7) were non-Hispanic White. None of the patients who lost weight achieved a BMI less than the 40 kg/m² threshold for IVF. Patients were more likely to lose any amount of weight the lower their presenting BMI was, with White race associated with higher odds of weight loss (OR 3.04) vs. any other race (OR 0.46).

CONCLUSIONS: Ethnic minorities are more likely to be older at initial presentation, have elevated BMIs, and are less likely to lose weight over time. As such, the policy of deferring IVF to achieve weight loss could potentially exacerbate disparities in access to fertility care which are already disproportionately accessed by non-Hispanic White women.

IMPACT STATEMENT: Given that underrepresented minorities tend to be older with a higher BMI at initial presentation and are less likely to lose weight sufficient to cross an arbitrary BMI threshold, a paradigm shift regarding BMI and fertility care may be warranted.


Laredo SE. Obesity, PCOS, infertility treatment: asking obese women to lose weight before treatment increases stigmatisation. BMJ. 2006;332(7541):609.
P-211 6:30 AM Monday, October 24, 2022

THE EFFECT OF LOW AMH AS A PREDICTOR OF EARLY PREGNANCY LOSS IN IVF /ICSI CONCEPTIONS—A RETROSPECTIVE OBSERVATIONAL STUDY.
Durga Gedela Rao Dr., MRCOG. Oasis Fertility, Hyderabad, India.

OBJECTIVE: To study low Serum AMH(Anti- Mullerain Hormone) level as a predictor of early pregnancy loss in IVF/ICSI(Invitro Fertilisation/Intracytoplasmic Sperm Injection) conceptions.

MATERIALS AND METHODS: It is a retrospective observational study at a private hospital between January 2018 – December 2020.

- Poor responders by POSEIDON CRITERIA i.e., those with an AMH <1.2ng/ml and normo-responders i.e., with AMH between 1.3-3.36 ng/ml are compared for IVF/ICSI pregnancy outcomes. All AMH measurements are done with in 12months before the date of stimulation. Serum samples are analyzed using the Gen 2 Beckman Coulter Inc., CA, USA.

RESULTS: Baseline variables of patients were comparable between both arms.

- Early pregnancy loss, Implantation rate (IR), clinical pregnancy rate (CPR), live birth rate (LBR) are similar between both the groups.

- Mean number of oocytes retrieved, mean number of mature oocytes, mean number of stimulations, mean number of days of stimulation, mean gonadotropin dose are the secondary outcomes studied.

OUTCOMES BETWEEN LOW AND NORMAL AMH-IMPLANTATION RATE- 74.77 % VS 72.22 %
- EARLY PREGNANCY LOSS- 25.6% VS 24 %
- CLINICAL PREGNANCY RATE- 74 .13% VS 71.88 %
- LIVE BIRTH RATE- 72.1% VS 80 %

IR, CPR, EPL, LBR are similar between both the groups

Secondary outcomes- low vs normal AMH

- Mean number of stimulations - 1.33 +/-8.39 vs 1.26 +/- 0.47 (p-value 0.4-not significant)
- Mean number of days of stimulation- 17.33+-/ 8.39 vs 14.99+/-.41 (p-value 0.08- not significant)

E-POSTER ABSTRACT SESSION: 22
Mean dose of gonadotropins – 5314 +/- 2239.85 vs 4675 +/- 2577.26 (p-value 0.15, not significant) are comparable between both the groups.

Mean number of mature oocytes - 7.16 vs 10.67 (p-value <0.01, highly significant).

CONCLUSIONS: Data from this retrospective study concludes that although low AMH levels are associated with less number of mature oocytes, low AMH levels does not increase the rate of early pregnancy loss when compared normal AMH levels in IVF/ICSI conceptions. There is conflicting evidence regarding the role of AMH and antral follicle count as qualitative markers for reproductive outcomes. A recent meta-analysis showed a positive association between low AMH and early pregnancy loss but a casual association could not be established. Further studies with large sample size are needed to evaluate AMH as a qualitative marker of ovarian reserve.

IMPACT STATEMENT: The study provides reassuring data that low AMH per se is not a risk factor for early pregnancy loss in IVF/ICSI conceptions. Although the dose of gonadotropins required is slightly higher and number of mature oocytes are lower, the chance of conception and pregnancy outcomes are similar between low AMH ans normal AMH. AMH is a quantitative marker but not qualitative marker for ovarian reserve.

REFERENCES:


P-213 6:30 AM Monday, October 24, 2022

ENDOMETRIAL MICROBIOTA AND CHRONIC ENDO-
METRITIS PROFILES FOLLOWED BY INTRAVAGI-
NAL PROBIOTIC SUPPLEMENTATION AND/OR ANTI-
BIOTIC ADMINISTRATION AND REPRO-
DUCIVE OUTCOMES IN 429 IVF CYCLES. Mauricio B. Chehin, MD, PhD,1 Marjorie Fasolin, MD,3 Renata Fioravanti Schaal, MD,1 Selma F. M. Moreira, BSc,1 Leticia Costa Da Silva, BSc,1 Aline R. Lorenzon, PhD1 Huntington Medicina Reproductiva - Eugen Group, São Paulo, Brazil;2 Huntington Medicina Reproductiva - Eugen Group, Sao Paulo, Brazil.

OBJECTIVE: Endometrial microbiota may vary with infections and sexual routine besides ethnicity and habits. Chronic endometritis is known to produce a negative impact on reproductive outcomes. The aim of this study is to investigate the endometrial microbiota and chronic endometritis profiles in IVF patients and verify their reproductive outcomes after following an intravaginal probiotic supplementation and/or antibiotic administration, according to a commercial screening test provider.

MATERIALS AND METHODS: Prospective, observational cohort study, including patients (n=390) that underwent IVF cycles (n=429) and performed the EMMA (Endometrial Microbiome Metagenomic Analysis) and ALICE (Analysis of Infectious Chronic Endometritis), Igneomax® tests from July/2019 and July/2021 in a private clinic. Most indication for EMMA/ALICE test was for implantation failure (50.3%). The majority of patients (68.3%) had a previous embryo transfer (ET) negative result. Endometrial biopsies and follow-up were performed according to test provider’s protocol. Reproductive outcomes were compared according to the microbiota and endometritis profiles. Comparison statistical tests, chi-square and Fisher’s exact test were applied. A p-value of <0.05 was considered significant.

RESULTS: Mean age was 38.51 ± 4.47 years old. There were no difference in age between normal, altered, low biomass microbiota, neither in positive and negative chronic endometritis. Normal microbiota profile was reported in 21.21% of samples, which is lower (p=0.04) compared to EMMA’s reference study (43.90%, Moreno et al., 2016). Altered microbiota (disbiosis and abnormal profile) was reported in 48.95% and ultralow biomass in 29.94% of samples, higher (p=0.0015) compared to Moreno’s. Top 5 bacterial genera were Lactobacillus (64.98%), Gardnerella (8.29%), Streptococcus (3.11%), Bifidobacterium (2.02%) and Klebsiella (1.94%), instead of Prevotella, as reported in reference study. Chronic endometritis were positive in 46 samples (10.7%), all of them with an altered result for EMMA test. Patients underwent ET (n=252) after following the treatment proposed (probiotics and/or antibiotic) in the case of altered/ultralow biomass and/or positive for endometritis. Clinical pregnancy (CP) in normal (60.5%), altered (44.6%, that includes all endometritis positive samples) and ultralow microbiota (47.8%) were not significantly different (p=0.25). The proportion of fresh and frozen ET was similar between groups (~94% frozen, p=0.062) as well the number of euploid ET (~65.6%, p=0.58), and patient’s age (~38.4 y, p=0.79).

CONCLUSIONS: Despite some differences in the proportion of normal and ultralow biomass profiles in comparison to the reference study, clinical pregnancy rate after intervention for altered or ultralow biomass and/or positive for chronic endometritis were similar to normal profile.

IMPACT STATEMENT: The use of probiotic and/or antibiotic treatment for patients with an altered/diminished endometrial microbiota and/or endometritis profile resulted in similar CP rate from those with a normal profile.

REFERENCES:

SCHISTOSOMIASIS INDUCED ASHERMAN’S SYNDROME IN A PATIENT UNDERGOING ASSISTED REPRODUCTIVE TECHNOLOGY (ART): A CASE REPORT AND LITERATURE REVIEW.

Virginia-Arlene Acosta Go, MD,1 Yetunde Ibrahim, M.D., M.S.C.2 UT Health San Antonio, San Antonio, TX; 2University of Texas Health Science Center At San A, San Antonio, TX.

OBJECTIVE: Female genital schistosomiasis occurs as a result of exposure to a waterborne parasite. Several cases of schistosomiasis related tubal disease have been reported, particularly in endemic areas, but given the rare occurrence of Asherman’s syndrome and subsequent uterine factor infertility, awareness is limited and reports are scarce in the literature. One case report describes Asherman’s syndrome caused by schistosomiasis but nothing to our knowledge has been published describing diagnosis and treatment in the setting of ART. Our objective is to report a rare case of schistosomiasis infection found during ART cycle and outline the management course.

MATERIALS AND METHODS: Case report from a university-based fertility clinic and literature review with keyword search terms including schistosomiasis, female infertility, amenorrhea, Asherman syndrome, assisted reproductive technology.

RESULTS: An HIV-positive patient from Ethiopia with persistent secondary amenorrhea despite correction of mildly elevated prolactin underwent controlled ovarian stimulation due to severe male factor infertility. She had normal ovarian reserve testing and otherwise normal saline infusion sonography. During ovarian stimulation with gonadotropins, her endometrial lining remained thin and hyperechoic on ultrasonography but appropriately rising estradiol. The endometrial biopsy at the time of oocyte retrieval revealed granulomas and the pathology of the non-calcified eggs consistent with an old parasitic infection, schistosomiasis. After an interdisciplinary review with pathology and infectious disease specialists, the patient underwent a prolonged Praziquantel course and hysteroscopic dilation and curettage to remove the granulomas in attempts to optimize her uterine cavity prior to frozen embryo transfer (FET). Hysteroscopic findings revealed numerous 1-2mm white plaques throughout the cavity that dense plaque at the fundus. At conclusion of hysteroscopy, the uterine cavity appeared overall normal however the patient failed to bleed after a prolonged estradiol course and progesterone withdrawal. Her endometrial lining remained thin during preparation for hormone replacement FET with oral estradiol. As the patient had only one frozen blastocyst from her stimulation, the decision was made to repeat hysteroscopy prior to attempting FET. A biopsy of the uterus was performed with a dilated surgical curette and a malignant process was ruled out.

CONCLUSIONS: Both active and prior schistosomiasis pelvic infection should be considered in the differential diagnosis of secondary amenorrhea and uterine factor infertility in patients at high risk, including HIV positive status and prior exposure to endemic areas. Early diagnosis and treatment could help prevent long standing disease, distortion of the uterine cavity and future infertility.

IMPACT STATEMENT: The literature on management and ART outcomes of patients with schistosomiasis induced Asherman’s Syndrome is lacking. Further investigation is needed to better characterize treatment options for these cases to best care for infertility patients of all backgrounds and exposures through travel.

REFERENCES:


THE RATIO BETWEEN THE LENGTH OF THE SECOND AND FOURTH DIGIT (2D:4D RATIO) AS A BIOMARKER OF OVARIAN RESERVE IN INFERTILE PATIENTS. Joana Peñarrubia, PhD,1 Sara Falgas, MD,2 Sol Gomez, MD,3 Marga Esbert, PhD,4 David Amoros, BSc,5 Agustín Ballesteros, PhD1 IVIRMA Barcelona, Barcelona, Spain; 2IVIRMA Barcelona, Barcelona, Spain; 3IVIRMA Barcelona, Barcelona, Spain; 4IVIRMA Barcelona, Barcelona, Spain.

OBJECTIVE: Ovarian reserve is established during intrauterine life, with a peak at 20 weeks of gestation. The 2D:4D ratio, which is also established during prenatal life, has been proposed as a non-invasive biomarker of the prenatal hormonal environment. It has been suggested that an intrauterine environment rich in androgens induces a development of the 2D:4D ratio < 0.85, which is reminiscent of the male fetus. A study by Woodall and colleagues showed a significant association between the 2D:4D ratio and female infertility. However, whether 2D:4D ratio can be used to could predict ovarian reserve status needs further investigation.

The present study aimed to: i) correlate the 2D:4D ratio with two classic markers of ovarian reserve, Anti-Mullerian Hormone (AMH) and Antral Follicle Count (AFC); ii) study the possible relationship between the 2D:4D ratio and the reproductive prognosis after In Vitro Fertilization (IVF) based on the POSEIDON (Patient Oriented Strategies Encompassing Individualized Oocyte Number) criteria.

MATERIALS AND METHODS: Prospective observational cohort study. 2D:4D ratio was measured in 142 nulligravid patients attending a single fertility clinic from December 2020 to April 2022. Patients diagnosed with polycystic ovary syndrome, endometriosis or having previous ovarian or genital surgery were excluded. Photographs were taken of both hands and the lengths of the second (2D) and fourth (4D) digits were determined to the nearest 0.1 millimeter using digital calipers by the same experienced observer. 2D:4D ratios for each hand were calculated by dividing the length of 2D by the length of 4D. The AFC was determined by transvaginal ultrasound by the same observer.

RESULTS: We compared BMI, donor age, TSH, AMH, HCG post trigger, LH post trigger, P4 pre trigger, eggs retrieved, number of matured eggs, fertilized eggs, and E2 before HCG respectively between the vaccinated (n=58) and non-vaccinated (n=48) groups. Results showed that there was no significant difference between the two groups for the considered parameters (p>0.05).

CONCLUSIONS: Our findings suggest that COVID-19 vaccination does not influence the BMI, donor age, TSH, AMH, HCG post trigger, LH post trigger, P4 pre trigger, eggs retrieved, number of matured eggs, fertilized eggs, and E2 before HCG respectively between the vaccinated and non-vaccinated groups. This study showed that COVID-19 vaccination does not influence the BMI, donor age, TSH, AMH, HCG post trigger, LH post trigger, P4 pre trigger, eggs retrieved, number of matured eggs, fertilized eggs, and E2 before HCG respectively between the vaccinated and non-vaccinated groups. Results showed that there was no significant difference between the two groups for the considered parameters (p>0.05).

IMPACT STATEMENT: Our findings will help in understanding of the impacts of COVID-19 vaccination on parameters which are considered important for assisted reproductive technology with respect to female partner.

SUPPORT: This work was supported in part by the IVFMD, South Florida Institute for Reproductive Medicine.
RESULTS: The clinical characteristics of the patients were: age 34.5±4.2 years; BMI 23.8±4.7 kg/m²; AMH 2.16±1.17 ng/ml; AFC 13.5±11.3. A significant negative correlation was found between the 2D:4D ratio of both hands and the AMH levels (right hand: r = -0.48 p<0.01; left hand: r = -0.17; p=0.58) and the AFC (right hand: r = -0.47 p<0.01; left hand: r = -0.19 p = 0.021). The 2D:4D ratio was significantly higher in women with low ovarian reserve defined by AMH < 1 ng/ml (n=32) than in patients with normal ovarian reserve in both hands (right hand: 1.02±0.02 vs 0.98±0.04 = 0.035; left hand: 1.01±0.02 vs 0.99±0.04 p = 0.025). Similarly, POSEIDON groups 3 and 4 patients (n=37) had a higher 2D:4D ratio in both hands than patients with good reproductive prognosis (right hand: 1.02±0.02 vs 0.98±0.04 p < 0.01; left hand: 1.01±0.03 vs 0.99±0.04 p < 0.01).

CONCLUSIONS: Infertile patients with low ovarian reserve and those with worse prognosis expected by poor expected ovarian response (POSEIDON groups 3 and 4) have a higher 2D:4D ratio. Our results provide the first evidence of an association between a biomarker of hormonal prenatal environment (2D:4D ratio) and ovarian reserve as well as with fertility prognosis, suggesting that the ovarian follicular pool could be affected by endocrine disruptors in prenatal life.

IMPACT STATEMENT: The 2D:4D ratio is a possible non-invasive biomarker of ovarian reserve in infertile patients.

P-218 6:30 AM Monday, October 24, 2022

RACIAL DIFFERENCES IN ENDOMETRIOSIS – A REFLECTION OF WHO PROCEEDS WITH SURGERY FOR PELVIC PAIN? Aaditi G. Naik, B.A., Ellen Betchold, M.D.,1 Obianuju Sandra Madueke Laveaux, M.D.,1,2 Isa Haasain, B.S., MSc,1 Amanda Adeleye, M.D.1 The University of Chicago, Chicago, IL. 2The University of Chicago.

OBJECTIVE: Endometriosis is thought to be more prevalent in White women than Black women. Few studies have reported whether reported racial differences in the prevalence of endometriosis can be explained by racial disparities in access to surgery for chronic pelvic pain. We aimed to identify whether patient factors such as race were associated with whether women with pelvic pain proceeded to surgery or were diagnosed with endometriosis.

MATERIALS AND METHODS: In this cross-sectional study, we administered a survey to new and return patients who presented to an academic gynecology practice between January 1, 2015 and December 31, 2020 with an ICD 9 or 10 code of ‘pelvic and perineal pain.’ Patients were sent an electronic survey querying: their demographics (race, employment and insurance status, zip code); provider demographics, the nature of their chronic pelvic pain, their history of pelvic pain; 42% (n=10). No Asian, Native American or Mixed-race participants pursued surgery in our cohort. There was no difference in the proportion of women that pursued surgery for pelvic pain by race (White 25%, Black 35%) p=0.70. Importantly a similar number of women reported being diagnosed with endometriosis when comparing race (n= 2 white women and n = 3 Black women) p = 0.99. Other factors such as education, insurance status, or racial concordance with providers were not associated with whether or not women pursued surgery (p=0.9, 0.24, 0.35 respectively). Patients had a variety of reasons for not pursuing surgery for their pain and this did not differ by race p =0.54. When patients felt encouraged by their providers to pursue surgery for pelvic pain, this was a significant predictor of women completing surgery for pelvic pain p=0.018.

CONCLUSIONS: In our study, the single most important factor for women pursing surgery for pelvic pain was feeling encouraged by their providers to do. Contrary to common belief, there was no racial difference in the reported incidence of endometriosis in our population. This may be due to similar perceptions of provider encouragement for surgery independent of race.

IMPACT STATEMENT: We may need to rethink the notion that the prevalence of endometriosis differs by race. Rather, racial differences in endometriosis may reflect differences in whether patients with pelvic pain are encouraged to pursue surgery.

SUPPORT: None

P-219 6:30 AM Monday, October 24, 2022

EXTRACELLULAR VESICLES SECRETED BY ENDOMETRIAL ORGANIODS FROM ADENOMYOSIS PATIENTS CONTAIN MiRNAs IMPLICATED IN DISEASE DEVELOPMENT, EMBRYO IMPLANTATION FAILURE AND PREGNANCY DISORDERS. Elena Juarez-Barber, MS,1 Marina Segura-Benitez, MSc,2 Carolina Carbajo-Garcia, MSc,3 Alba Bas-Rivas, MSc,3 Amparo Faus, B.Sc.,4 Antonio Pellicer, M.D.,4 Hortensia Ferrero, PhD1 IIS La Fe - IVI Foundation, Spain; 2Universidad de Valencia - IVI Foundation, Valencia, Spain; 3Universitat de València, Valencia, Spain; 4IVI Foundation - Hs La Fe, Spain; 5IVI Foundation - La Fe Health Institute, Valencia, Spain; 6Instituto Valenciano Infertilidad (IVI), Rome, Italy; 7IVI Foundation - Instituto de Investigación Sanitaria INCLIVA, Valencia, Spain.

OBJECTIVE: To describe microRNA (miRNA) cargo of extracellular vesicles (EVs) secreted by adenomyosis-derived endometrial organoids and to evaluate the role of miRNAs in adenomyosis pathogenesis and consequent impaired implantation and embryo development.

MATERIALS AND METHODS: Organoids from eutopic endometrium of women with adenomyosis (n=4) were established and supplemented with ovarian (E2, P4 and cAMP) and pregnancy (hPL and PRL) hormones to induce secretory and gestational endometrial differentiation, respectively. EVs were secreted by secretory and gestational organoids into culture media were isolated by ultracentrifugation and characterized by Western Blot and Nanoparticle Tracking Analysis (NTA). miRNAs from EVs were extracted and NextSeq High Output miRNA-sequencing was performed. Count per million were analyzed to select the most expressed miRNAs. Functional enrichment analysis of genes targeted by top 20 most expressed miRNAs was performed with ShinyGo.

RESULTS: EVs showed a size within 100-400 nm by NTA and were characterized by identification of intraluminal (HSP70, TSG101) and transmembrane (CD9, CD81) proteins by Western Blot. miRNA-seq showed presence of 80 miRNAs in secretory phase EVs and 60 miRNAs in gestational phase EVs. Functional enrichment analysis of genes targeted by top 20 most expressed miRNAs revealed their involvement in biological processes such as differentiation, proliferation, apoptosis, cell cycle, and response to extracellular stimulus. In secretory phase EVs, we identified hsa-miR-21-5p, hsa-miR-24-3p, hsa-miR-26a-5p, hsa-miR-26b-3p, hsa-miR-30a-5p, hsa-miR-30c-5p, hsa-miR-223-3p, hsa-miR-423-5p, hsa-miR-423-3p and hsa-miR-423-5p which promote an inflammation status, induce epithelial endometrial cell proliferation, impair damaged tissue healing, inhibit invasion and migration of trophoblast, and are involved in recurrent implantation failure. Gestational phase EVs contained hsa-miR-21-5p, hsa-miR-26a-5p, hsa-miR-30a-5p, hsa-miR-30c-5p, hsa-miR-223-3p, hsa-miR-423-5p associated with maternal immunotolerance regulation, preeclampsia, miscarriage, reduced developmental competence of blastocysts, proliferation and DNA integrity in embryos. Between the genes targeted by the highest number of miRNAs, we found PTEFb and MDM4, PLAGL2, CELF1, whose down-regulation contributes to adenomyosis pathogenesis and embryonic development impairment, leading to implantation failure and miscarriages.

CONCLUSIONS: miRNA cargo of EVs secreted by eutopic adenomyotic endometrium are involved in triggering adenomyosis onset, implantation failure and preeclampsia, suggesting eutopic endometrium from women with adenomyosis to be altered.

IMPACT STATEMENT: This study represents a step forward in the development of the role of miRNAs as potential non-invasive biomarkers of adenomyosis and further reproductive outcomes predictors.

SUPPORT: FI19/00110, FPU18/03735, ACIF/2019/139, CP20/00120.
P-220 6:30 AM Monday, October 24, 2022

**RACIAL DISPARITIES IN PRESENTATION TO INFERTILITY CONSULTATIONS AND TELEHEALTH USE DURING THE COVID-19 PANDEMIC.** Surabhi Tewari, BS,1 Kathryn D. Coyne, MD,2 Rachel S. Weinerman, MD,2 Rebecca Flyckt, MD,3 Cleveland, OH; 3University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH; 1University Hospitals Cleveland Medical Center/Case Western Reserve University, Beachwood, OH.

**OBJECTIVE:** Investigate the impact of the COVID-19 pandemic on characteristics of initial infertility consultations for patients of different racial backgrounds.

**MATERIALS AND METHODS:** A retrospective cohort study was completed of patients aged 21 to 45 years presenting for an initial infertility consultation between January 1st, 2019 and June 1st, 2021. 500 patients presenting before March 1st, 2020 were randomly selected for the Pre cohort, and 500 patients presenting after March 1st, 2020 were randomly selected for the Post cohort. The electronic health record was queried for demographic and initial consultation data.

**RESULTS:** In comparison to the Pre cohort, the Post cohort had fewer African American (AA) patients (33.0% vs. 27.0%, p = 0.038) and more patients with private insurance (64.4% vs. 72.8%, p = 0.004). Rates of missed appointments did not differ between the Pre and Post cohorts (p = 0.78), but patients were more likely to no-show in the Pre cohort (49.4% vs. 27.8%, p < 0.0001) versus cancel in the Post cohort (50.6% vs. 72.2%, p < 0.0001). There were no significant differences in rates of rescheduled visits (23.6% vs. 25.8%, p = 0.99) or IVF initiation (17.4% vs. 17.3%, p = 0.96) between the Pre and Post cohorts, respectively. In-person visits were more prevalent in the Pre cohort and telehealth was utilized more in the Post cohort (99.8% vs. 35.8% and 1.2% vs. 64.2%, p < 0.0001). AA patients in comparison to patients of all other (AO) races in both the Pre and Post cohorts, respectively, were less likely to have private insurance (41.2% vs. 75.8%, p < 0.0001 and 57.0% vs. 78.6%, p < 0.0001); present to their scheduled appointment (52.7% vs. 73.7%, p < 0.0001 and 48.1% vs. 74.8%, p < 0.0001); and cancel rather than no-show at appointments (30.8% vs. 6.8%, p < 0.0001 and 64.3% vs. 78.3%, p = 0.049). AA and AO patients had statistically significant differences in appointment length in the Pre cohort (p = 0.021), but similar differences were not seen in the Post cohort (p = 0.47). In comparison to AO patients, AA patients in the Post cohort were less likely to have a telehealth visit (57.0% vs. 66.8%, p = 0.042) or initiate IVF in both the Pre (6.9% vs. 21.4%, p = 0.001) and Post (6.4% vs. 20.1%, p = 0.005) cohorts. In a multivariable regression model controlling for Pre- vs. Post- COVID-19 and insurance status, AA race was a negative predictor (OR 0.37, 95% CI 0.28-0.50) and telehealth was a positive predictor (OR 1.54, 95% CI 1.04-2.27) for presentation to initial consultation.

**CONCLUSIONS:** Implementation of telehealth did not significantly reduce missed appointments for initial infertility consultation, but there was a significant shift from no show to cancellation. Importantly, the pandemic has highlighted a disparity in utilization of telehealth and presentation for initial consultation in AA versus AO patients.

**IMPACT STATEMENT:** The COVID-19 pandemic necessitated a change in practice patterns in fertility clinics across the country. However, this study demonstrates that the pandemic has impacted how fertility care is accessed, and more importantly, that AA patients may have decreased access to telehealth compared to other patients.

**SUPPORT:** None

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**P-662 10:00 AM Tuesday, October 25, 2022

**RISK PROFILE OF MULTIFETAL IN VITRO FERTILIZATION (IVF) PREGNANCIES VS SPONTANEOUS MULTIFETAL PREGNANCIES, A STUDY OF A LARGE AMERICAN POPULATION DATABASE INCLUDING ALMOST 100,000 MULTIPLE GESTATIONS.** Samar Mandourah, MD,1 Ahmad Badeghiesh, M.D., MPH,2 Haitham Baghlaf, MD, MPH,2 Michael H. Dahan, M.D.3 Montreal, QC, Canada; 4McGill University Health Centre, Montreal, QC, Canada; 5Division of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada.

**OBJECTIVE:** This study aims to assess risks associated with in vitro fertilization (IVF) in multifetal pregnancies (MFP) when compared to spontaneous conception. Very few population based studies addressed this topic.

**MATERIALS AND METHODS:** This is a retrospective cohort study using the Health Care Cost and Utilization Project-Nationwide Inpatient Sample (HCUP-NIS) database. The study included 90,552 spontaneous MFP and 3,219 IVF MFP, from 2008-2014, inclusively. Multivariate logistic regression analyses were performed comparing maternal and neonatal outcomes, whilst adjusting for confounding differences between groups. Subject was located using ICD-9 codes for multifetal gestation: 651.X and 76.1 and ICD-9 code for IVF: 23.85. Each pregnancy was included once, by limiting to deliveries or maternal deaths.

**RESULTS:** Women who underwent IVF were more likely to be >35 years old, be Caucasian, Asian or Pacific islanders, have an income of $63,000 or more, have private health insurance, and thyroid disease (p < 0.0001). Spontaneous MFP were more likely to be obese (p = 0.024), have a previous CS (p < 0.0001), smoke (p < 0.0001) or use illicit drug (p < 0.0001). When controlling for these confounders, MFPs conceived through IVF had increased risk of pregnancy induced hypertension(aOR:1.31, 95%CI:1.20-1.43), gestational hypertension(aOR:1.21, 95%CI:1.04 - 1.41), preeclampsia(aOR:1.31, 95%CI:1.19 - 1.45), gestational diabetes(aOR:1.26, 95%
A NEW ENDOMETRIAL TRANSCRIPTOMIC STRATIFICATION IN THE MID-SECRETORY PHASE REVEALS A NEW TAXONOMY FOR ENDOMETRIAL PROGNOSIS IN INFERTILITY. Josefa Maria Sanchez-Reyes, MSc,1 Antonio Parraga-Leo, MSc,1 Patricia Sebastián León, PhD,2 Katharina Spath, PhD,3 Carmen Vidal, MD, PhD,3 Manuel Gorriz-Bellet, MSc,2 Almudena Devesa-Peiro, PhD,3 Jose Remohi Gimenez, MD PhD,3 Dagan Wells, PhD,6 Antonio Pellicer, MD PhD,7 Patricia Diaz Gimeno, PhD7 Biomedical Research Institute La Fe, IVI Foundation - University of Valencia, Valencia, Spain; 2Biomedical Research Institute La Fe, IVI Foundation, Valencia, Spain; 3Juno Genetics, Oxford, United Kingdom; 4IVIRMA Valencia, Valencia, Spain; 5IVIRMA - University of Valencia, Valencia, Spain; 6Juno Genetics - University of Oxford, Oxford, United Kingdom; 7IVIRMA Rome - University of Valencia, Roma, Italy.

OBJECTIVE: To develop a precision medicine strategy, identifying and stratifying distinct endometrial molecular profiles associated with different pregnancy prognoses. MATERIALS AND METHODS: A multicenter prospective study was performed in IVF patients undergoing endometrial evaluation and embryo transfer in a hormone replacement therapy cycle. Endometrial biopsies were collected in the mid-secretory phase and whole transcriptome RNA-Seq analysis was performed. To identify the transcriptomic patterns associated with different reproductive outcomes, transcriptomic variation affected by the progression of the cycle was removed. Patients (n=131) were clinically classified as pathological (>3 implantation failures, n=32) and controls (<3 implantation failures, n=99) transferring high quality embryos. An artificial intelligence probabilistic model supervised clinically by reproductive success was utilized for stratifying the patient population. Pregnancy (PR), live birth (LBR), clinical and biochemical miscarriage rates (CMR and BMR) were calculated in the first embryo transfer after biopsy collection. Cumulative PR was also calculated.

RESULTS: A new transcriptomic taxonomy that identifies 4 different endometrial molecular profiles in mid-secretary phase were identified. Patients were stratified according to a risk score of pathology in P1 (n=24), P2 (n=14), C2 (n=32) and C1 (n=61). Pregnancy and Live birth rates were significantly lower in pathological profiles (PR=29-57%; LBR=50-78%) than in controls profiles (PR=71-78%; LBR=76-91%) while miscarriage rates were higher in pathological profiles (BMR=12-43%; CMR=0-43%) than in controls (BMR=0-8%; CMR=9-17%) (p-values<0.05). C1 was the profile with the significant highest LBR (91%) while C2 was the profile with the highest PR (78%). In contrast, P1 showed the lowest PR (29%) and the highest BMR (43%) and P2 exhibited a low PR (57%) and the highest CMR (43%) (p-value=0.05). Cumulative PR was lower in pathological profiles, showing a 15% increasing rate from P1 to C1 (P1=38%>P2=76%>C2=81%>C1=93%). CONCLUSIONS: We have identified for the first time molecular profiles in the mid-secretory phase associated with a gradient of prognosis in implantation failure and risk of miscarriage. We identified two profiles associated with poor prognoses, one of them with high risk of biochemical loss and the other with high risk of clinical miscarriage.

IMPACT STATEMENT: Current endometrial dating tools are based on detecting endometrial progression. However, their relation to fertility status remains controversial. These findings stratify the infertile population in a different way, according to an increasing risk of implantation failure and miscarriages, opening up the possibility of a new generation of endometrial evaluation tools that represent further progress towards precision reproductive medicine.

SUPPORT: This research was funded by IVI-RMA IVIFoundation (1706-FV-DP-RD), ISCIII (PI19/00537) co-funded by ERDF, “A way to make Europe”, and by Miguel Servet program (CP20/00118) from ISCIII awarded to Patricia Diaz-Gimeno (Spanish Government). Josefa Maria Sanchez-Reyes was supported by the ACIF/2018/072 and BEFPI/2020/028 predoctoral program fellowship from Generalitat Valenciana (Spanish Government). Antonio Parraga-Leo was supported by the FPU18/01777 predoctoral program fellowship (Ministry of Spain) and Almudena Devesa-Peiro was supported by the FPU15/01398 predoctoral program fellowship (Ministry of Spain) and IVIFoundation.

P-664 10:00 AM Tuesday, October 25, 2022

IS IT SAFE TO PERFORM OVARIAN CRYOPRESERVATION AND TRANSPLANTATION IN PATIENTS WITH LEUKEMIA A 5-YEAR SURVIVAL ANALYSIS

DATA. Murat Sonmez, M.D., 1 Yavuz Emre Sükrü, M.D., 1 Koray Gökrem Sağcın, M.D., 2 Sinan Ozkavukcu, M.D., 2 Duygu Kankaş, M.D., 3 Güldane Cengiz Seval, M.D., 3 Cem Somer Atabekoglu, M.D., 3 Kutluh Oktay, M.D., Ph.D. 4 Ankara University School of Medicine, Ankara, Turkey; 4University of Dundee, Dundee, United Kingdom; 4Ankara University School of Medicine, Ankara, Turkey; 4Yale University School of Medicine.

OBJECTIVE: Although ovarian tissue cryopreservation is performed in patients with leukemia undergoing Allogenic Hematopoietic Stem Cell Transplantation (Allo-HSCT), auto-transplantation of these tissues have raised concerns with the risk of reintroducing cancer cells. We performed this retrospective study, spanning 14 years to investigate the safety of performing autologous ovarian tissue transplantation in acute leukemia survivors.

MATERIALS AND METHODS: Clinical, histopathological and molecular data of four women with AML and two with ALL referred to the fertility preservation units at two major academic centers in Europe and US were reviewed. All patients received high dose multiagent alkylating chemotherapy before undergoing Allo-HSCT. Ovarian cortical tissue harvesting was performed by laparoscopic surgery. The cortical strips thawed prior to transplantion underwent a detailed histologic, immunohistochemical and molecular evaluation where appropriate to rule out leukemic cell infiltration. All patients underwent a detailed hematologic evaluation as a part of routine disease follow-up.

RESULTS: The median age of the patients was 19 years (15-32) at cryopreservation and 25 years (23-39) at transplantation. Serum AMH levels were 1.4±1.8 ng/ml before cryopreservation, 0.02±0.01 ng/ml and 0.24±0.17 ng/ml prior to transplantation and six months after transplantation, respectively. Ovarian transplantation was performed laparoscopically with or without robot-assistance, after a median of 74.5 months (41-120) following cryopreservation. All patients achieved full donor chimerism following Allo-HSCT. Immunohistochemical staining against CD3, CD20, CD34, CD 117, PAX5 and TDT antigens, and using BCR/ABL p190 molecular marker revealed no blastic infiltration in the removed/transplanted ovarian tissues. The median follow-up after transplantation was 41 months (12-62 months). All patients remained relapse-free, as confirmed by detailed hematologic evaluations by their hematologists. Of these 6, ovarian function was restored in all patients, and 2 had at least 1 child. Ovarian grafts were removed in one patient during cesarean section and no blastic infiltration was detected in detailed immunohistochemical staining.

CONCLUSIONS: Our long-term follow-up data demonstrated no evidence of disease relapse after ovarian tissue transplantation in patients with acute leukemia who received Allo-HSCT. This safety profile may be explained by the fact that these patients are induced into remission by induction chemotherapy, which is not gonadotoxic, before undergoing ovarian tissue cryopreservation. Furthermore, the allogeneic bone marrow in the survivors likely cause a reverse graft vs host reaction to any limited residual leukemic cells, if any, and result in the immunological elimination.

IMPACT STATEMENT: Ovarian autotransplantation with cryopreserved tissue seems to be safe. Young leukemia survivors with high risk for POI due to preconditioning chemotherapy prior to Allo-HSCT should be offered ovarian tissue cryopreservation as a fertility preservation option.
DNA-BASED ANCESTRY VS SELF-REPORTED ANCESTRY: A CASE FOR PAN-ETHNIC CARRIER SCREENING IN GAMETE DONOR PROGRAMS. Natalia Zarytska, B.S., 1 Kara Baldwin, MS, CGC, 2 Pamela Callum, MS, CGC, 3 Kathryn Lockwood, MS 3 Los Angeles, CA; 4Generate Life Sciences (Cooper Surgical), Los Angeles, CA; 5Generate Life Sciences, Los Angeles, CA.

OBJECTIVE: The American College of Obstetrics and Gynecology (ACOG) currently recommends ethnicity-based carrier screening. As such, individuals planning pregnancies may not be offered screening for conditions like hemoglobinopathies or Tay Sachs unless they self-report an ethnicity associated with increased risk for these disorders. In 2021, the American Society of Reproductive Medicine (ASRM) began recommending pan-ethnic carrier screening for gamete donors; however, the carrier screening performed on donors remains varied. This study aims to compare these screening methods using data from a U.S. sperm donor population.

MATERIALS AND METHODS: DNA-based ancestry testing was performed on sperm donors during 2020 and 2021 by a reference laboratory. These donors provided their self-reported ancestries and had pan-ethnic carrier screening for 260+ recessive conditions. Donors’ DNA-based ancestry results were compared to their self-reported ancestries to evaluate if the opportunity for ACOG-recommended ethnic-based testing would have been missed using self-reported ancestries alone. A minimum threshold of 5% of a DNA-detected ethnicity was used for the purposes of this study to capture at least 4 ancestral generations for the tested individuals. The pan-ethnic carrier screening results for donors with discrepant ancestries were reviewed to determine if any significant results would have been missed in this cohort if tested via an ethnicity-based screening modality.

RESULTS: DNA-based ancestry testing was performed on 365 donors. 245 donors (67.1%) had >5% of an ethnicity (Asian, African, Hispanic, Mediterranean, Middle Eastern, and West Indian) at increased risk for hemoglobinopathies. 35 (14.3%) of these donors did not self-report the relevant ancestry. 5 of the 35 donors (14.3%) were carriers for alpha thalassemia or thalassemia intermedia by molecular testing. 49 donors had >5% Ashkenazi Jewish (AJ) DNA-based ancestry. 9 of the 49 donors (18.4%) did not self-report Jewish ancestry. 2 of the 9 (22.2%) donors were carriers for one condition common in the AJ population (Usher Syndrome Type 1F: Familial Dysautonomia).

CONCLUSIONS: Donor gametes are used by numerous recipients of varying ethnic ancestries. The use of self-reported ancestries for carrier screening has significant limitations and can result in the birth of affected offspring. Donor programs and donor recipients benefit from pan-ethnic carrier screening of gamete donors to increase detection of carriers and allow opportunity for reciprocal screening. Healthcare providers should be aware of ethnicity-based screening limitations and variations of carrier screening within donor programs to help determine appropriate screening for patients using donor gametes.

IMPACT STATEMENT: Pan-ethnic carrier screening is a preferred screening approach for donors to aid in identification of reproductive risks independent of self-identified ethnicity. Results of this study are generalizable to the greater population thus pan-ethnic carrier screening should be considered as an option for all reproductive couples.

Support: Generate Life Sciences.

P-665 10:00 AM Tuesday, October 25, 2022

MATERNAL AND PERINATAL OUTCOMES IN ASSISTED REPRODUCTIVE TECHNOLOGY CONCEIVED PREGNANCIES IN BRITISH COLUMBIA. Rebecca Eckler, M.D., 1 Arianne Y. K. Albert, Ph.D., 2 Amrita Pooni, M.D., 3 Mohamed Ali Bedaiwy, MD, PhD, 4 University Of British Columbia, Vancouver, BC, Canada; 5Women’s Health Research Institute, Vancouver, BC, Canada; 6Division of Reproductive Endocrinology and Infertility, McGill University Health Care Center, Montreal, QC, Canada; 7University of British Columbia, Obstetrics and Gynaecology, Vancouver, BC, Canada.

OBJECTIVE: Pregnancies resulting from assisted reproductive technology (ART) are known to confer greater risks to both mothers and their neonates compared to those achieved by natural conception. However, it is difficult to distinguish the effect of ART from its confounding factors such as advanced maternal age and multilaternal gestations. Given these concerns, we aim to investigate maternal and perinatal outcomes in ART conceived pregnancies while controlling for reproductive age and excluding multilaternal pregnancies.

MATERIALS AND METHODS: Neonatal and maternal outcome data were collected from singleton, primiparous women who conceived both naturally and by ART from 2008-2018 using the British Columbia Perinatal Data Registry. All outcomes were analyzed using generalized additive models to allow for flexible, non-linear relationships between the outcomes and age. P-values were calculated using likelihood ratio tests. Categorical outcomes were analyzed using log-binomial models to allow for the estimation of relative risk.

RESULTS: After excluding for multifetal pregnancies and multiparous women, during the ten-year study period there was a total of 182,869 deliveries. 176,335 (96.4%) of these deliveries were conceived naturally and 6,534 (3.6%) were conceived using ART. After controlling for age, when comparing ART conceived pregnancies to naturally conceived pregnancies, there was a significant increased risk in gestational diabetes (RR 1.15, CI 1.08-1.22), gestational hypertension (RR 1.27, CI 1.17-1.37), longer maternal postpartum length of stay in hours (RR 2.30, CI 1.27-3.32), preterm birth (RR 1.36, CI 1.27-1.46), low birth weight (RR 1.36, CI 1.24-1.46), and NICU admissions (RR 1.20, CI 1.11-1.31). There was no statically significant difference in the risk of stillbirth (RR 1.31, CI 0.93-1.82) and APGARs at 5 minutes <7 (RR 1.11, CI 0.97-1.27).

CONCLUSIONS: There is an increased risk of developing multiple adverse maternal and neonatal outcomes in singleton pregnancies conceived by ART across all maternal ages. The mechanisms underlying these associations require further research.

IMPACT STATEMENT: Our findings add to the growing body of evidence suggesting an association between ART and adverse reproductive outcomes. Improved understanding of this relationship can help guide patient counseling, medical care, and future research.

Support: None.

REFERENCES


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P-666 10:00 AM Tuesday, October 25, 2022

DOES ANTI MULLERIAN HORMONE (AMH) AFFECT EUPLOIDY RATES IN DIFFERENT AGE GROUPS. Yousef M. Y. Alhelou, M.SC., 1 Michael H. Fakh, MD, 2 Fakhiv IVF Fertility Center, Abu Dhabi, Abu Dhabi, United Arab Emirates; 3Abu Dhabi, Abu Dhabi, United Arab Emirates.

OBJECTIVE: This study pursues to determine whether patients with a low AMH undergoing ICSI with preimplantation genetic screening for aneuploidy (PGT-A) have aneuploidy rates that differ from patients with normal AMH levels.

MATERIALS AND METHODS: In this retrospective cohort study, data was collected from all ICSI cycles with PGT-A conducted at three referral fertility centers from June 2018 to December 2021. We excluded cycles without serum AMH, endocrinopathies or recurrent pregnancy loss, males with total sperm count of less than 5 million and total motility less than 20%.
30%, and those with parental chromosomal abnormalities. Cycles were divided into two main cohorts based on the patient’s AMH level: low (≤ 1.1 ng/mL) and normal (>1.1 ng/mL). Our primary outcome was aneuploidy rate with secondary outcomes of blastulation rate. Outcomes were analyzed using analysis of variance, chi-squared tests, Fisher’s exact tests. Multiple linear regression models were used to examine the association of AMH with aneuploidy rates.

RESULTS: Of the 13863 cycles in our initial sample, 5065 cycles met inclusion criteria. Within our study, 1524 (30.1%) of cycles were in the low cohort, 3541 (69.9%) of cycles were in the normal cohort. Each cohort was subdivided into 6 age sub-cohorts as follow (35 to < 38), (38 to < 40), (40 to 42), (42 to < 44), (>44). The low AMH cohort had significantly average older age in comparison to the normal cohorts (39.2 ± 3.8, 34.8 ± 3.9 respectively p=0.006). The mean aneuploidy rate did not differ substantially between the low and normal AMH cohorts and the related sub-cohorts in our primary outcome. The euploid percentage was (60.2% ± 31.2%, 60.6% ± 41.1% respectively p=0.57). The regression analysis did not show significant mean increase in the aneuploidy rate amongst the two cohorts after adjusting for age. Average aneuploidy rates rise considerably with each year of age (RC 3.91; 95% CI: 3.20-4.88). Our secondary outcomes of blastulation rate were not significantly different (p<0.05). The observed associations is a plausible consideration that merits attentive discussion.

CONCLUSIONS: Our study found no differences in aneuploidy rates between patients with normal AMH and those with intermediate or low AMH in the same age group.

IMPACT STATEMENT: In patients having IVF/ICSI with PGT-A, our study found no evidence that AMH might be utilized as a biomarker to predict increased aneuploidy.

P-669 10:00 AM Tuesday, October 25, 2022

DUAL TRIGGERING (DT) WITH GONADOTROPIN RELEASING-HORMONE AGONIST (GNRHA) AND HUMAN CHORIONIC GONADOTROPIN (hCG) IN AN ULTRASHORT FLARE (USF) PROTOCOL MOUNTS AN EFFECTIVE LUTEINIZING HORMONE (LH) SURGE. Ariri Taggar, M.D., M.P.H, Lawrence Engmann, MD, Daniel R. Grow, MD, MHCM, Claudio A. Benadiva, MD, HCLD University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT.

OBJECTIVE: The use of a DT in poor prognosis patients has not been previously published. We aim to study whether the potential benefit of applying a DT among a poor prognosis patient population using the USF protocol improves oocyte maturity rates, and if this population mounts an effective LH surge.

MATERIALS AND METHODS: A query of IVF cycles using the USF protocol at a single academic institution was performed. Cycles using a DT (leuprolide acetate 1mg + hCG dosed base on estradiol levels) were compared to cycles triggered with hCG alone (HT). The primary outcome was oocyte maturity rate. Secondary outcomes included the blastocyst development rate per oocyte and post trigger serum LH surge levels. Subgroup analyses were performed for pregnancy outcomes among those who had fresh embryo transfers (ET), as well within the DT group for patients that failed the GnRH trigger (LH surge < 15 mIU/mL). Descriptive statistics with independent t-tests for continuous data, and chi squared tests for categorical data were used. A two-sided p-value of <0.05 was considered statistically significant.

RESULTS: Of the 79,416 FET single ET cycles meeting eligibility criteria, racial & ethnic representations were: W: 35, 654 (45%), B: 2,255 (2.8%), As: 10.015 (12.6%), Unk (31, 378 (39.5%), H: 3, 168 (4.0%). Outcomes of pregnancies resulting from single genetically tested ET were significantly compromised in women of non-W race & of H ethnicity compared to W & non-H women (Table). EP & EL were unreported to race or ethnicity (p<0.05).

CONCLUSIONS: Concerning racial & ethnic differentials in pregnancy outcomes of IVF PGT-A cycles utilizing transfer of single thawed blastocysts were noted.

IMPACT STATEMENT: Among women of color achieving pregnancy following transfer of genetically tested single embryos in the US, Black women are at a disproportionately higher risk for concerning obstetric outcomes including late PL, PTB & SB. Systemic racism as underpinning to the observed associations is a plausible consideration that merits attentiveness.

SUPPORT: None

P-668 10:00 AM Tuesday, October 25, 2022

RACIAL DISPARITIES IN OUTCOMES OF PREGNANCIES RESULTING FROM PGT-A SINGLE BLASTOCYST TRANSFER - ANALYSIS OF 79, 416 FROZEN-EMBRYO TRANSFER CYCLES IN SART CORS. Lubna Pal, MBBS,1 Meredith Akerman, MS,2 Sata Kuokkanen, MD, PhD1 Yale University, Orange; NYU Langone - Long Island Hospital, Mineola, NY; NYU Langone, Mineola, NY.

OBJECTIVE: To examine if pregnancy outcomes following transfer of thawed single genetically tested (PGT-A) blastocysts differ by race & ethnicity.

MATERIALS AND METHODS: SARS CORS data on autologous single embryo transfer (ET) PGT-A cycles were analyzed. Recurrent pregnancy loss, gestational carrier, donor egg & donor ET cycles were excluded. Racial categories available in SART CORS are: White (W), Black (B), Asian (As), Pacific Islander (PI) & Unknown (Unk). Ethnic categories are Hispanic (H) & non-Hispanic (nH). SART specified pregnancy outcomes include preterm birth (PTB), stillbirth (SB), ectopic pregnancy (EP) & live birth (LB). Term birth (TB, birth at gestation ≥37 weeks), early loss (EL, loss at gestation<13 weeks) & late loss (LL, loss between ≥13 and <20 weeks) were computed. Multivariable analysis examined relationship between race & ethnicity with specified outcomes, after adjusting for age, BMI, smoking, endometrial thickness (mm), infertility diagnoses of uterine & tubal factor & AMH (linked with fresh cycle).

RESULTS: Of the 79,416 FET single ET cycles meeting eligibility criteria, racial & ethnic representations were: W: 35, 654 (45%), B: 2,255 (2.8%), As: 10.015 (12.6%), PI: 115 (0.14%), Unk (31, 378 (39.5%), H: 3, 168 (4.0%). Outcomes of pregnancies resulting from single genetically tested ET were significantly compromised in women of non-W race & of H ethnicity compared to W & non-H women (Table). EP & EL were unreported to race or ethnicity (p<0.05).

CONCLUSIONS: Concerning racial & ethnic differentials in pregnancy outcomes of IVF PGT-A cycles utilizing transfer of single thawed blastocysts were noted.

IMPACT STATEMENT: Among women of color achieving pregnancy following transfer of genetically tested single embryos in the US, Black women are at a disproportionately higher risk for concerning obstetric outcomes including late PL, PTB & SB. Systemic racism as underpinning to the observed associations is a plausible consideration that merits attentiveness.

SUPPORT: None

P-667 10:00 AM Tuesday, October 25, 2022

AN EFFECTIVE LUTEINIZING HORMONE (LH) SURGE. Arti Taggar, M.D., M.P.H, Lawrence Engmann, MD, Daniel R. Grow, MD, MHCM, Claudio A. Benadiva, MD, HCLD University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT.

OBJECTIVE: The use of a DT in poor prognosis patients has not been previously published. We aim to study whether the potential benefit of applying a DT among a poor prognosis patient population using the USF protocol improves oocyte maturity rates, and if this population mounts an effective LH surge.

MATERIALS AND METHODS: A query of IVF cycles using the USF protocol at a single academic institution was performed. Cycles using a DT (leuprolide acetate 1mg + hCG dosed base on estradiol levels) were compared to cycles triggered with hCG alone (HT). The primary outcome was oocyte maturity rate. Secondary outcomes included the blastocyst development rate per oocyte and post trigger serum LH surge levels. Subgroup analyses were performed for pregnancy outcomes among those who had fresh embryo transfers (ET), as well within the DT group for patients that failed the GnRH trigger (LH surge < 15 mIU/mL). Descriptive statistics with independent t-tests for continuous data, and chi squared tests for categorical data were used. A two-sided p-value of <0.05 was considered statistically significant.

RESULTS: 147 cycles were identified for the DT group, and 134 were identified for the HT group. There was no difference in the mean age, AMH, antral follicle count, BMI, day3 FSH level, number of stimulation days, or total gonadotropin dose among the two groups. The mean trigger dose of hCG was 8296 ± 289 in the DT group and 8941±249 IU in the HT group, p=0.11. There were no differences in the mean oocyte maturity (DT: 6.4 ± 2.6% vs HT: 6.3 ± 3.4%, p=0.66) or the blastocyst development (DT: 2.4% ± 1.9% vs HT: 2.4 ± 2.3%, p=0.89) rates per oocyte retrieved.
27/147 patients in the DT group and 41/134 patients in the HT group had a fresh ET. The live birth/ongoing pregnancy rates (DT: 29.2% vs HT: 12.2%, p=0.015) and miscarriage rates (DT: 18.5% vs HT: 28.3%, p=0.32) were not statistically different.

Within the DT group, the mean number of days from the initial flare GnRHa doses to the DT was 13.7 ±0.8 and 92.5% of the DT patients exhibited an adequate LH surge of 34.6 mIU/mL (95% CI: 32.9, 39.5). When compared to rest of the 136/147 cycles in the DT group that had an effective LH surge, there were no differences among the 11/147 cycles that failed the GnRHa trigger in their oocyte maturity (Surged: 6.5 ± 2.7% vs Failed: 6.6 ± 7.6%, p=0.90) or blastocyst development (Surged: 2.5 ± 2.0% vs Failed: 1.8 ± 4.8%, p=0.38) rates per oocyte retrieved.

CONCLUSIONS: DT was effective in producing an LH surge despite having received 3 previous GnRHa flare doses at the beginning of the stimulation, indicating that the pituitary remains responsive to the GnRHa trigger in most patients. Though the difference did not reach statistical significance, the DT group showed a trend towards higher pregnancy and lower miscarriage rates, suggesting a potential benefit of this trigger modality for poor prognosis patients. Further prospective randomized studies are warranted to evaluate any benefits of a DT for this challenging group of patient cycles.

IMPACT STATEMENT: DT in an USF protocol amounts an adequate LH surge among poor responders and outcomes may be superior to patients trying with hCG alone.

**P-671 10:00 AM Tuesday, October 25, 2022**

**DYSGREGULATED GATA2 AND GATA6 TRANSCRIPTION FACTOR EXPRESSION IN PATIENTS WITH ADENOMYOSIS: IMPLICATIONS FOR IMPAIRED ENDOMETRIAL DECIDUALIZATION.** Zoran I. Pavlovic, M.D.,1 Angel H. Pai, M.D.,2 Tzu-Ti Hisao, M.S.,2 Asli Ozmen, PhD,3 Emad Mikhail, M.D.,3 Anthony N. Imudia, M.D.,1 Maha Al Jumaily, MBBS,4 Xiaofang Guo, M.S. M.D.,5 Charles J. Lockwood, MD, MHC,1 Chih-Feng Yen, MD, PhD,1 Ozlem Guzeloglu-Kayisli, PhD,6 Umit Kayisli, PhD,1 University of South Florida, Tampa, FL;6 Linkou Chang Gung Memorial Hospital, Taoyuan City, Taiwan;1 University of South Florida, Morsani College of Medicine, Tampa, FL;1 University of South Florida, College of Medicine, Tampa, FL;2 Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital at Linkou, Chang Gung University College of Medicine, Kwei-Shan, Taoyuan, Taiwan;5 Department of Obstetrics and Gynecology, Morsani College of Medicine, University of South Florida, Tampa, FL.

OBJECTIVE: GATA binding protein 2 and 6 (GATA2 and GATA6) are zinc-finger transcription factors involved in proliferation of hematopoietic and endocrine cell lineages, and in cell differentiation and organogenesis, respectively, which are important mechanisms in early pregnancy. Binding of GATA2 to the progesterone receptor (PGR) gene promoter induces PGR expression. GATA2 also interacts with PGR and contributes to PGR-mediated transcription. GATA2 deficiency is due to impaired uterine response associated with lower PGR levels and attenuated progesterone signaling and defective decidualization. Additionally, elevated GATA6 levels increase aromatase activity with concomitant aberrant activation of estrogen synthesis in studies of endometriosis. It has previously been shown that several decidualization mediators such as LIF, IL11R and PGR are dysregulated in endometrium of adenomyosis patients during the implantation window. Thus, we hypothesized that dysregulated GATA2 and GATA6 expression may contribute to adenomyosis-associated implantation failure by impairing decidualization.

MATERIALS AND METHODS: GATA2 and GATA6 immunohistochemistry (IHC) and H-SCORE was performed on mid-secretory phase endometrial tissue from adenomyosis patients (n=9) and leiomyoma control patients (n=9). Human endometrial stromal cells (HESCs) were isolated from patients with confirmed adenomyosis and from fertility proven leiomyoma patients who served as controls. Control HESC (n=2) and adenomyosis HESC (n=2) cultures were treated with either placebo, 10^-8 M estradiol (E2), or decidualization media (EMC) containing 10^-8 M E2, 10^-7 M medroxyprogesterone acetate, and 5x10^-5 M cAMP for 10 days. Additionally, control HESC cultures (n=4) were transfected with scrambled siRNA (control) or GATA2-specific siRNAs (n=2). GATA2, GATA6, PGR and Prolactin (PRL) mRNA levels were analyzed by qPCR using TaqMan Gene Expression assays.

RESULTS: HIC revealed a 3-fold lower GATA2 and 5-fold higher GATA6 H-Score level in endometrial stromal cells of adenomyosis patients vs. controls (p<0.05). Decidual induction with EMC resulted in a 1.4-fold lower GATA2 and 2.1-fold higher in GATA6 mRNA levels in HESC cultures from adenomyosis patients vs. controls. Decidualized HESCs from adenomyosis patient also displayed 1.8- and 4.1-fold lower PGR and PRL levels respectively, compared to controls (n=2). GATA2 siRNA transfection in control HESC cultures resulted in a 1.6-fold higher GATA6 mRNA levels (p=0.01).

CONCLUSIONS: These results demonstrate that there is an inversely correlated relationship between endometrial GATA2 and GATA6 levels with adenomyosis patients having diminished GATA2 and concurrent elevated GATA6 levels. In vitro results showing lower GATA2 and higher GATA6 levels, together with decreased PGR and PRL mRNA levels in HESCs from adenomyosis patients, supports impaired decidualization.

IMPACT STATEMENT: Dysregulated expression of the inversely related GATA2 and GATA6 transcription factors contribute to adenomyosis-associated implantation failure leading to infertility.

SUPPORT: None

**P-672 10:00 AM Tuesday, October 25, 2022**

**SOCIODEMOGRAPHIC AND ECONOMIC CHARACTERISTICS OF INFERTILE PATIENTS REFERRED TO A PUBLIC UNIVERSITY CENTER IN BRAZIL. FOR ASSISTED REPRODUCTION THERAPY.** Bruna Lopes de Magalhães, MD, Natália Beltrami, MD, Olivia Patatas, MD, Mayra Satiko Lemos Nakano, MD, Dani Ejzenberg, MD PhD, Pedro AA. Monteleone, MD, PhD, Edmund Chada Baracat, MD, PhD University of São Paulo, São Paulo, Brazil.

OBJECTIVE: To evaluate the sociodemographic and economic profile as well as the time attempting conception of couples who were referred for fertility treatment in the main public hospital in Brazil.

MATERIALS AND METHODS: This was a retrospective study that analyzed data of 128 couples who sought fertility treatment in Hospital das Clinicas of University of São Paulo in the year of 2018. The following variables were studied: age, ethnicity, length of time trying to conceive, time of union, years of schooling, parity, monthly household income and distance from residence to hospital.

RESULTS: The mean age of patients was 33 years (21-43 range). 67.19% declared themselves white, 12.5% brown/mixed and 5.47% black. Mean time of relationship between couples was 7.8 years and 50.8% had primary infertility. Most female patients were high school graduates (46.9%). Most couples had about 8 to 14 years of schooling. The monthly household income ranged from $773.67 to $1,574.34 US dollars. The mean distance from residence to hospital was 22.2 miles (range 0.6 to 351 miles). Average time attempting conception was 4.2 years, ranging from 1 to 14 years.

CONCLUSIONS: Patients in this study had an average age of 33 years old, while according to data from the Latin American Network of Assisted Reproduction (REDLARA) of 20181, 32% of the patients treated in private clinics in Latin America had 40 years or more and only 26.4% had less than 34 years of age. This could happen because there is a limit of 37 years of age for infertility treatment in this public service in Brazil. The short number of public centers that provide fertility treatments might be one of the reasons for the duration of infertility (4 years), which is longer, for example, than the mean time trying to conceive of infertile patients in the United Kingdom (18 months).2

IMPACT STATEMENT: The delay in diagnosis and referral of infertile patients for treatment in the public service demonstrates a difficulty of access when compared to European fertility centers. The social disparities in IVF treatments are a reality in developing countries like Brazil. Despite the growing number of IVF cycles in the country in the past years (a 16% increase from 2017 to 2018 and a rise of 859 cycles from 2018 to 2019), this fact is mostly due to the private sector. The International Committee for Monitoring Assisted Reproductive Technologies (ICMART) and other international initiatives must pay attention to infertile couples from developing countries who are suffering from disparities in access to fertility treatment.

REFERENCES:
OBJECTIVE: Historically, transvaginal ultrasound (TVU) has been considered superior to transabdominal ultrasounds (TAU) in measuring the thickness of uterine lining (Marasini JP et al., 2009; Karavani G, et al., 2018). In addition, endometrial thickness is directly correlated with ART success with poorer outcomes when the endometrial thickness is < 7 mm. However, nearly all studies have utilized an abdominal probe to measure the endometrial thickness at the time of ET, and to our knowledge no previous studies have compared whether there are differences between an abdominal measurement and that of the supposedly more accurate vaginal approach at the time of embryo transfer (ET). We therefore aimed to determine if TVU endometrial measurement is more accurate than TAU.

MATERIALS AND METHODS: This single center study prospectively evaluated 132 patients undergoing Frozen Embryo Transfers (FETs) between 2020 and 2022. All patients signed an informed consent for ET and underwent the same procedures, measuring uterine lining at ET via TVU and TAU. Both measurements were recorded and compared. Patients with endometrial thickness < 7 mm were excluded (only one patient). All transfers were performed under abdominal guidance immediately after measuring the endometrial thickness vaginally and abdominally. All measurements were performed by a single physician (FIS).

RESULTS: Results were divided into TVU lining and TAU. TVU mean measurements were 9.9 ± 2.11 mm. TAU mean measurements were 10.0 ± 2.1 mm. There was no significant difference between using TVU or TAU (P = 0.69) to measure endometrial thickness at embryo transfer.

CONCLUSIONS: The use of transvaginal ultrasound at the time of embryo transfer is not necessary to have an accurate representation of endometrial thickness. Using solely transabdominal ultrasound decreases potential patient discomfort, and does not sacrifice accuracy of endometrial thickness at embryo transfer.

IMPACT STATEMENT: Abdominal ultrasound measurements of endometrial thickness is as accurate as vagal ultrasound measurements. SUPPORT: None

P-222 6:45 AM Tuesday, October 25, 2022
EVALUATION OF ULTRAST ULTRASOUND GEL TO INDUCE A TEMPORARY DISTENSION OF THE UTERINE CAVITY TO IMPROVE UTERINE SONOGRAPHY.

Paul Pirtea, M.D., 1 Laurentiu Cornel Pirtea, M.D. Ph.D.1 1Hospital FOCH, Paris, France; 2Vittor Babes University, Timisoara, Romania.

OBJECTIVE: To demonstrate that a small amount (up to 5mL) of Ultras Gel induces a slight, temporary distension of the uterine cavity while exploring by regular ultrasound. Also, to assess the tolerability of using Ultras gel for ultrasound examination.

MATERIALS AND METHODS: Prospective single-center open-label cohort study. 21 patients, with or without uterine bleeding disorders, between 20 and 50 years old were included. All were in the follicular phase of their menstrual cycle (day 4-10) when the examination was performed. Ultras Gel was instilled by a single physician. All patients had a history of minimal or moderate pain during transvaginal ultrasound. None had complaints over the course of the exam. One subject reported acute abdominal pain, 5th after gel injection, which resolved within 15 minutes after one dose of a non-steroidal anti-inflammatory agent.

RESULTS: All subjects rated the exam as tolerable, and no one had complaints over the course of the exam. One subject reported acute abdominal pain, 5th after gel injection, which resolved within 15 minutes after one dose of a non-steroidal anti-inflammatory agent.

CONCLUSIONS: Ultras Gel allows visualization of the inner uterine cavity while performing a regular ultrasound. All subjects showed uterine distension with a sono-transparent interface following administration of Ultras Gel and in all, the distension had rescinded 25 minutes later.

IMPACT STATEMENT: The use of Ultras Gel – well accepted by women – constitutes a seminal invention in diagnostic imaging of the uterine cavity, permitting SIS-like uterine images to be obtained with a regular ultrasound.

SUPPORT: Ultras Gel samples were provided by Ultras Inc., New York.
age as well as side effects (e.g., breast tenderness, leg cramps, skin irritation, heart disease and carcinogenesis). Hence, Stem cells, which have been reported for their paracrine effects including anti-inflammatory, augment cell proliferation, and cell-cell communication, are in the spotlight as a treatment to improve ovarian function. Some reports of ovarian tissue banking using various stem cells are increasing, but their evidence is insufficient. Therefore, our aim of this study is to investigate the recovery mechanisms of stem cells for improving ovarian granulosa cells (OGCs).

**MATERIALS AND METHODS:** To analyze the effect of Umbilical cord mesenchymal stem cells (UC-MSCs) on damaged OGCs, we induced damage using cyclophosphamide with busulfin and used the condition media (CM) of UC-MSCs for restoring OGCs. At this time, CM was exposed at 80% cell confluency for 24h using basal media without FBS. To confirm the effect of UC-MSCs, we analyzed the factors of granulosa cell function and apoptosis on damaged OGCs. To confirm the recovery mechanism by UC-MSCs, we analyzed the mitochondrial function including antioxidant effect,OXPHOS, biogenesis, metabolism, and dynamics on damaged OGCs.

**RESULTS:** As a result, we confirmed that the CM of UC-MSCs recovered the function of damaged OGCs through the anti-apoptotic effect and decreased the oxidative stress by chemotheraphy through the antioxidant activities. And then, the CM of UC-MSCs enhanced the mitochondrial OXPHOS and biogenesis in damaged OGCs. Based on these results, we confirmed that the CM of UC-MSCs changed phenotype of damaged OGCs to energetic condition by restoring the mitochondrial function reduced by chemotherapy to a normal level. Also, the CM of UC-MSCs enhanced the mitochondrial metabolic activity (e.g., Glucose, Fatty acid, and Glutamine pathway) degraded by chemotherapy in damaged OGCs.

**CONCLUSIONS:** Our data demonstrated that UC-MSCs induce functional recovery through quality control of mitochondria by mitophagy in damaged OGCs by chemotherapy.

**IMPACT STATEMENT:** Our findings are important in identifying mechanisms for the treatment of ovarian dysfunction using stem cells. Taken together, the findings offer new insights into further understanding of stem cell therapy for reproductive systems and should provide new avenues to develop more efficient therapies.

**SUPPORT:** This study was financially supported by start-up funds from University of Chicago (AA).

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**P-227  6:45 AM Tuesday, October 25, 2022**

**MARKERS OF OVARIAN RESERVE AS PREDICTORS OF FUTURE FERTILITY.** Benjamin S. Harris, MD, MPH,1 Anne Marie Z Jukic, PhD,1 Tracy Truong, MS,2 Caroline Turner Nagle, MPH,1 Aalattin Erkanli, PhD,1 Anne Z. Steiner, MD, MPH1 2Durham, NC; 3National Institute of Environmental Health Sciences, Durham, NC; 4Department of Biostatistics & Bioinformatics, Duke University Medical Center, Durham, NC; 5Duke University School of Medicine, Morrisville, NC; 6Duke University, Durham, NC.

**OBJECTIVE:** Ovarian reserve biomarkers have been shown to be poor predictors of current reproductive capacity. However, their value predicting future reproductive capacity is uncertain. This study sought to determine the association between ovarian reserve biomarkers and future fertility among late reproductive-age women.

**MATERIALS AND METHODS:** This community-based cohort study included participants enrolled in Time to Conceive (TTC), a time-to-pregnancy cohort study of ovarian reserve biomarkers. Participants were 30-44 years old, without a history of infertility, and recruited between 2008-2016. Participants who provided blood samples at enrollment and agreed to future follow-up completed a web-based questionnaire between October 2020 and February 2021 on pregnancy attempts following TTC. Primary outcomes were probability of achieving a live birth > 3 years following TTC enrollment, diagnosis of infertility, and time to pregnancy in future pregnancy attempts.

**RESULTS:** Women with diminished ovarian reserve (DOR), defined as AMH < 0.7 ng/mL or FSH > 10 μIU/mL, did not have a lower probability of future live birth (Relative Risk [RR] 1.32; 95% CI, 0.95-1.83 and RR 1.28; 95% CI, 0.97-1.70, respectively) compared to women with normal ovarian reserve after adjusting for age at blood draw, race, obesity, use of hormonal contraception, and year of enrollment in original study. Among women in the cohort who attempted to conceive, there was not a significant association between DOR as measured by AMH or FSH and risk of future infertility (RR 0.65; 95% CI, 0.21-2.07 and RR 1.60; 95% CI, 0.86-3.31, respectively). Similarly, there was no association between DOR as measured by AMH and FSH and fecundability (Fecundability Ratio [FR] 0.97; 95% CI, 0.59-1.60; and FR 0.86; 95% CI 0.53-1.36, respectively) during pregnancy attempts following TTC.

**CONCLUSIONS:** Diminished ovarian reserve is not associated with reduced future reproductive capacity, as measured by probability of achieving a live birth > 3 years after assessment, risk of infertility, or fecundability in future pregnancy attempts.

**SUPPORT:** NIH/NICHD (R21 HD060229-01 and R01 HD067683-01) and Intramural Research Program of the National Institute of Environmental Health Sciences (Z1ESI053333). Support for this investigation was provided in part by the Office of Research on Women’s Health (ORWH), NIH. This study was supported by the Charles Hammond Research Fund, Duke University School of Medicine, Durham, NC.

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**THE NEW FOLLICULAR WAVE: DUOSTIM VS MICRODOSE FLARE CYCLE OUTCOMES IN DIMINISHED OVARIAN RESERVE.** Anisa Hassain, B.S., M.A.1 Jacqueline Sehring, B.S., M.A.1 Tyler Soy, MA,1 Lauren Grimm, MA,1 Caroline Peschansky, MA,1 Kayla Vitale, BS,1 Janelle M. Jackman, MBBS,2 Angelene Beltsos, MD,3 Roohi Jeelani, MD1 Vios Fertility Institute, Chicago, IL;2Kindbody, Los Altos, CA;3Kindbody/Vios Fertility Institute Chicago, Chicago, IL.

**OBJECTIVE:** To optimize ovarian stimulation in patients with diminished ovarian reserve (DOR), by comparing IVF cycle outcomes in DOR patients who underwent DuoStim protocol compared to those who underwent Microdose Lupron Flare (MDF) protocol.

**MATERIALS AND METHODS:** Chart review of patients with DOR who underwent DuoStim or MDF stimulation protocol for IVF and embryo vitrification was conducted at a multisite fertility practice in the US. DOR was defined by AMH < 1 ng/mL. Patients were divided into two groups: DuoStim and MDF. DuoStim protocol consisted of two phases: follicular phase stimulation (FPS) and luteal phase stimulation (LPS). During FPS, patients underwent ovarian stimulation via antagonist protocol, recombinant hCG trigger, and oocyte retrieval. This was immediately followed by LPS, which consisted of a microdose Lupron flare with recombinant FSH, recombinant hCG trigger and oocyte retrieval. MDF protocol consisted of a single ovarian stimulation cycle with microdose Lupron and recombinant FSH with hCG trigger, followed by oocyte retrieval. Cycle outcomes (total oocytes retrieved, fertilization rate, and total embryos frozen) between each phase of DuoStim and MDF cycles were compared via one-way ANOVA (FPS vs. FPS vs. MDF). Further, unpaired t-test compared the aforementioned parameters between complete DuoStim cycles and MDF cycles (FPS + LPS vs. MDF). Statistical tests were performed using Graph Pad, LLC.

**RESULTS:** There was no significant difference between oocytes retrieved, fertilization rate, and embryos frozen between FPS, LPS, and MDF groups (p=0.29, p=0.62, p=0.1; see Table 1). There was no significant difference between total oocytes retrieved, fertilization rate, and total embryos frozen between a complete DuoStim cycle (FPS + LPS) and MDF cycle (p=0.12, 0.71, 0.74; see table 1). Of note, there was no significant difference in the oocytes retrieved, fertilization rate, and embryos frozen between FPS and LPS of DuoStim cycles (p=0.21, 0.22, 0.78; see table 1).

**CONCLUSIONS:** In this study, we compared the cycle outcomes in DOR patients who underwent IVF with DuoStim and MDF protocols. Whereas trends indicated that patients with DOR who underwent DuoStim had a higher number of total oocytes retrieved, compared to those who underwent MDF, this trend was statistically insignificant. Additionally, there was no significant difference in fertilization rate or number of embryos frozen between the two groups.

**IMPACT STATEMENT:** These preliminary results suggest that DuoStim cycles, which can be costly for patients and institutions, may not improve cycle outcomes in patients with DOR.

**SUPPORT:** None

**REFERENCES:** None

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THE USE OF ENDOMETRIAL CULTURE FOR TARGETED TREATMENT OF ENDOMETRITIS IN PATIENTS EXPERIENCING INFERTILITY AND RECURRENT PREGNANCY LOSS. Sarah Hmaidan, D.O.,¹ Edwin Holt, M.D.,¹ Zoe Finer, MS-2,¹ Donna R. Session, M.D.,² Michelle Roach, M.D.¹ Vanderbilt University Medical Center; °Vanderbilt University School of Medicine.

OBJECTIVE: To evaluate whether endometrial culture in addition to endometrial biopsy reduces time to clear chronic endometritis (CE) and fewer endometrial biopsies in patients experiencing infertility and recurrent pregnancy loss (RPL).

MATERIALS AND METHODS: This retrospective cohort study was performed at an academic tertiary care facility. We included patients (N=92) with endometritis (defined as either endometritis on pathologic evaluation or 5 plasma cells per high power field) who were evaluated in the reproductive infertility and endocrinology clinic for infertility or RPL from March 2018 to January 2022. In March 2021, the clinic implemented routine use of endometrial culture in addition to endometrial biopsy as part of the evaluation of infertility or RPL. We hypothesized that treatment of specific endometrial pathogens with reported sensitivities to antibiotics would result in a reduction in length of treatment to clear CE and fewer number of biopsies per patient. Patients evaluated prior to March 2021 with only endometrial biopsy (n=46) were compared to patients evaluated after March 2021 with endometrial culture in addition to endometrial biopsy (n=46). Patients who did not follow up to evaluate for clearance of endometritis were excluded from the study. Mean time to clearance and average number of biopsies were compared via students t-test.

RESULTS: The mean time needed to clear CE in the endometrial biopsy only cohort was 73.1 days, while the average time needed in the endometrial culture plus endometrial biopsy cohort was 51.4 days (p=0.018). The average number of biopsies per patient in the endometrial biopsy only cohort was 2.89, while the average number of biopsies in the endometrial culture plus endometrial biopsy cohort was 1.98 (p=0.00001).

CONCLUSIONS: Endometrial culture in addition to endometrial biopsy leads to a statistically significant decreased time to treat patients with CE and significantly fewer endometrial biopsies required per patient. Endometrial culture is a diagnostic tool that could reduce time needed to treat CE by targeting specific pathogens. Futures studies should investigate if this simple diagnostic tool reduces time to pregnancy in patients with CE.

IMPACT STATEMENT: CE is present in up to 40% of patients with infertility and 28% of patients with RPL (1). With pathogen targeted evaluation of the endometrial microbiome comes the ability to tailor therapy and potentially improve reproductive outcomes (2).

REFERENCES:


Giudice LC. Challenging dogma: the endometrium has a microbiome with functional consequences!
OBJECTIVE: To investigate the effectiveness of UI±OS for women with “overt” or “subtle” TFI (such as those with endometriosis) in comparison to those with unexplained infertility (UI).

MATERIALS AND METHODS: Design: Retrospective cohort.

Setting: Academic Center.

Patients: 4613 UI±OS cycles from 1625 women with one of the following diagnoses: TFI (269 cycles, 105 women), endometriosis (ENDO: 242 cycles, 87 women), or UI (4102 cycles, 1433 women).

Interventions: UI±OS.

Outcomes:

Primary: Ongoing pregnancy rate (OPR).

Secondary: Clinical (CPR) and ectopic pregnancy rate (EcPR), as well as spontaneous abortion rate (SABR).

Statistics: Chi-square, Fisher’s exact, analysis of variance, and Kruskal-Wallis tests were used as appropriate. Risk ratios (RR) and 95% confidence intervals (CI) for the incidence of ectopic pregnancy were calculated. Odds ratios (OR) and 95% CI were calculated with generalized estimating equations (GEE) logistic regression models and adjusted for maternal age, BMI, day-3 FSH, prior parity, OS regimen, and total progressive motile sperm count.

RESULTS: CPRs and SABRs did not differ significantly between groups (CPR: 10.0% vs. 10.3% vs. 12.6%, p=0.304; SABR: 25.9% vs. 8.0% vs. 17.9%, p=0.221; for TFI vs. ENDO vs. UI, respectively). Yet EcPR in TFI was 8.17 times that of UI group (11.1% vs. 1.4%, p=0.010; RR: 8.17, 95%CI: 2.24-29.87, UI: ref.). No ectopic pregnancies were observed in ENDO group.

OPRs per identified clinical pregnancy were lowest among patients with TFI (63.0% vs. 92.0% vs. 80.8%, for TFI vs. ENDO vs. UI, respectively, p=0.025). Following adjustments for confounders, TFI cycles had 47% lower odds to result in an ongoing pregnancy compared to those with UI (adj-OR: 0.53, 95% CI: 0.31-0.91, p=0.021, UI: ref.), while no such association was observed for ENDO (adj-OR: 0.81, 95% CI: 0.46-1.42, p=0.457, UI: ref.).

Interestingly, although cumulative OPRs after 3 or 4 UI cycles were lowest in TFI group, the differences among groups did not reach statistical significance (3 cycles: 16.2% vs. 17.2% vs. 22.5%, p=0.178; 4 cycles: 16.4% vs. 18.8% vs. 24.7%, p=0.080; for TFI vs. ENDO vs. UI, respectively).

CONCLUSIONS: Overt TFI seemed to be associated with impaired UI outcomes with regard to increased EcPR and decreased OPR as compared to UI, whereas our results do not suggest such associations for women “at-risk” for TFI such as those with endometriosis.

IMPACT STATEMENT: Because of the potential higher risk of ectopic and lower chances of ongoing pregnancy, women with overt tubal factor infertility may benefit from earlier transition to IVF.

SUPPORT: None.

P-233 6:45 AM Tuesday, October 25, 2022

PREDICTING THE DIAGNOSIS OF POLYCYSTIC OVARIAN SYNDROME (PCOS) AMONG AT RISK WOMEN WITHIN AN ELECTRONIC HEALTH RECORD (EHR) DATABASE. Victoria S. Jiang, MD, 1 Kaitlyn E. James, PhD, 2 Irene Souter, MD 1 1Massachusetts General Hospital Fertility Center, Boston, MA; 2Harvard T.H. Chan School of Public Health, Boston, MA.

OBJECTIVE: To determine informative predictor variables associated with the diagnosed and undiagnosed polycystic ovarian syndrome (PCOS) through an electronic health record (EHR) database.

MATERIALS AND METHODS: Design: Retrospective cohort study conducted using a database containing 144,561 laboratory accessions that were submitted between January 1, 2016 and December 9, 2019 by 129,883 patients. These patients collected urine samples on filter paper at home and sent the collections to the laboratory to be processed. Urinary concentrations of androsterone, dehydroepiandrosterone sulfate (DHEA-S), epi-testosterone, etiocholanolone, testosterone, 5a-androstanediol, 5a-androstanediol, and 5a-dihydrotestosterone (DHT) were measured. The database included a total of 2050 patients with a reported diagnosis of PCOS and 27488 patients who did not report a PCOS diagnosis. A “urinary androgen index” was created comprising all measured androgen metabolites. Mixed models were then created to determine sensitivity, specificity, and predictive values of the components of this urinary androgen index.

RESULTS: Mixed models determined that for patients with a measured urinary androgen index greater than or equal to 4 (or more androgen metabolites above the reference range) the sensitivity was 0.44, the specificity was 0.78, the positive predictive value was 0.13, and the negative predictive value was 0.95. For patients with a measured epi-testosterone, etiocholanolone, or testosterone above the reference range the sensitivity was 0.70, the specificity was 0.53, the positive predictive value was 0.10, and the negative predictive value was 0.96. For patients with a measured urinary testosterone higher than the 75th percentile of the reference range, the sensitivity was 0.47, the specificity was 0.76, the positive predictive value was 0.13, and the negative predictive value was 0.95.

CONCLUSIONS: Urinary androgen metabolites measured using a dried urine sample and a validated GC-MS/MS assay demonstrated low positive predictive values, but high negative predictive values for PCOS suggesting that these measures may be of use in ruling out PCOS.

IMPACT STATEMENT: In this large general population study, a dried urine sampling method measuring androgen metabolites demonstrated the potential to be effective at ruling out PCOS. This method may represent a new, convenient, at-home, non-invasive tool for clinicians and researchers to use in settings where barriers exist to in-person patient evaluation or ultrasound. When combined with additional information available from urine sampling, this tool may provide a comprehensive panel of results to inform both clinical investigation and decision making.

P-233 6:45 AM Tuesday, October 25, 2022

Sensitivity, Specificity, and Predictive Value of Urinary Androgen Metabolites for the Diagnosis of Polycystic Ovary Syndrome. Mark Newman, MS, 1 Doreen Saltiel, MD, JD, 1 Bryan P. Mayfield, PharmD, 1 Frank Z. Stanczyk, PhD 1 Precision Analytical, Inc, McMinnville, OR; 2University of Southern California, Los Angeles, CA.

OBJECTIVE: The objective of this study was to determine if urinary androgen metabolite concentrations measured using an at-home dried urine sampling method and an accompanying gas chromatography-tandem mass spectrometry (GC-MS/MS) assay could be used to confirm or rule out polycystic ovary syndrome (PCOS).

MATERIALS AND METHODS: This was a retrospective observational cohort study conducted using a database containing 144,561 laboratory accessions that were submitted between January 1, 2016 and December 9, 2019 by 129,883 patients. These patients collected urine samples on filter paper at home and sent the collections to the laboratory to be processed. Urinary concentrations of androsterone, dehydroepiandrosterone sulfate (DHEA-S), epi-testosterone, etiocholanolone, testosterone, 5a-androstanediol, 5a-androstanediol, and 5a-dihydrotestosterone (DHT) were measured. The database included a total of 2050 patients with a reported diagnosis of PCOS and 27488 patients who did not report a PCOS diagnosis. A “urinary androgen index” was created comprising all measured androgen metabolites. Mixed models were then created to determine sensitivity, specificity, and predictive values of the components of this urinary androgen index.

RESULTS: Mixed models determined that for patients with a measured urinary androgen index greater than or equal to 4 (or more androgen metabolites above the reference range) the sensitivity was 0.44, the specificity was 0.78, the positive predictive value was 0.13, and the negative predictive value was 0.95. For patients with a measured epi-testosterone, etiocholanolone, or testosterone above the reference range the sensitivity was 0.70, the specificity was 0.53, the positive predictive value was 0.10, and the negative predictive value was 0.96. For patients with a measured urinary testosterone higher than the 75th percentile of the reference range, the sensitivity was 0.47, the specificity was 0.76, the positive predictive value was 0.13, and the negative predictive value was 0.95.

CONCLUSIONS: Urinary androgen metabolites measured using a dried urine sample and a validated GC-MS/MS assay demonstrated low positive predictive values, but high negative predictive values for PCOS suggesting that these measures may be of use in ruling out PCOS.

IMPACT STATEMENT: In this large general population study, a dried urine sampling method measuring androgen metabolites demonstrated the potential to be effective at ruling out PCOS. This method may represent a new, convenient, at-home, non-invasive tool for clinicians and researchers to use in settings where barriers exist to in-person patient evaluation or ultrasound. When combined with additional information available from urine sampling, this tool may provide a comprehensive panel of results to inform both clinical investigation and decision making.
RESULTS: Within Model I, the predictive model achieved an AU(C) in D(95) of 80.9% (1.2). MLP score (PC = 0.62) and obesity (PC = 0.43) were positively correlated with PCOS diagnosis. Pregnancy (gravimetry PC = 0.55; positive pregnancy test PC = 0.49), normal BMI (PC = 0.22), and smoking (PC = 0.18) were inversely correlated with PCOS diagnosis.

Within Model II, the predictive model achieved an AU(95) of 75.0% (1.8). MLP score (PC = 0.56), obesity (PC = 0.18), normal BMI (PC = 0.15), negative pregnancy test (PC = 0.11), and normal HDL (PC = 0.09) were positively correlated with undiagnosed PCOS. Age (PC = 0.27), pregnancy (gravimetry PC = 0.24; positive pregnancy test PC = 0.2), and Hispanic race (PC = 0.18) were inversely correlated with undiagnosed PCOS.

CONCLUSIONS: These predictive models are a novel approach to identifying barriers to PCOS diagnosis. While some factors like age, pregnancy status, obesity, and hypertension were predictive of PCOS diagnosis, other factors like norm BMI and normal blood pressure were predictive of undiagnosed PCOS. PCOS may suggest leaner phenotypes can potentially lead to missed PCOS diagnosis or that disease severity may be a factor in diagnosis.

IMPACT STATEMENT: As the use of machine learning expands, these algorithms may serve as an important tool in conjunction with the EHR to assist in predicting diagnoses that may be otherwise missed.

P-234 6:45 AM Tuesday, October 25, 2022
PRENATAL ANDROGEN EXPOSURE IN MICE LEADS TO A METABOLICALLY DISTINCT PCOS WITHOUT OBESITY.
Alexandra Gannon, M.D., Janet Bruno-Gaston, M.D., Vipin A. Vidyadhara, Pharm.D., Marta L. Fiorotto, Pharm.D., Shaji Chucko, PhD., Juan Marini, PhD., Amy K. Schutt, MD, MSCI, William Gibbons, MD, Chellakkatt Selvanesan Blesson, B.SC., M.PHIL., M.S.C. PH.D., Baylor College of Medicine, Dept of Obstetrics & Gynecology, Houston, TX; 2Baylor College of Medicine, Houston, TX; 3Houston, TX.

OBJECTIVE: Our objective was to elucidate the mechanisms of glucose metabolism in a lean polycystic ovary syndrome (PCOS) mouse model.

MATERIALS AND METHODS: Lean PCOS mice were created by administering dihydrotestosterone prenatally on days 16.5, 17.5 and 18.5 of gestation.

RESULTS: Serum luteinizing hormone and androgen levels, and SC abdominal fat positively correlated with those of serum log nonHDL values (P = 0.034), SC abdominal stem cell lipid accumulation in vitro (P = 0.004) and placebo treatment for 6-months. Clinical characteristics and SC abdominal stem cell lipid accumulation in vitro were compared between PCOS and control subjects. Changes in abdominal fat mass and SC abdominal stem cell lipid accumulation in vitro were compared between female- and placebo-treated PCOS women and correlated with endocrine-metabolic outcomes. An unpaired Student’s t-test, two-way ANOVA with repeated measures and Pearson correlation coefficients, adjusting for serum free testosterone (T) levels, were used.

RESULTS: Serum luteinizing hormone and androgen levels, and SC abdominal stem cell lipid accumulation in vitro, were greater in PCOS than control women (all values, P < 0.01). During flutamide versus placebo treatment, treatment-time interactions existed for percent (% android) fat (P = 0.040), SC abdominal stem cell lipid accumulation in vitro (P = 0.004) and log serum nonHDL (P = 0.026) and log LDL (P = 0.034) values. After adjusting for serum free T levels, only percent android fat (P = 0.013) and SC abdominal stem cell lipid accumulation in vitro (P = 0.008) remained significant. Flutamide versus placebo treatment in PCOS women reduced % android fat (P = 0.040), serum log nonHDL (P = 0.056) and log LDL (P = 0.034) values, and partially lowered SC abdominal stem cell lipid accumulation in vitro relative to control cells (P = 0.004). In all PCOS subjects, changes in % android fat positively correlated with those of serum log nonHDL values (P = 0.069, P = 0.019) and also were affected by hyperandrogenemia (adjusting for serum free T; nonHDL, R = 0.56, P = 0.096; log LDL, R = 0.31, P = 0.385). Changes in SC abdominal stem cell lipid accumulation in vitro and serum lipid levels were unrelated.

CONCLUSIONS: Low-dose flutamide administration to normal-weight PCOS women lowers abdominal fat mass and serum atherogenic lipoprotein levels, and partially reduces accelerated SC abdominal stem cell lipid accumulation in vitro and if so whether such changes alter metabolism.

MATERIALS AND METHODS: Twelve normal-weight, NIH-defined PCOS women and 12 age- and body mass index (BMI)-matched normo- androgenic ovulatory (control) women underwent circulating hormone/meta- determinations, intravenous glucose tolerance testing, total-body dual-energy x-ray absorptiometry and SC abdominal fat biopsy. Interventions were repeated in PCOS women after randomization to flutamide (125 mg orally daily) or placebo treatment for 6-months. Clinical characteristics and SC abdominal stem cell lipid accumulation in vitro were compared between PCOS and control subjects. Changes in abdominal fat mass and SC abdominal stem cell lipid accumulation in vitro were compared between female- and placebo-treated PCOS women and correlated with endocrine-metabolic outcomes. An unpaired Student’s t-test, two-way ANOVA with repeated measures and Pearson correlation coefficients, adjusting for serum free testosterone (T) levels, were used.

RESULTS: Serum luteinizing hormone and androgen levels, and SC abdominal stem cell lipid accumulation in vitro, were greater in PCOS than control women (all values, P < 0.01). During flutamide versus placebo treatment, treatment-time interactions existed for percent (% android) fat (P = 0.040), SC abdominal stem cell lipid accumulation in vitro (P = 0.004) and log serum nonHDL (P = 0.026) and log LDL (P = 0.034) values. After adjusting for serum free T levels, only % android fat (P = 0.013) and SC abdominal stem cell lipid accumulation in vitro (P = 0.008) remained significant. Flutamide versus placebo treatment in PCOS women reduced % android fat (P = 0.040), serum log nonHDL (P = 0.056) and log LDL (P = 0.034) values, and partially lowered SC abdominal stem cell lipid accumulation in vitro relative to control cells (P = 0.004). In all PCOS subjects, changes in % android fat positively correlated with those of serum log nonHDL values (P = 0.069, P = 0.019) and also were affected by hyperandrogenemia (adjusting for serum free T; nonHDL, R = 0.56, P = 0.096; log LDL, R = 0.31, P = 0.385). Changes in SC abdominal stem cell lipid accumulation in vitro and serum lipid levels were unrelated.

CONCLUSIONS: Low-dose flutamide administration to normal-weight PCOS women lowers abdominal fat mass and serum atherogenic lipoprotein levels, and partially reduces accelerated SC abdominal stem cell lipid accumulation in vitro.

IMPACT STATEMENT: Androgen receptor blockade in normal-weight PCOS women alters metabolism by reducing abdominal fat mass relative to accelerated SC abdominal stem cell differentiation into adipocytes in vitro.

SUPPORT: National Institutes of Health awards P50HD071836 and P51 OD011092

REFERENCES:
THE DYSREGULATION OF TRYPTOPHAN METABOLISM IN LEIOMYOMAS. Tsaiyer Chuang, PhD,1 Derek Quintanilla, BS,2 Drake Boos, BS,3 Omid Khorram, MD, PhD1,2,3 The Lundquist Institute At UCLA Medical Center, Torrance, CA; 2Torrance, CA; 3Harbor-Ucla Medical Center, Torrance, CA.

OBJECTIVE: To determine the expression of enzymes in tryptophan (Trp) catabolism and the influence of race and MED12 (Mediator Complex Subunit 12) mutation on their expression in fibroids and matched myometrium.

MATERIALS AND METHODS: The expression of enzymes in Trp catabolic pathway, tryptophan transporters, CYP1B1 (Cytochrome P450 1B1) in fibroids and matched myometrium of women from different race/ethnic groups and in tumors with MED12-mutation-positive and mutation-negative tumors was determined by qRT-PCR. The levels of serotonin, kynurenine acid (KYNA) and NAD (nicotinamide adenine dinucleotide) were determined by ELISA (enzyme-linked immunosorbent assay).

RESULTS: Fibroids overexpressed TPH1 (Tryptophan hydroxylase 1), KAT2 (Kynurenine amino transferase 2), SLCTA5 (Large neutral amino acid transporter small subunit 2) and SLCTA5 (Large neutral amino acids transporter small subunit 1) mRNA and reduced expression of KYNU (Kynurenine synthase), WARS1 (Tryptophan TRNA ligase 1) mRNA with no changes in the expression of WARS2, AFMID (Kynurenine formamidase), KMO (Kynurenine 3-monooxygenase), KAT1, KAT3 and KAT4 as compared with matched myometrium (n=81). The mRNA expression of CYP1B1, a marker of AhR (aryl hydrocarbon receptor) activation was higher in fibroids. Furthermore, we demonstrated increased nuclear levels of AhR protein in leiomyoma as compared to matched myometrium, indicative of AhR nuclear translocation in fibroids and indicative of AhR activation. Tumors bearing the MED12 mutation expressed more CYP1B1, and lower WARS1, KAT1, KAT3 and KAT4 mRNA levels as compared to MED12-mutation-negative tumors. Race/ethnicity affected the expression of KYNU in tumors with African Americans and Hispanic patients expressing lower levels of KYNU mRNA as compared with Caucasians. We also quantified the levels of serotonin, KYNA and NAD which are the end products of Trp catabolism. There were no significant differences in levels of serotonin and KYNA, while levels were lower in fibroids as compared to paired myometrium. This reduction in NAD level was independent of race/ethnicity.

CONCLUSIONS: In addition to TDO2 (tryptophan 2,3-dioxygenase) there is marked dysregulation in the expression of other enzymes in Trp metabolic pathway and Trp transporters in fibroids. Both MED12 mutation status and race/ethnicity had selective effects on the expression of components of this pathway. Trp metabolism in fibroid is selectively shuttled in the KYN pathway with downstream activation of AhR. The reduced expression of KYNU in fibroids results in reduced generation of NAD.

IMPACT STATEMENT: These findings indicate that dysregulation of Trp metabolism could be a significant pathogenic mechanism underlying fibroid tumors and a potential target for future therapies.

SUPPORT: National Institutes of Health (NIH: HD100529 and HD101852).

P-236 6:45 AM Tuesday, October 25, 2022

COMPARISON OF CYCLIC URINARY ESTROGEN AND PROGESTERONE METABOLITE PATTERNS BETWEEN WOMEN REPORTING MENSES AND WOMEN REPORTING NO MENSES. Mark Newman, MS1, Doreen Saltiel, MD, JD,1 Bryan P. Mayfield, PharmD,1 Frank Z. Stanczyk, PhD1 Precision Analytical, Inc, McMinnville, OR; 1University of Southern California, Los Angeles, CA.

OBJECTIVE: To determine if monthly urinary patterns of estrogen and progesterone, collected as dried urine samples and measured with a GC-MS/MS assay, differ between women who reported menses and women who reported no menses.

MATERIALS AND METHODS: This was a retrospective observational cohort study conducted using a database containing 144,561 laboratory accesses that were submitted between January 1, 2016 and December 9, 2019 by 129,883 individuals. From this database, 1604 individuals completed a cycle collection and met inclusion criteria for the study (female sex, age between 17 and 50 years, body mass index [BMI] between 16 and 55 kg/m2, and urinary creatinine > 0.1 ng/mL). Progesterone was measured as its urinary metabolites 5α-pregnanediol-3α, 20α-diol (α-pregnanediol) and 5β-pregnanediol-3α, 20α-diol (β-pregnanediol), with total pregnanediols calculated as α-pregnanediol plus β-pregnanediol. Estrogen was also measured via the urinary metabolites with total estrogens calculated as the sum of all 10 measured metabolites. Ovulation was defined as a peak β-pregnanediol > 600 ng/mg-Cr and a peak α-pregnanediol > 200 ng/mg-Cr or a change in total estrogens > 850 ng/mg-Cr. Mixed models to account for repeated measures were used to compare hormone patterns between women who showed evidence of ovulation and those who did not.

RESULTS: Of the 1604 patients included in the study, 83% (1366) showed evidence of ovulation. The mean age (± SD) was 36.5 ± 6.8 for the group that showed evidence of ovulation and 34.3 ± 9.3 for the group that did not. The mean BMI was 24.1 ± 4.6 for the ovulation group and 24.6 ± 5.5 for the anovulatory group. No statistically significant difference existed between the mean age (p = 0.15) or BMI (p = 0.43). A mixed model showed that the difference in the trajectories of total pregnanediols between those who ovulated and those who did not differed significantly (mean difference = 545.67 ± 28.2 ng/mg-Cr/day; p<0.0001). Similarly, in the mixed model evaluating differences in the patterns of total estrogens over the month, the trajectories differed between those who did and did not ovulate (mean d=13.2±3.5 ng/mg-Cr/d). The individual pregnanediol and estrogen measures resulted in similar findings when analyzed separately.

CONCLUSIONS: The method used in this study effectively captured the expected estrogen and progesterone metabolic patterns in women who showed laboratory evidence of ovulation. The results also showed clear and significant differences in these patterns between women who ovulated and women who did not. Further research comparing this method with more definitive methods of ovulation confirmation, such as ultrasonography, is needed.

IMPACT STATEMENT: The results of this study demonstrate the potential for this tool to provide an easy to collect, lower cost, non-invasive option for clinicians and researchers investigating clinical scenarios involving ovulation status.

P-238 6:45 AM Tuesday, October 25, 2022

URINARY ESTROGEN AND PROGESTERONE METABOLITE PATTERNS IN OVULATORY AND ANOVULATORY WOMEN. Mark Newman, MS1, Doreen Saltiel, MD, JD,1 Bryan P. Mayfield, PharmD,1 Frank Z. Stanczyk, PhD1 Precision Analytical, Inc, McMinnville, OR; 1University of Southern California, Los Angeles, CA.

OBJECTIVE: To determine if monthly urinary patterns of estrogens and progesterone, collected as dried urine samples and measured with a GC-MS/MS assay, differ between women who reported menses and women who reported no menses.

MATERIALS AND METHODS: This was a retrospective observational cohort study conducted using a database containing 144,561 laboratory accesses that were submitted between January 1, 2016 and December 9, 2019 by 129,883 individuals. From this database, 1604 individuals completed a cycle collection and met inclusion criteria for the study (female sex, age between 17 and 50 years, body mass index [BMI] between 16 and 55 kg/m2, and urinary creatinine > 0.1 ng/mL). Progesterone was measured as its urinary metabolites 5α-pregnanediol-3α, 20α-diol (α-pregnanediol) and 5β-pregnanediol-3α, 20α-diol (β-pregnanediol), with total pregnanediols calculated as α-pregnanediol plus β-pregnanediol. Estrogen was also measured via the urinary metabolites with total estrogens calculated as the sum of all 10 measured metabolites. Mixed models to account for repeated measures were used to compare urinary estrogen and progesterone patterns between women who reported menses and women who reported no menses.

RESULTS: Of the 1604 patients included in the study, 99% (1584) reported menses and 7% (110) reported no menses. Estrogen was measured via the urinary metabolites with total estrogens calculated as the sum of all 10 measured metabolites. Mixed models to account for repeated measures were used to compare urine estrogen and progesterone patterns between women who reported menses and women who reported no menses.

CONCLUSIONS: The method used in this study effectively captured the expected estrogen and progesterone metabolic patterns in women who showed laboratory evidence of ovulation. The results also showed clear and significant differences in these patterns between women who ovulated and women who did not. Further research comparing this method with more definitive methods of ovulation confirmation, such as ultrasonography, is needed.

IMPACT STATEMENT: These findings indicate that dysregulation of Trp catabolism and the influence of race and MED12 (Mediator Complex Subunit 12) mutation on their expression in fibroids and matched myometrium. Tumors bearing the MED12 mutation expressed more translocation in fibroids and indicative of AhR activation. Tumors bearing the MED12 mutation expressed more CYP1B1, and lower WARS1, KAT1, KAT3 and KAT4 mRNA levels as compared to MED12-mutation-negative tumors. Race/ethnicity affected the expression of KYNU in tumors with African Americans and Hispanic patients expressing lower levels of KYNU mRNA as compared with Caucasians. We also quantified the levels of serotonin, KYNA and NAD which are the end products of Trp catabolism. There were no significant differences in levels of serotonin and KYNA, while NAD levels were lower in fibroids as compared to paired myometrium. This reduction in NAD level was independent of race/ethnicity.

CONCLUSIONS: In addition to TDO2 (tryptophan 2,3-dioxygenase) there is marked dysregulation in the expression of other enzymes in Trp metabolic pathway and Trp transporters in fibroids. Both MED12 mutation status and race/ethnicity had selective effects on the expression of components of this pathway. Trp metabolism in fibroid is selectively shuttled in the KYN pathway with downstream activation of AhR. The reduced expression of KYNU in fibroids results in reduced generation of NAD.

IMPACT STATEMENT: These findings indicate that dysregulation of Trp metabolism could be a significant pathogenic mechanism underlying fibroid tumors and a potential target for future therapies.

SUPPORT: National Institutes of Health (NIH: HD100529 and HD101852).
CONCLUSIONS: The method used in this study effectively captured the expected estrogen and progesterone patterns in women who reported menses. Additionally, there were clear and significant differences in these patterns between women who reported menses and women who reported no menses.

IMPACT STATEMENT: This convenient, at-home collection method and the accompanying validated assay represents a tool that may be useful in a variety of clinical and research settings as it decreases the need for office visits and staff to perform collections needed to evaluate estrogen and progesterone patterns over the course of a menstrual cycle.

P-239 6:45 AM Tuesday, October 25, 2022

AT-HOME SAMPLE COLLECTION FOR THE DETECTION OF AGE-RELATED CHANGES IN FEMALE REPRODUCTIVE HORMONAL PATTERNS: A COHORT STUDY. Natalie M. Daumeyer, PhD,1 Kathleen M. Gavin, PhD,2 Daniel Kreitzberg, PhD,1 Timothy A. Bauer, PhD2 1Everly Health, Inc., Austin, TX; 2Denver, CO.

OBJECTIVE: To evaluate hormonal patterns in a large cohort of women using at-home collection and mail-in lab testing.

MATERIALS AND METHODS: A retrospective analysis was performed using real world data from female consumers who purchased at-home sample collection kits for laboratory analysis of reproductive hormones between September 2017 and March 2022. Dried blood spot (DBS) samples were collected on day 3-4 of the menstrual cycle for Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH). Salivary samples were collected on day 19-21 of the cycle for estradiol (E2), free testosterone, and progesterone. No women taking birth control were included. Further, ages 18-39 years were in the expected cycle timed range, except for progesterone patterns over the course of a menstrual cycle.

RESULTS: Observed medians and interquartile ranges (IQRs) from 35,400 women are presented in Table 1. All biomarker medians for women ages 18-39 years were in the expected cycle timed range, except for progesterone, possibly because women taking birth control were included. Further, median LH and FSH levels were higher with advancing age while E2, free testosterone, and progesterone were lower among the 50-59 and 60+ age groups.

CONCLUSIONS: This real world evidence demonstrates that DBS and salivary samples collected by women in an at-home setting reveal, at a population level, the expected physiological patterns within cycles and across the reproductive lifespan. At-home sample collection is a convenient and useful testing option for adult women across the age-spectrum in need of laboratory testing for reproductive hormones.

IMPACT STATEMENT: At-home lab testing for reproductive hormones can be used to demonstrate expected menstrual cycle specific values as well as patterns across the reproductive life cycle.

Table 1. Medians (M) with different superscripts within a given column are significantly different from each other.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>LH, IU/L (DBS) N M(IQR)</th>
<th>FSH, IU/L (DBS) N M(IQR)</th>
<th>Estradiol, pg/mL (Saliva) N M(IQR)</th>
<th>Free Testosterone, pg/mL (Saliva) N M(IQR)</th>
<th>Progesterone, pg/mL (Saliva) N M(IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 to 29</td>
<td>5,445 5.1 (4.6)</td>
<td>5,605 6.4 (3.9)</td>
<td>4,691 1.6 (1.2)</td>
<td>3,975 37 (24.0)</td>
<td>4,013 51.0 (73)</td>
</tr>
<tr>
<td>30 to 39</td>
<td>14,364 5.0 (4.2)</td>
<td>15,270 6.4 (3.3)</td>
<td>12,283 1.8 (1.2)</td>
<td>10,501 37 (24.0)</td>
<td>11,120 61.5 (75)</td>
</tr>
<tr>
<td>40 to 49</td>
<td>10,055 5.7 (5.5)</td>
<td>10,375 9.3 (9.1)</td>
<td>8,383 1.8 (1.4)</td>
<td>7,150 32 (19.8)</td>
<td>7,783 56.0 (72)</td>
</tr>
<tr>
<td>50 to 59</td>
<td>3,551 28.9 (37.3)</td>
<td>3,366 61.4 (89.3)</td>
<td>3,091 1.1 (1.2)</td>
<td>2,574 34 (21.0)</td>
<td>2,992 62.0 (75)</td>
</tr>
<tr>
<td>≥ 60</td>
<td>664 35.4 (22.9)</td>
<td>665 90.3 (57.2)</td>
<td>663 0.9 (0.8)</td>
<td>551 26 (20.0)</td>
<td>656 21.0 (19)</td>
</tr>
</tbody>
</table>

P-241 6:45 AM Tuesday, October 25, 2022

CONCORDANCE OF Reproductive and Thyroid Hormone Measurements Between Venipuncture and Capillary Blood Samples Throughout the Menstrual Cycle. Natalie Getreu, BSc, MSc, PhD1, Tharni Vasavan, BSc, Msc, PhD,2 Adrian Timpson, PhD,3 Helen C. O’Neill, BSc., MSc., PH.D.1 1UCL Institute for Women’s Health, London, United Kingdom; 2Ruislip, Middlesex, United Kingdom; 3University College London.

OBJECTIVE: At-home testing of reproductive and thyroid hormones are commercially available to assess reproductive health, however, there is limited evidence of the reliability and validity of the capillary blood sampling method utilised in these tests. Previous literature reports blood volume and collection tube type affects the measurement of hormones in venipuncture samples. We sought to assess the intra and inter sample variability in venipuncture and capillary blood and the effect of blood collection tube type on reproductive and thyroid hormone measurement.

MATERIALS AND METHODS: To assess intra and inter sample variability, four venipuncture and capillary blood samples (two replicates of each method) were taken from a fasting 23 year old eumenorrheic participant with no pre-existing reproductive conditions on alternate days of an entire 32 day menstrual cycle. Immunoassays were used to measure 13 analytes in all samples: Anti-Müllerian Hormone (AMH), Estradiol (E2), Follicle-Stimulating Hormone (FSH), Luteinising Hormone (LH), Prolactin, Progesterone, Sex Hormone-Binding Globulin, Testosterone (T2), Free Thyroxine, Free Triiodothyronine, Thyroid-Stimulating Hormone, Anti-Thyroglobulin antibodies and Anti Thyroid Peroxidase antibodies.

Analytes which had significant inter sample variability in the above data were measured again in a separate cohort of 11 premenopausal female participants to assess whether variability was due to collection tube type. Measurements were taken from two venipuncture and capillary samples collected in red top tubes (without serum-separating gel) and gold top tubes (with serum-separating gel).

All data was log-transformed prior to statistical analysis via paired t-tests. P values < 0.05 were considered statistically significant.

RESULTS: No significant intra or inter sample variability was found for 13/13 and 11/13 analytes respectively. Measurements of E2 (p < 0.001, n = 15) and T2 (and p = 0.001, n = 15) were significantly lower in capillary samples, however, T2 measurement in a larger cohort with different tube types did not yield significant differences. Measurements of E2 were significantly lower in gold top capillary samples compared to gold top venipuncture (p<0.001, n = 11) and red top capillary samples (p=0.012, n = 11); no other pairwise comparisons were found to be significant. Further assessment of AMH, FSH and LH levels in this cohort also found significant differences in gold top capillary measurements that were not present between other sample or tube types.
CONCLUSIONS: Reproductive and thyroid hormone measurements taken from venipuncture and capillary samples are concordant, however, capillary samples collected in gold top tubes yielded consistently different measurements which are likely due to the interference of serum-separating gel within the tube. Capillary collection tubes without gel perform comparably to venipuncture for these analytes.

IMPACT STATEMENT: Capillary blood sampling is a valid and reliable method for hormone testing, however, blood collection tube type should be considered when assaying common reproductive biomarkers

SUPPORT: Funding and participation recruitment was via Hertility Health Limited.

P-242 6:45 AM Tuesday, October 25, 2022
REDEFINING LABORATORY REFERENCE RANGES FOR FEMALE REPRODUCTIVE AND THYROID HORMONES. Helen C. O’Neill, B.S.C., M.S.C., PH.D., Tharni Vasavan, BSc, MSc, PhD, Adrian Timpson, PhD, Natalie Getreu, BSc, MSc, PhD 1 UCL Institute for Women’s Health, London, United Kingdom; 2Ruislip, Middlesex, United Kingdom; 3University College London.

OBJECTIVE: The diagnoses and clinical management of many reproductive health conditions rely on categorically interpreting hormone measurements as either within or outside a ‘normal’ reference range. Historically these ranges represent the 95% confidence intervals of a small population without regard to the distributional asymmetry expected by compositional data. We establish a more robust statistical framework that considers continuous quantities, derived from a large dataset, in order to better define normal reference ranges of reproductive and thyroid hormone levels.

MATERIALS AND METHODS: Capillary blood samples taken on day 3 of the menstrual cycle from 2180 UK women aged 18 to 53 years were assayed for the following hormones: Anti-Müllerian hormone (AMH), Estradiol (E2), Luteinising Hormone (LH), Follicle-Stimulating Hormone (FSH), Free Thyroxine (FT4), Thyroid-Stimulating Hormone (TSH) and Prolactin (Prl). Participants who had a previous diagnosis or symptoms of polycystic ovary syndrome, hyper- or hypo-thyroïdism, premature ovarian insufficiency or menopause, hypogonadotropic hypogonadism, endometriosis or fibroids were excluded from analysis. Participants with no diagnosis but self-reported their suspicion of a reproductive problem were also excluded. Participants who were >35 years old, had a BMI >30 or <18.5 kg/m2, a menstrual cycle length of <21 or >35 days or a period length of >38 or <3 days were also excluded. Nine further participants were excluded as outliers, resulting in a subset of 292 individuals to represent a model cohort of healthy women for statistical analysis. All data were log-transformed and the distribution of measurements of each hormone was tested for normality (Shapiro-Wilks test). Summary statistics were derived from these distributions.

RESULTS: Measurements of AMH, E2, FSH, FT4, TSH and Prl levels did not significantly deviate from normality at the confidence level of 0.05. OCT: report mean and standard deviation of log-transformed values, and the Standard Error of the Mean (SEM) to indicate the uncertainty due to finite sample sizes: logAMH (mean = 3.085, SD = 0.670, SEM = 0.040), logE2 (mean = 4.4902, SD = 0.393, SEM = 0.026), logLH (mean = 1.788, SD = 0.375, SEM = 0.025), logFSH (2.039, SD = 0.289, SEM = 0.019), logFT4 (mean = 2.772, SD = 0.128, SEM = 0.008), logTSH (mean = 0.753, SD = 0.478, SEM = 0.029), logPrl (mean = 5.949, SD = 0.560, SEM = 0.047), all values in ln(UL).

CONCLUSIONS: Our empirical results support the theory that hormone values are log-normally distributed, permitting the mean and standard deviation of log-transformed values to be a full and fair representation of the data. Normal distribution of hormone values confirms this dataset can be used to derive normal reference ranges to better interpret hormone values from the female population.

IMPACT STATEMENT: We establish an improved framework for the clinical reporting and interpretation of hormone measurements with respect to a normal distribution derived from a large cohort of healthy women.

SUPPORT: Funding and participation recruitment was via Hertility Health Limited.

P-244 6:45 AM Tuesday, October 25, 2022
UTILITY OF HORMONE GENETIC RISK SCORES IN IDENTIFYING REPRODUCTIVE DYSFUNCTION ASSOCIATED WITH POLYCYSTIC OVARY SYNDROME. Ky’Era V. Actkins, PhD, Lea K. Davis, PhD 1 National Institute of Environmental Health Sciences, Durham, NC; 2Vanderbilt University Medical Center, Nashville, TN.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is characterized by impairments in ovarian hormone regulation that lead to an assortment of reproductive and metabolic symptoms. Abnormal hormone levels can be driven by the genetic risk of PCOS, but it is unclear if the genetic susceptibility of hormones can lead to the onset of ovarian dysfunction experienced by patients. Polygenic risk scores (PRS) are emerging as a promising tool for studying the genetic contribution of complex conditions and can aid in the understanding of etiologies that have been difficult to elucidate. Due to the strong genetic overlap between hormones and PCOS, we aimed to understand the capability of hormone genetic predictors in identifying PCOS and its reproductive symptoms.

MATERIALS AND METHODS: Using genome-wide association studies from various sources, including TwinsUK and UK Biobank, we developed PRS for total testosterone, bioavailable testosterone, dehydroepiandrosterone (DHEAS), free androgen index (FAI), estradiol, sex-hormone binding globulin (SHBG), follicle stimulating hormone (FSH), luteinizing hormone (LH), progesterone, prolactin, and anti-müllerian hormone (AMH). Each PRS was tested against a validated diagnosis of PCOS in 365 female cases and 6,996 controls of European ancestry using a multivariable logistic
regression model adjusted for age and genetic ancestry. Sensitivity analyses were applied to account for body mass index (BMI). PRS models were then examined against reproductive symptoms related to PCOS including infertility (168 cases and 25,175 controls), ovarian dysfunction (578 cases and 31,368 controls), and polycystic ovaries (476 cases and 31,368 controls). Cases were identified using billing codes from their medical records.

RESULTS: PRS for LH (OR = 0.84, p = 9.96x10^{-10}) was the top association for a PCOS diagnosis, followed by DHEASPRS (OR = 1.14, p = 0.02) and SHBGPRS (OR = 0.89, p = 0.04). Although LHPRS and DHEASPRS remained significant with PCOS after adjusting for BMI, the association with PRS for bioavailable testosterone (OR = 1.12, p = 0.02) and FAI (OR = 1.14, p = 0.05) improved. When reproductive symptoms were examined, PRS for bioavailable testosterone increased risk of polycystic ovaries and ovarian dysfunction while PRS for progesterone (OR = 1.20, p = 3.79x10^{-5}) and AMH (OR = 1.20, p = 7.54x10^{-5}) increased risk of infertility. After adjustment of BMI, AMHPRS showed a suggestive association with polycystic ovaries (OR = 1.10, p = 0.04) and ovarian dysfunction (OR = 1.09, p = 0.03).

CONCLUSIONS: PRS associations varied across symptoms, illustrating the differences in the underlying genetic risk of hormones that contribute to reproductive phenotypes. Anthropometric features can also cause variations in risk and warrants further investigation to understand the role of hormone genetic predisposition on different manifestations of reproductive dysfunction.

IMPACT STATEMENT: Genetic risk scores of reproductive hormones provide biological insight into disorders affected by ovarian dysfunction.

P-245 6:45 AM Tuesday, October 25, 2022

ESR1 HINGE REGION VARIANT IN A PATIENT WITH UNEXPLAINED INFERTILITY. Robert A. Roman, MD, Haijuo Liu, MD, Lynn Chorich, B.S, M.S., Yin Li, PhD, Janet E. Hall, MD, MS, Michael P. Diamond, MD, Kenneth S. Korach, PhD, Lawrence C. Layman, MD, Medical College of Georgia at Augusta University, Augusta, GA; 2Medical College of Georgia at Augusta University; 3National Institute of Environmental Health Sciences/NIH, Durham, NC; 4National Institute of Environmental Health Sciences/NIH.

OBJECTIVE: Estrogen is vital to human reproduction and acts primarily through two receptors: estrogen receptor alpha (ERα, encoded by ESR1) and estrogen receptor beta (ERβ, encoded by ESR2). Severe ESR1 variants lead to complete estrogen insensitivity and abnormal pubertal development, as evidenced by an ESR1 homozygous missense variant (p.Glu375His) in the ERα ligand-binding domain (LBD) with decreased estrogen response. We performed whole exome sequencing on 200 females with unexplained infertility to evaluate the potential role of ESR1 variants in this population. We identified 4 likely pathogenic ESR1 heterozygous missense variants confirmed by Sanger sequencing. Functional analysis of a variant in the LBD was associated with incomplete estrogen insensitivity. In this study, we performed in vitro functional analysis to determine whether a second variant, p.Arg271Cys, in the binding site of ESR1 signaling was pathogenic. MATERIALS AND METHODS: The p.Arg271Cys variant plasmid was constructed using site-directed mutagenesis, and confirmed by Sanger sequencing. An in vitro cell model was used to evaluate estrogen activity. HepG2 cells were transiently transfected with WT ESR1, p.Arg271Cys, or p.Glu375His plasmid, along with the Firefly estrogen response element (ERE) luciferase reporter (3X ERE TATA luc) and Renilla luciferase (pRL-TK luc) plasmids using the Effectene transfection protocol. Cells were treated with 17β-estradiol (0, 0.01, 0.1, 1, 10, and 100 nM). A dual luciferase reporter assay was used to compare relative Firefly and Renilla luciferase activity between WT ESR1, p.Arg271Cys, and p.Glu375His plasmids using a luminometer. Estrogen response curves were generated to calculate the area under the curve (AUC) and half maximal effective concentration (EC50) of WT, p.Arg271Cys, and p.Glu375His plasmids. A one-way ANOVA was used to compare the relative luciferase activity across WT and variant plasmids using GraphPad Prism v9. Differences were considered significant at p < 0.05.

RESULTS: One-way ANOVA found a statistically significant difference across WT ESR1, p.Arg271Cys, and p.Glu375His AUC (p < 0.01). Tukey’s test did not show a statistically significant difference in AUC between WT ESR1 and p.Arg271Cys (p = 0.71). WT ESR1 had a larger AUC compared to p.Glu375His (p < 0.001). The p.Arg271Cys variant plasmid also had a larger AUC compared to p.Glu375His (p < 0.01). The EC50 showed that the p.Arg271Cys variant had a 1.8-fold decrease in luciferase activity compared to WT. In comparison, the p.Glu375His variant had a 1.76-fold decrease in luciferase activity when compared to WT.

CONCLUSIONS: The ESR1 p.Arg271Cys hinge region variant does not significantly impair estrogen signaling in vitro. Potential deleterious mechanisms for the p.Arg271Cys variant could include reduced receptor expression, altered cellular localization, or dysregulation of steroid coactivators and/or corepressors, which are currently being analyzed.

IMPACT STATEMENT: In vitro functional analysis of ESR1 variants can assess their pathogenicity in patients with unexplained infertility.

P-246 6:45 AM Tuesday, October 25, 2022

ASSOCIATION OF FOLLICULAR FLUID KISSPEPTIN LEVELS AND OVARIAN RESPONSE TO STIMULATION. Erin Ahart, MD, Michael W. Wolfe, Ph.D., Courtney A. Marsh, MD, MPH University of Kansas Medical Center, Kansas City, KS.

OBJECTIVE: This study aims to evaluate the association of follicular fluid kisspeptin-54 (Kp-54) levels and response to controlled ovarian hyperstimulation in women undergoing egg retrieval for in vitro fertilization.

MATERIALS AND METHODS: Study participants included patients who underwent egg retrieval at the University of Kansas Center for Advanced Reproductive Medicine in 2019. Participants were separated into categories based on response to controlled ovarian hyperstimulation. Moderate responders were defined as having 6-15 oocytes; high responders were defined as having ≥ 20 oocytes. The follicular fluid from each study participant was evaluated for Kp-54 concentration using enzyme-linked immunosorbent assay (ELISA) and measured by optical density. Age, body mass index (BMI), gravidity, parity, live births per embryo transfer, and mean Kp-54 levels were compared between the moderate and high responder groups by T test. Correlations between clinical characteristics and Kp-54 level were evaluated using Pearson’s correlation coefficients.

RESULTS: The moderate responder (n = 23) and high responder (n = 22) groups showed no difference in age (p = 0.1253), BMI (p = 0.2978), gravidity (p = 0.5812), or parity (p = 0.3720). The mean Kp-54 level of the moderate responder group (n = 23) was 0.2077 ± 0.124. The mean Kp-54 level of the high responder group (n = 22) was 0.1905 ± 0.0896. These Kp-54 levels were found to be not statistically significant (p = 0.5971). There were no statistically significant correlations between Kp-54 level and age (r = -0.05872, p = 0.6983), BMI (r = -0.02957, p = 0.8507), gravidity (r = -0.13335, p = 0.4904), parity (r = -0.10447, p = 0.5896), or live births per embryo transfer (r = -0.21297, p = 0.1553). The moderate and high responder groups also showed no difference in the number of live births per embryo transfer (p = 0.8836).

CONCLUSIONS: In this study population, follicular fluid Kp-54 levels were not significantly different between low and high responders to ovarian hyperstimulation. These groups also showed no difference in the number of live births per embryo transfer.

IMPACT STATEMENT: This is the first study to our knowledge that compares the follicular fluid Kp-54 levels between low and high responders to ovarian hyperstimulation. Further research is needed to determine its efficacy as a fertility biomarker.

SUPPORT: N/A

P-247 6:45 AM Tuesday, October 25, 2022

REPRODUCTIVE AND METABOLIC EFFECTS OF A NUTRITIONAL INTERVENTION FOR KETOSIS INDUCTION ADDED TO IVF IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME. Cecilia Palafóx-Gómez, Mcs.1 Ginnia Milena Ortiz, MD.2 Ivan Madrazo, M.D.2 Leonardo M. Porchia, PhD,1 Esther Lopez-Bayghen, PhD1 1Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional (CINVESTAV-IPN), México City 07360, México., México, DF, Mexico; 2Ingenes Mexico, Mexico City, DF, Mexico; 3Instituto Regenera SC, México City 05320, México, Mexico.

OBJECTIVE: High-carbohydrate diets (glucotoxicity) and hyperinsulinaemia contribute to PCOS disturbances and infertility; a ketogenic diet could mitigate the harmful effects of insulin resistance (IR) and improve PCOS women’s fertility results when combined with IVF.

MATERIALS AND METHODS: 20 PCOS patients recruited from Ingenes Mexico signed informed consent. Inclusion criteria: failure in the previous IVF attempt, no previous treatment with Ovulation Induction and/or Clomiphene. Women were randomly stratified into two groups, the moderate responder group (n = 23) was 0.2077 ± 0.124. The mean Kp-54 level of the high responder group (n = 22) was 0.1905 ± 0.0896. These Kp-54 levels were found to be not statistically significant (p = 0.5971). There were no statistically significant correlations between Kp-54 level and age (r = -0.05872, p = 0.6983), BMI (r = -0.02957, p = 0.8507), gravidity (r = -0.13335, p = 0.4904), parity (r = -0.10447, p = 0.5896), or live births per embryo transfer (r = -0.21297, p = 0.1553). The moderate and high responder groups also showed no difference in the number of live births per embryo transfer (p = 0.8836).

CONCLUSIONS: In this study population, follicular fluid Kp-54 levels were not significantly different between low and high responders to ovarian hyperstimulation. These groups also showed no difference in the number of live births per embryo transfer.

IMPACT STATEMENT: This is the first study to our knowledge that compares the follicular fluid Kp-54 levels between low and high responders to ovarian hyperstimulation. Further research is needed to determine its efficacy as a fertility biomarker.

SUPPORT: N/A
pressure systolic ≥ 130, and diastolic ≥ 85 mm Hg or fasting glucose ≥ 100 mg/dL); exclusion: previous endocrine pathologies. Patients were instructed to follow a ketogenic diet, daily consumption of 50g of total carbohydrates, 1.5 grams of protein per kg of ideal body weight, adjusting with fat, 15, 25, and 30g of total carbohydrates for OB, NW and OBD, respectively. Nutritional education (video) focused on controlling glucose load and avoiding processed food, starches, juices, bread, sweets, sugared beverages, and carbohydrate-rich food. Every third day, the patient reported all food consumption to the dietician to calculate and correct macronutrients consumption. The presence of ketones in urine was auto-monitored twice a week with reactive strips. Once ketosis and correction of IR in more than 50% were achieved, patients proceeded to IVF. Pregnancy achievement was recorded, and the reproductive results were analyzed and compared against the previous cycle.

RESULTS: 20 patients included in the study were closely followed and constantly advised and monitored throughout the nutritional intervention of five months (average); the decrease in carbohydrate consumption was consistently lowered from an average of 194 g/day to less than 50 g/day (measured by a dietitian). Weight loss ranged from 4 to 14%, with an average of 10% (+/-1%, SE). Urine ketones appeared in all patients in nine days (average); positive ketosis was considered at 40 mg/dL and was recorded in all patients following the nutritional program (15 to 160 mg/dL). We found an average of 60% +/- 12.19 decrease in HOMA-IR values (20.7 to 4.7 as maximal change). Metabolic parameters improve in all patients being the Tri-glyceride/HDL-C ratio the most consistent change (1.69 to 1.08 on average).

Considering the implantation rate in the previous cycle as zero, after the nutritional intervention, 90% of treated patients achieved biochemical pregnancy (beta-hCG positive), and 20% had an early loss; 70% progressed to clinical pregnancy, 57% presented an ongoing pregnancy, 43% delivered a live newborn.

CONCLUSIONS: Through a carefully followed restriction in the consumption of carbohydrates as the only additional intervention, it is possible to improve insulin resistance, decrease the waist-to-height and triglycerides/HDL-C ratio and achieve ongoing pregnancy in 70% of the PCOS cases.

IMPACT STATEMENT: In IR-PCOS patients, pregnancy achievement through in vitro fertilization can be enhanced by over 70%, focusing on lowering insulin resistance via ketosis induction.

SUPPORT: None to declare

P-248 6:45 AM Tuesday, October 25, 2022

DIET SUPPLEMENTATION RESTORES OBESITY-INDUCED MITOCHONDRIAL DYSFUNCTION IN GRANULOSA CELLS FROM THE EQUINE PREOVULATORY FOLLICLE. Kyle Fresa, B.S., 1 Giovana Di Donato Catandi, DVM, 2 Adam J. Chicco, PhD, 2 Elaine M. Carnevale, DVM, PhD. 1Fort Collins, CO; 2Colorado State University.

OBJECTIVE: Determine the potential of dietary supplementation to attenuate adiposity-associated disturbances of mitochondrial function in the granulosa cells (GC) of preovulatory follicles in a mare model.

MATERIALS AND METHODS: Mares were assigned to groups: Normal Weight (NW, n=6, 17.8±1.8 yr, grass/alfalfa hay), Obese (OB, n=7, 18.6±2.5 yr, grass/alfalfa + corn/oats), and Obese + Dietary Supplement (OBD, n=6, 18.1±1.3 yr, grass/alfalfa + corn/oats + a proprietary blend of nutrients, including vitamins, minerals, probiotics, antioxidants, chromium and L-carnitine). After ≥ 6 wk, obesity was confirmed by adiposity markers, including percent of body fat, GCs were collected from dominant, follicular-phase follicles after maturation induction and prior to ovulation. Using the Oroboros Oxygraph-2k high-resolution respirometer, oxygen consumption rate (aerobic metabolism) and reactive oxygen species (ROS) production were determined in fresh, intact GCs under basal conditions (fueled only by endogenous substrates). Isolated protein samples were used for western blots to quantify expression of Complexes I-V of the electron transport system (ETS) and antioxidant enzymes, including cytosolic CuZn superoxide dismutase (SOD1), mitochondrial Mn superoxide dismutase (SOD2), and glutathione peroxidase 1 (GPX1). Data were compared using one-way ANOVA with post-hoc Tukey’s multiple comparison tests.

RESULTS: Oxygen consumption rates did not differ among groups. ROS production was higher in OB than NW and OBD (p<0.0005). Total protein expression of Complexes I-V was lower in OB compared to NW and OBD (p<0.0005). However, the ratio of Complexes I+III (major ROS producing sites of ETS) to Complexes II, IV and V was higher (p<0.004) in OB than NW and OBD. GPX1 expression was higher (p<0.04) in NW than OB and OBD. SOD2 expression was higher (p<0.005) in NW and OB than OBD. SOD1 was not different among groups.

CONCLUSIONS: GCs from obese mares produce more ROS, possibly due to altered ETS organization and reduced antioxidant enzyme expression. However, ROS production in GCs was mitigated in obese mares with dietary supplementation. Expression of SOD2 was decreased in the GCs of obese mares fed the diet supplementation (OBD), suggesting that the dietary supplement may be mitigating production of oxidants and/or supplying exogenous antioxidant molecules that lessen demand for endogenous antioxidant enzyme expression.

IMPACT STATEMENT: Obesity results in insulin dysregulation, reproductive alterations, and offspring health concerns in mares and women. The mare is a monogastric animal with similar follicular growth patterns as women, providing a promising animal model. In the present study, maternal obesity affected the metabolic function of GCs in the preovulatory follicle, and short-term dietary supplementation was used to mitigate ROS production by GCs in vivo. The study demonstrates methodology to assess effects of maternal factors and diet on GC mitochondrial function. Additional studies are being conducted to further define the impact of obesity on GCs, including using similar methodology with human GCs.

SUPPORT: USDA NIFA Animal Health and Disease No. 1026913

The Cecil and Irene Hylton Foundation

Abney Foundation Scholarship

P-249 6:45 AM Tuesday, October 25, 2022

IMPACT OF COVID-19 INFECTION AND mRNA VACCINATION ON MENSTRUAL CYTOKINE PROFILES. Zainub Dhanani, AB, 1 Norma Jimenez Ramirez, BS, 2 Jennifer Nguyen, BS, 3 Yael Rosenberg Hasson, PhD. 1 Sara Naseri, MD. 1 Bertha Chen, MD. 1 Ryan Kellogg, PhD 2 Stanford University School of Medicine, Stanford, CA; 3Stanford School of Medicine, Stanford, CA; 4Stanford University, Stanford, CA.

OBJECTIVE: Reports have emerged on changes in length and amount of menstrual flow after COVID-19 mRNA vaccination.1 While there is documentation of serum immune marker elevations with COVID-19 infection,2 similar menstrual symptom changes after infection have not been reported. To evaluate this discrepancy in symptoms, we examined differences in menstrual cytokine expression in women who have had COVID-19 and/or mRNA vaccination.

MATERIALS AND METHODS: Menstrual blood from the first heavy day of menses was collected using a modified menstrual pad with an embedded dried blood sample collection strip. Women 20-40 years old with no gynecologic conditions, use of intrauterine birth control or smoking history, were included. Samples were collected from four groups: 1) controls (COV-/Vax-), 2) vaccinated with no known COVID-19 (COV-/Vax+), 3) unvaccinated with a history of COVID-19 (COV+/Vax-), and 4) vaccinated with a history of COVID-19 (COV+/Vax+). Samples were extracted and run on a H48 plex immune assay and analyzed for cytokine expression.

RESULTS: We found notable trends in the expression of nine cytokines when compared to cytokines from control women with no infection or vaccination (table below). Notably, vaccination-only is associated with upregulation of EGF, IL-1ra, IL-2, MDC, and MIP-1b and downregulation of IL-1b and IL-6. Cov+ patients shared similar cytokine profiles whether they received the vaccine or not, with the exception of EGF, IL-6 and VEGF.

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CONCLUSION: Obesity results in insulin dysregulation, reproductive alterations, and offspring health concerns in mares and women. The mare is a monogastric animal with similar follicular growth patterns as women, providing a promising animal model. In the present study, maternal obesity affected the metabolic function of GCs in the preovulatory follicle, and short-term dietary supplementation was used to mitigate ROS production by GCs in vivo. The study demonstrates methodology to assess effects of maternal factors and diet on GC mitochondrial function. Additional studies are being conducted to further define the impact of obesity on GCs, including using similar methodology with human GCs.
CONCLUSIONS: Both COVID-19 infection-only and vaccination-only groups presented with differential cytokine profiles compared to the control (COV-Vax-) group. The cytokine profile of these two groups showed similar trends in five out of the nine cytokines that were differentially expressed suggesting that the vaccine may be inducing COVID-like immune responses that call for caution in menstruall blood. Increased expression of EGF, a cytokine involved in the regulation of endometrial angiogenesis, in the vaccinated groups may be associated with the transient changes in quality of menstrual flow.

IMPACT STATEMENT: The differential expression of several cytokines noted between healthy individuals and those infected with or vaccinated against COVID-19 may offer further insight into the inflammatory reactions followed by infection detection and the menstrual changes reported by women after vaccination. Further, menstrual cytokine tracking may offer a non-invasive method of monitoring vaccine response and COVID infection rates in the future.

REFERENCES:

P-250 6:45 AM Tuesday, October 25, 2022

CURRENT PRACTICES IN INFERTILITY AND FERTILITY PRESERVATION COUNSELING AMONG PATIENTS WITH TURNER SYNDROME.
Gabriela Beroukhim, M.D.1 Rama Kastury, D.O.2 Kerri A. Davidson, B.A.3 Jenna Bergmann, B.A.3 Alla Vash-Margita, MD1 New Haven, CT; 1Yale School of Medicine, New Haven, CT; 2Yale School of Medicine; 3Fairfield, CT.

OBJECTIVE: To determine current practices in counseling on infertility and fertility preservation (FP) among patients with Turner syndrome (TS) at a large academic institution and to examine patient or provider characteristics associated with delivery of counseling and pursuit of oocyte cryopreservation (OC) or in vitro fertilization (IVF).

MATERIALS AND METHODS: This retrospective medical record review, approved by the Institutional Review Board, included biologically female patients with classic or mosaic TS who were evaluated from 1997 to 2020. Inclusion criteria were ages 0-33 years and documented karyotype 45,X or 46,XX/45,X. Exclusion criteria included presence of Y chromosome or insufficient data. Variables such as demographics, comorbidities, and type of provider and specialty were collected. Descriptive statistics, t-test and Chi-square test were applied. Prism-Graphpad Version 9.3.1 was used for the analysis.

RESULTS: Of 108 included patients, 43 (39.81%) were classified as mosaic TS and 65 (60.19%) as classical TS. The mean age was 18.57 ± 9.34 years. Patients with classical TS were more likely to have cardiac anomalies (46.15% vs 13.95%, p = 0.0007), hypertension (28.13% vs 6.98%, p = 0.0067), and osteopetrosis/osteopenia (21.31% vs 4.65%, p = 0.022). There was no significant difference in age, race, or incidence of short stature, renal anomaly, hypothyroidism, celiac disease, sensorineural hearing loss, depression and anxiety between the mosaic and classical TS population. Patients who were counseled about FP were more likely to pursue OC or IVF (20.00% vs 0%, p = 0.0005). Age of receipt of counseling and pursuit of OC ranged from 13 to 25 years. Counseling was provided by various providers: pediatric and adolescent gynecology, reproductive endocrinology and infertility (REI), genetics, pediatric endocrinology, pediatrics, gynecology, and endocrinology. A higher number of mosaic TS patients received counseling compared to classical TS (43.95% vs 22.03%, p = 0.027). Other factors, such as race, ethnicity, and cardiac anomalies, were not associated with receipt of counseling. Only 30 (27.78%) patients received infertility or FP counseling, of which 6 (5.56%) pursued OC or IVF. None of the six patients had cardiac anomalies. All OC and IVF occurred in or after 2017, which is notable as the Disorders of Sex Development (DSD) Program was implemented at our institution. AMH, FSH, and number of oocytes retrieved ranged from 0.23-3.06 ng/mL, 0.84-9.11 IU/mL, and 0-16 oocytes (mean 5.66), respectively.

CONCLUSIONS: Our findings indicate that few TS patients receive infertility or FP counseling and even fewer pursue OC or IVF.

IMPACT STATEMENT: TS patients are at high risk of infertility and pregnancy-related morbidity and mortality. Relevant and timely infertility and FP counseling should be routinely provided to all TS patients. Our large cohort study highlights the need for and implementation of system-wide measures to standardize the content and delivery of counseling to TS patients including development of the multidisciplinary approach such as DSD Program.

E-POSTER ABSTRACT SESSION: T4

P-251 6:45 AM Tuesday, October 25, 2022

DETECTION OF THE OVULATION TIME VIA HORMONE LEVELS IN THE PERIPHERAL BLOOD OF THE SUBFERTILE WOMEN WITH REGULAR MENSTRUAL CYCLE.
Turgut Aydin, MD,1 2 3 Nadiye Koroglu, MD1 Nazli Albayrak, MD1 Mert Akin Akin Insel, MSc1 4Acibadem MAA University; 2Acibadem MAA University Atakent Hospital; 3Acibadem MAA University Atakent Hospital, Istanbul, Turkey; 3Besiktas, Istanbul, Turkey; 5Yildiz Technical University, Istanbul, Turkey.

OBJECTIVE: In order to detect the ovulatory disorders, ovulation physiology is needed to be fully understood, and the cut-off values related to the changes in hormone levels are to be defined. This study aimed to define the cut-off values showing the ovulation with serial evaluation of the serum hormone levels of progesterone (P), estradiol (E2), and luteinizing hormone (LH), besides ultrasonographic assessments of the subfertile women having regular menstrual cycle.

MATERIALS AND METHODS: In this prospective observational study, 50 subfertile women aged between 18-40, having regular menstruation with a cycle length between 24-38 days, and women accepting blood tests with full attendance to the follow-up visits are included. All participants are provided informed consent. Patients who are fully attended the follow-ups with no ovulation are excluded. Participants are invited for transvaginal ultrasonographic examination (TVUE) and peripheral blood test on the second day of the menstruation and two days prior to the estimated ovulation day, and after the ovulation in order to detect the corpus luteum. During the evaluation, and the analysis of the data, follicle size, E2, LH, P, and endometrial thickness are taken into account.

RESULTS: 50 participants with mean age 31.3±4.2 years underwent serial TVUE, and serial analysis of hormone levels in blood. Mean cycle length was 28.8±1.6 days, and the mean follicle size on the ovulation day was measured as 18.6±1.5 mm in size. The effect of P levels on determining the ovulation day was investigated. It was observed that the data shows an exponential trend, hence an exponential regression was carried out to construct the mathematical model which relates days until and after ovulation with serial evaluation of the P levels of each patient. The R²; the sum of squared estimate of errors (SSE), and root-mean-square error (RMSE) values of the constructed model was evaluated as 0.99, 0.61, and 0.35, respectively, which show that the model is highly sufficient in estimating the P levels. P levels were measured as 0.57±0.19 ug/L two days prior to the ovulation, 0.79±0.20 ug/L one day prior to the ovulation, 1.31±0.31 ug/L on the ovulation day, 2.10±0.48 the day after the ovulation, 4.45±2.36 ug/L two days after the ovulation, and 12.91±6.01 ug/L on the 5th day after the ovulation which can be scheduled for the blastocyst transfer for the natural frozen thaw cycles.

CONCLUSIONS: Progesterone has a particular increasing pattern in menstrual cycle which enables the prediction of the ovulation day in order to schedule the embryo transfer day in natural frozen thaw cycles.

IMPACT STATEMENT: This model may be utilized to determine the ovulation day for patient directly from their P levels, which would assist the physician in assigning appointments accordingly and avoid unnecessary appointments.

P-252 6:45 AM Tuesday, October 25, 2022

LUTEINIZING HORMONE SUPPLEMENTATION WITH HUMAN MENOPAUSAL GONADOTROPIN VERSUS LOW-DOSE HUMAN CHORIONIC GONADOTROPIN DURING STIMULATION DOES NOT AFFECT PREGNANCY OUTCOMES AFTER FRESH EMBRYO TRANSFER.
Linnea Fischler, B.A.1 Rebecca K. Chung, MD2 Sung Tae Kim, PhD, HCLD,3 Rebecca Flyckt, MD3 Rachel S. Weinerman, MD 2 1Cleveland, OH; 2University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH; 3Cleveland Clinic Foundation, Cleveland, OH.

REFERENCES:
OBJECTIVE: To determine whether Luteinizing hormone (LH) supplementation with human Menopausal Gonadotropin (hMG) compared to low-dose human Chorionic Gonadotropin (LD-hCG) during controlled ovarian stimulation (COS) affects pregnancy outcomes after fresh embryo transfer (FET).

MATERIALS AND METHODS: Patients undergoing fresh ET after standard long or antagonist protocols supplemented with either hMG (75-200 IU) or LD-hCG (50-100 IU) during COS from 2017-2021 at our academic center were included. The primary outcome was rate of live birth (LB) or ongoing clinical pregnancy (CP). Additional pregnancy outcomes included biochemical pregnancy (Biochem) and clinical miscarriage (SAB). We also assessed the number mature oocytes, 2pm embryos, and high-quality blastocysts (grade ≥3BB) per cycle. Demographic parameters included maternal age at transfer, BMI, and AMH. Cycle characteristics included maximum daily FSH dose, number of days of COS, and estradiol level (E2) at trigger.

Statistical analysis was performed with T-tests, chi square, multiple linear regression, and multiple logistic regression. Our regression analysis controlled for maternal age, BMI, and AMH.

RESULTS: 216 cycles were analyzed. Patients in the hMG group were slightly older (34.5 ± 4.0 vs 33.1 ± 3.9, p = 0.01) but had similar mean BMI (28.2 ± 7.1 vs 28.6 ± 6.7, p = ns) and AMH values (4.3 ± 3.2 vs 4.4 ± 3.5, p = ns) compared to LD-hCG patients. Cycles with hMG (n = 121) vs LDhCG (n = 95) had a higher mean maximum daily FSH dose (290 ± 96 vs 223 ± 71, p < 0.001), higher mean number of days of COS (9.1 ± 8 vs 7.1 ± 4.4, p = 0.005), and lower mean E2 (2033 ± 846 vs 2719 ± 801, p < 0.0001). However, the number of mature oocytes and number of 2pm embryos did not differ between hMG and LD-hCG (9.1 ± 4.3 vs 9.5 ± 3.4 and 7.0 ± 3.9 vs 7.2 ± 3.3 respectively, p = ns). The number of high-quality blasts also did not differ for hMG vs LD-hCG (2.5 ± 2.8 vs 2.6 ± 2.5, p = 0.281). hMG compared to LD-hCG did not affect rates of CP/LB (42% vs 50%, p = Biochem (8.0% vs 2.1%, p = ns), or SAB (11.6% vs 13.1%, p = ns) per transfer.

Multiple logistic regression showed no association between hMG or LD-hCG and CP/LB rate for agonist (OR = 0.267, 95% CI = 0.65 - 1.18), antagonist (OR = 0.868, 95% CI = 0.461 - 1.63), or both protocols combined (OR = 1.28; 95% CI = 0.73 - 2.2). Multiple linear regression showed no association between hMG or LD-hCG and number of high-quality blasts for agonist, antagonist, or both protocols combined.

CONCLUSIONS: In fresh ET, there was no difference in oocyte or blastocyst yield and no difference in LB, Biochem, or SAB rates when patients’ stimulations were supplemented with hMG or LD-hCG in either standard long or antagonist cycles.

IMPACT STATEMENT: LH supplementation has been shown to improve success in IVF. This study demonstrates that there is flexibility in dosing regimens for supplemental LH that may take into account patient or physician preferences, cost concerns, as oocyte yield, embryo quality, and pregnancy outcomes for hMG vs LD-hCG supplementation in fresh ET were not significantly different.

P-253 6:45 AM Tuesday, October 25, 2022

WHAT IS THE IDEAL LETROZOLE REGIMEN FOR OVULATION INDUCTION IN WOMEN WITH POLYCYSTIC OVARY SYNDROME? Rachel S. Mandelbaum, MD, Ravi Agarwal, MD, Caroline Violette, MD, Zachary Anderson, MD, Samuel J. F. Melville, BS, Lynda K. Mcginnis, PHD,1 Jacqueline Ho, M.D,2 Sharon A. Winer, M.D., M.P.H.,1 Donna Shoupe, M.D, M.P.H, 1 Donna Shoupe, MD, 1 Koji Matsuo, MD, PhD, 1ern California, Los Angeles, CA; 2Keck School of Medicine, University of California, Los Angeles, CA; 3Keck School of Medicine, University of Southern California, Los Angeles, CA; 4Keck School of Medicine, University of California, Los Angeles, CA.

OBJECTIVE: To determine the optimal letrozole regimen for ovulation induction (OI) in women with polycystic ovary syndrome (PCOS)

MATERIALS AND METHODS: This is a retrospective cohort study conducted at a single institution from 2015 – 2022. Four letrozole regimens were compared: 2.5mg for 5 days, 2.5mg for 10 days, 5mg for 5 days, and 5mg for 10 days. Response to the index letrozole regimen was determined by follicle size >14mm on ultrasound, positive ovulation predictor kit, mid-luteal progesterone >3 ng/dL, or positive pregnancy test. If there was no response, letrozole was re-prescribed with a higher dose or longer duration sequentially until a response was observed. Primary outcomes included response to the initial regimen, multifollicular development, and clinical pregnancy rate (CPR), which were analyzed with a multivariable binary logistic regression adjusting for age, gravidity, body mass index (BMI), diabetes, hypertension, and hyperlipidemia.

RESULTS: Of 49 PCOS patients included in the study who underwent 189 OI cycles, the mean age was 30.9 years (standard deviation (SD) 3.6) and BMI was 32.1 (SD 4.0). Distribution of patients by index letrozole regimen and primary outcomes are shown in Table 1. 2.5mg for 5 days was most frequently used (32.8%) but had the lowest response rate (45.2% vs. 73.7-88.2%). Odds of a response were significantly higher with the 5mg dose and/or a 10-day duration (Table 1). There was no significant difference in response between groups 2, 3 and 4 (P > 0.05). In all groups, 88.9-100% of patients ovulated eventually after dose adjustments (P < 0.05), yet those who received 5mg and/or 10 days initially achieved response sooner. CPR was 15.7%; this did not differ by group, and there were no multiple gestations.

CONCLUSIONS: This study showed improved response rates with letrozole 5mg and an extended 10-day regimen. This may shorten time to ovulation and potentially to pregnancy by allowing patients to complete more OI cycles as well as decrease direct costs for patients.

IMPACT STATEMENT: Letrozole 2.5mg for 5 days for OI is associated with a lower response rate, thus there may be benefit to starting at a higher dose or for a longer duration without increasing rates of multifollicular development.

SUPPORT: none

P-255 6:45 AM Tuesday, October 25, 2022

CORRELATION OF BASAL SERUM AMH VALUES OF PCOS PATIENTS TO OVARIAN RESPONSE FOLLOWING STIMULATION WITH OVULATION INDUCTION AGENT CLOMIPHENE CITRATE - A PROSPECTIVE COHORT STUDY. Pilibani Sarkar Fellow. Reproductive Endocrinology and Infertility, PGIMER, Chandigarh, India.

OBJECTIVE: To correlate basal serum AMH values of PCOS patients with ovarian response, following stimulation with oral ovulation induction agent clomiphene citrate.

MATERIALS AND METHODS: Study Design - Prospective observational cohort study

Sample Size - 87 patients

Setting - Department of Obstetrics and Gynecology, Post Graduate Institute of Medical Education & Research, Chandigarh, India

Duration - 6 months (August 2021 - January 2022)

Inclusion Criteria -
- Diagnosed PCOS (using Rotterdam criteria)
- No previous pelvic surgeries for infertility
- Husband semen analysis (Normal)
- Willingness to participate

Exclusion Criteria -
- Previous history of established endometriosis & tuberculosis
- Other causes of anovulation like hypothryoidism, hyperprolacteinemia, Cushing’s disease & Type 2 Diabetes

Method - Basal serum AMH, FSH, LH, Prl, DHEAS, 17-OHP, Total testosterone, SHBG levels were done on Day 2/3 of spontaneous or progesterin induced withdrawal bleeding. Serum AMH Levels assayed using electrochemiluminescence assay(ECLIA)(E-2020,Roche Diagnostics Basel, Switzerland). Baseline TVS done for AFC, Ovarian volume, uterine size, endometrial cavity. Patients underwent ovulation induction with clomiphene for up to 3 cycles maximum dose 150mg. Folliculometry was done on Day 11, 15 & 18 for response.

RESULTS: 87 anovulatory PCOS women presenting with infertility underwent a total of 205 cycles of ovulation induction with clomiphene citrate. Ovulation rate per cycle was 79.51%. 35(40.2%) ovulated with 50 mg dose, 24(26.7%) ovulated with 100 mg and 14(16.1%) with 150 mg dose of clomiphene. 14(16.1%) patients did not respond to max dose of 150 mg (no response). Serum AMH level in the ‘no response’ group was significantly higher (p < 0.047) than the response group. Clinical pregnancy rate, ectopic pregnancy rate & miscarriage rate was 17.24%, 1.41 % & 3.4% respectively.

Women who ovulated with clomiphene citrate had lower mean AMH values (6.69mg/ml, 7.53mg/ml, 8.70mg/ml corresponding to 50mg, 100mg and 150mg dose of clomiphene respectively) compared to women who failed to show any ovarian response mean serum AMH value (11.74mg/ml). There was a gradient increase in mean serum AMH values across the increasing dose of clomiphene citrate to achieve ovulation. AMH also positively correlated with AFC, ovarian volume and LH level (p
<0.01) while negatively correlating with age, BMI (p <0.05) and waist circumference (p <0.01).

CONCLUSIONS: Higher levels of serum AMH in PCOS women required higher doses of oral ovulagen clomiphene citrate. Patients with ultra high levels of AMH may require adjuvant therapy.

IMPACT STATEMENT: Establishing predictive cutoff values for AMH with ovarian response will decrease time to pregnancy interval in PCOS anovulatory infertility by earlier institution of higher dose of oral ovulagens or need for adjuvant gonadotropins.

P-257 6:45 AM Tuesday, October 25, 2022
IS TRILAMINAR ENOUGH? COMPARING FET IMPLANTATION RATES OF PCOS AND NON-PCOS PATIENTS WITH FAVORABLE ENDOMETRIAL LINING. Kristina Hrvojevic, MD,1 Tyler Soy, MA,1 Roohi Jeelani, MD,1 Angeline Beltsos, MD,2 Julie Rhee, M.D.1 1Vios Fertility Institute, Chicago, IL; 2Kindbody/Vios Fertility Institute Chicago, Chicago, IL.

OBJECTIVE: To determine if there is a difference in implantation success rate (defined by positive initial beta hCG after embryo transfer) in frozen embryo transfers, between PCOS and non-PCOS patients with trilaminar endometrial linings.

MATERIALS AND METHODS: A retrospective chart review at a private, fertility clinic was conducted. Patients who underwent FET with a previously given diagnosis of PCOS, as well as those without a PCOS diagnosis were included. An optimal endometrial lining was determined based on ultrasound findings of an endometrial lining thickness between 7-14 mm with a trilaminar appearance at time of progesterone initiation. Implantation success was defined as a positive beta hCG obtained 10 days after embryo transfer. Baseline characteristics were evaluated and a two sample proportion t-test was used to analyze the data to determine if there was a statistically significant difference in the primary outcome between the two groups.

RESULTS: A total of 105 patients with an optimal endometrial lining who underwent FET were analyzed: 29 in the PCOS group and 76 in the non-PCOS group. The PCOS group had an implantation success rate of 79%, compared to 50% in the non-PCOS group. However, there was no statistically significant difference between the two groups in the primary outcome when accounting for population variance (p >0.05).

CONCLUSIONS: While it is known that implantation rates of PCOS patients are lower than patients without PCOS, the etiology of this finding still remains unclear. There are likely many contributing factors, including altered gene expression due to elevated testosterone levels and overall altered endocrine environment within the endometrial tissue. Our preliminary results indicate that there is no significant difference in successful implantation rates between PCOS and non-PCOS patients even when a lining appears favorable, as defined by a trilaminar appearance. Given the trilaminar appearance is an indicator of estrogen exposure to the lining, this demonstrates that the standard ways of analyzing an optimal lining may not be the most important factors when determining implantation success in PCOS patients. Further research is needed to determine if other pathological processes may be present within the endometrium of PCOS patients despite a visually favorable endometrial lining or only in those with an unfavorable lining. This may shed possible therapeutic targets in order to improve pregnancy outcomes in patients with PCOS. While a limitation of our study is the sample size, further data is being collected to allow analysis of a larger sample size.

IMPACT STATEMENT: Further research is needed to determine if other pathological processes may be present within the endometrium of PCOS patients despite a visually favorable endometrial lining or only in those with an unfavorable lining. This may shed possible therapeutic targets in order to improve pregnancy outcomes in patients with PCOS.

SUPPORT: None.

REFERENCES:

P-258 6:45 AM Tuesday, October 25, 2022
PREDICTIVE VALUES OF PROGESTERONE/ESTRA DIOL RATIO ON INTRAUTERINE INSEMINATION OUTCOMES. Nabil Sayme Dr. med,1 Thomas Krebs, Dipl.-Biol.,1 Dieter H. A. Maas, Prof. Dr. med.,1 Marija Kljajic, Master of Biology Science2 Team Kinderwunsch Hannover, Hannover, Germany;2Saarland University Medical Center, Homburg, Germany.

OBJECTIVE: During the luteal phase, progesterone is extremely important for creating decidualization changes required for implantation and pregnancy progress. The correlation between progesterone and estradiol was evaluated in several studies in different populations. The primary objective of this study was to investigate whether there is a correlation between serum progesterone/estradiol (P/E2) hormone ratio, 7 days after Intrauterine insemination (IUI) and the clinical pregnancy.

MATERIALS AND METHODS: We performed a retrospective analysis of data collected between February 2018 and August 2021, including 402 IUI cycles. Patients aged from 22 to 40 years with a BMI of 23.2 ± 3.6kg/m² were subjected to individually adjusted daily doses of 50-100 IU recombinant FSH. Cycles were triggered with recombinant-HCG (Ovitrelle) when the dominant follicle became 18 mm in diameter. Serum progesterone and estradiol levels were measured 7 days after IUI, always between 8 and 10 am, to limit the diurnal variation of hormones. β-HCG was tested on the 15th day of the post insemination day. The P/E2 ratio was calculated as [P (ng/mL) * 1000/E2 (pg/mL)]. Between-group comparisons were conducted with the Mann-Whitney U test. RESULTS: There were 54 (20.9%) women with a positive pregnancy test following controlled ovarian stimulation and the IUI cycle. Progesterone/Estradiol ratio values were compared within groups with and without positive pregnancy tests. The comparison revealed significantly increased values of the P/E2 ratio in the positive pregnancy group [148.47 (35.53-408.77 vs 132.87(0.64-386.81); retrospectively p<0.05]. What is more, logistic regression analysis confirmed the positive effect of the P/E2 ratio on pregnancy rate (p<0.05).

P-259 9:00 AM Tuesday, October 25, 2022
EVALUATION OF PROGESTERONE AND ESTRADIOL LEVELS DURING THE INTRAVENOUS INSEMINATION (IVI) CYCLE: A SYSTEMATIC REVIEW AND META-ANALYSIS. Valentina Pati, MD1,2,3,4,5, Eunice S Beraldo, MD, PhD2,3,4,5, Matheus B S Borges, MD1,2,3,4,5, Roberto M Bressan, MD1,2,3,4,5, Maria F K de Souza, MD, PhD1,2,3,4,5, 1Department of Biometry, Brazilian National Cancer Institute, Brasília, Brazil; 2School of Medicine, University of Brasília, Brasília, Brazil; 3Department of Obstetrics and Gynecology, Brazilian National Cancer Institute, Brasília, Brazil; 4Department of Biometry, School of Medicine, University of Brasília, Brasília, Brazil; 5Department of Biometry, Brazilian National Cancer Institute, Brasília, Brazil.
CONCLUSIONS: The increased P/E2 ratios seven days after insemination were found to be efficient predictive markers of cycle outcome. Further studies, including different stimulation protocols and patients with different infertility diagnoses, are needed in order to confirm the effect of the P/E2 ratio.

IMPACT STATEMENT: Based on the obtained results in the presented research, P/E2 ratio seven days after intrauterine insemination can be utilized as one of the clinical tests to predict the occurrence of clinical pregnancies.

SUPPORT: N/A

P-259 6:45 AM Tuesday, October 25, 2022

THE EFFECTIVENESS OF ADDITIONAL INTRAMUSCULAR LUTEAL PROGESTERONE SUPPORT IN WOMEN WITH ENDOMETRIAL CONTRACTILITY ON ULTRASOUND THE DAY PRIOR TO PROGRAMMED FROZEN EMBRYO TRANSFER. Jayapriya Jayakumaran, MD, Aashishtwariya Gulani, BS, Daniel Vesco, DO, Lauren Stadtmuhr, MD, PhD, Mark P. Trollese, MD, FACOG, FACS, FACE, Ponie Veda, FL; Fertility CARE: The IVF Center, Orlando, FL; Fertility CARE: The IVF Center, Winter Park, FL; Fertility CARE: The IVF Center; Professor, University of Central Florida College of Medicine, Orlando, FL.

OBJECTIVE: Increased contractility at the time of embryo transfer (ET) adversely affects embryo implantation and pregnancy rates in IVF (1). It has been postulated that the high uterine contraction frequency seen on the day of ET resulted from an insufficient response to the uteroleaxing properties of progesterone (2). Therefore, we decided to investigate the effectiveness of increasing luteal progesterone support based on endometrial contractility (EC) prior to programmed frozen embryo transfer (FET).

MATERIALS AND METHODS: This is a retrospective cohort study of all ART procedures at Fertility Care: The IVF Center from February 2018 to January 2021 at an academic private practice. Inclusion criteria were women under the age of 40 years, normal uterine cavity evaluation within 6 months, transfer of 1 or 2 good quality blastocysts compliant with ASRM guidelines, and a minimum endometrial thickness of 7mm. Women who received a combination of PIO and vaginal progesterone or only vaginal progesterone for luteal support were excluded from the analysis. Hormonal luteal support consisted of vaginal estradiol 2mg twice daily and 75 mg of intramuscular (IM) progesterone in oil daily. All women underwent a transvaginal ultrasound for assessment of endometrial contractions (EC) followed by next day embryo transfer, at the blastocyst stage occurring at 132±3 hours of PIO. A positive EC was defined as three or more waves visualized during a one-minute observation period on ultrasound. When positive EC was present, the woman was instructed to administer a second IM dose of 75 mg PIO in the evening prior to embryo transfer followed by resumption of a daily PRO dose beginning the evening of embryo transfer. The study cohort was divided into two groups: Group 1 had positive EC and received additional luteal progesterone support whereas Group 2 did not have significant EC and received standard luteal support. The primary outcome was live birth rates per cycle (LBR). Continuous variables were presented with mean ± SD. Categorical variables were compared between groups with Fisher’s exact test.

RESULTS: 425 women were included in the study (Group 1 = 191, Group 2 = 234). Groups were similar by age (35.46 ± 35.39, p = 0.8) and BMI (25.6 vs 26.3, p = 0.3). There was no statistically significant difference in the progesterone levels (32 ± 31.5, p = 0.6), endometrial thickness (10 mm vs 9.9 mm, p = 0.74), Preimplantation Genetic Testing (18% vs 20.4%, p = 0.61), and mean number of embryos transferred (1.19 vs 1.2, p = 0.8). Clinical pregnancy rates (68.1% vs 67.9%, p = 0.98), LBR (58.6% vs 55.1%, p = 0.46) and miscarriage rates (9.4% vs 12.8%, p = 0.27) were similar between groups. In patients undergoing programmed FET cycles with positive EC on the day prior to embryo transfer, additional supplementation with a 75 mg IM PIO dose results in LBR comparable to those of patients without significant endometrial contractility.

IMPACT STATEMENT: Our results suggest that additional intramuscular luteal progesterone support the day before embryo transfer nullifies the negative impact of positive EC resulting in no impairment on pregnancy outcomes in programmed FET cycles.

SUPPORT: None

REFERENCES:

DO MATERNAL PRECONCEPTION SERUM ANTI-MÜLLERIAN HORMONE (AMH) LEVELS CORRELATE WITH LIVE BIRTH SEX RATIO AFTER INTRAUTERINE INSEMINATION (IUI) WITH OR WITHOUT OVARIAN STIMULATION (OS)? Karissa C. Hammer, MD, Panagiota Cherouveim, MD, Kaitlyn E. James, PhD, Caroline Sherston, MD, Stylianos Vagios, MD, Caitlin R. Sacha, MD, Victoria W. Fitz, MD, MSCR, Victoria E. Jiang, MD, Irene Dimitriadis, MD, David Pepin, PhD, Mary E. Morris, M.D., Ph.D., Irene Souter, MD Massachusetts General Hospital Fertility Center, Massachusetts General Hospital and Harvard Medical School, Boston, MA; Massachusetts General Hospital Fertility Center, Boston, MA; Deborah Kelly Center for Outcomes Research, Massachusetts General Hospital and Harvard Medical School, Boston, MA; Pediatric Surgical Research Laboratories, Massachusetts General Hospital, Boston, MA; Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Massachusetts Chan Medical School, Worcester, MA.

OBJECTIVE: Follicular fluid AMH may impact oocyte and embryo development altering, among other, sex ratio of conceptuses. Consequently, we aimed to investigate the potential relationship between maternal AMH levels (ng/ml) and neonatal sex in IUI±OS conceptions.


Intervention: Births were stratified by AMH into quartiles (Q1-Q4).

Outcome: Neonatal sex.

Statistics: Odds ratios (OR) and 95% confidence intervals (CI) were calculated with generalized estimating equations logistic regression models adjusted for maternal age, body mass index, fresh vs. frozen sperm. AMH was analyzed either as a continuous variable or in quartile increments. Data were further stratified, in a subanalysis, by PCOS diagnosis.

RESULTS: Overall, there were 219 (52.1%) male and 201 (47.9%) female neonates. Mean AMH (Table) and incidence of PCOS diagnosis (22.9% vs. 22.3%, p = .87, male vs. female) did not differ significantly between sexes. Male sex frequency did not differ between AMH quartiles (54.2%, 52.8%, 55.0%, and 46.7%, p = .62; for Q1-Q4, respectively). AdjOR for male sex did not suggest significant associations with AMH levels, neither with AMH as a continuous variable nor as quartile increment.

After further stratification by PCOS diagnosis, results remained unchanged. CONCLUSIONS: Our results do not suggest an association between AMH levels and neonatal sex among IUI±OS conceived singletons.

IMPACT STATEMENT: A natural skew exists in terms of live birth that favors males over females. Our data suggest no association between AMH and sex of IUI±OS conceived newborns.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All</th>
<th>Mean ± SD</th>
<th>Non-PCOS</th>
<th>PCOS</th>
<th>p-value1</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMH (ng/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cycles</td>
<td>5.30±5.21</td>
<td>51.2±4.92</td>
<td>54.8±5.51</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>PCOS</td>
<td>4.92±5.45</td>
<td>3.77±3.87</td>
<td>3.81±4.25</td>
<td>0.90</td>
<td></td>
</tr>
<tr>
<td>b. AdjOR (95%CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous</td>
<td>10.43±5.47</td>
<td>10.33±5.12</td>
<td>10.53±5.82</td>
<td>0.85</td>
<td></td>
</tr>
<tr>
<td>Quartiles2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cycles</td>
<td>1.00</td>
<td>0.25</td>
<td>0.30</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Non-PCOS</td>
<td>(0.99, 1.02)</td>
<td>(0.83, 1.08)</td>
<td>(0.85, 1.13)</td>
<td>(0.78, 1.04)</td>
<td></td>
</tr>
<tr>
<td>PCOS</td>
<td>(0.97, 1.01)</td>
<td>(0.80, 1.08)</td>
<td>(0.76, 1.04)</td>
<td>(0.75, 1.03)</td>
<td></td>
</tr>
</tbody>
</table>

1. Male vs Female.

2. Ref: Q1.
P-261 6:45 AM Tuesday, October 25, 2022

ORAL GONADOTROPIN-RELEASING HORMONE ANTAGONISTS IN THE TREATMENT OF ENDOMETRIOSIS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS OF EFFICACY PARAMETERS AND ADVERSE EFFECTS. Erkan Kalafat, M.D. M.Sc.1 Savci Bekir Bekir Tekle, M.D.,2 Zeynep Gurbuz, Ms.,1 Baris Ata, M.D. M.Sc.1 1Koc University, School of Medicine, Istanbul, Turkey; 2Istanbul University Faculty of Medicine, Istanbul, Turkey.

OBJECTIVE: The aim of this systematic review is to synthesize evidence regarding the use of oral gonadotrophin-releasing hormone (GnRH) antagonist for the treatment of pain associated with endometriosis.

MATERIALS AND METHODS: Web of Science, and MEDLINE databases were searched electronically in March 2022. Only randomized controlled trials involving patients with surgically confirmed endometriosis treated with different doses of oral nonpeptide GnRH antagonists were included. A network meta-analysis using random effects was performed and treatments were ranked according to their P score.

RESULTS: Five randomized trials were included in the analyses. Included studies were found to be at low risk of bias. Endometriosis-associated pain was reported in 3 studies with 1626 participants. All regimens of elagolix were significantly better than placebo for controlling endometriosis-associated pain at 3 months and higher doses of elagolix (200mg BID) scored higher (mean difference [MD] in pain scores: -1.22, 95% CI: -1.31 to -1.15) compared to lower doses of 150mg OD (MD: -0.53, 95% CI: -0.61 to -0.44) and 250mg OD (MD: -0.48, 95% CI: -0.62 to -0.33). Dyspareunia scores were reported by 4 studies with 1406 participants. All doses of linzagolix and elagolix were significantly better than placebo for reducing dyspareunia scores at 3 months while relugolix was not better than placebo. The highest reduction in dyspareunia scores was achieved with Linzagolix 200mg OD (MD: -0.83, 95% CI: -1.18 to -0.49), followed by Elagolix 200mg OD (MD: -1.28, 95% CI: -2.49, P = 0.47). The same conclusion was reached when analyzing the 11 studies that described LBR per cycle (RR = 0.91 (95% CI: 0.63-1.30, P = 0.60)), or cumulative LBR after all IVF/ICSI cycles (7 studies: RR = 1.09 (95% CI: 0.61-1.92, P = 0.78)). Sensitivity analysis led to similar results and conclusions. Subgroup analysis according to the endometriosis phenotype (endometrioma (OMA) or deep infiltrating endometriosis) or the type of OMA surgery (transvaginal ethanol sclerotherapy, cysctectomy or other) showed similar results regarding LBR per cycle, when comparing prior endometriosis surgery followed by ART and those who did not (risk ratio (RR) = 1.28, 95% CI: 0.66-2.49, P = 0.47). Analyses were completed in R version 4.1.0 (Vienna, Austria).

CONCLUSIONS: The results of this systematic review and meta-analysis showed no statistically significant benefit for surgery before IVF in endometriosis patients.

IMPACT STATEMENT: These data urge the clinician to carefully weight the pros and cons before systematically referring infertile endometriosis patients to radical surgery.

SUPPORT: This work was sponsored by an unrestricted grant from GEDEON RICHTER France. The authors have no competing interests to declare.

P-263 6:45 AM Tuesday, October 25, 2022

RACIAL DISPARITIES IN ENDOMETRIOSIS. Anthony Bui, M.D., M.S.1 Audrey Garneau, M.D.,1 Steven L. Young, M.D., Ph.D.,2 Genevieve S. Neal-Perry, M.D., Ph.D.1 1University of North Carolina, Chapel Hill, NC; 2University of North Carolina School of Medicine, Chapel Hill, NC; 3University of North Carolina, Chapel Hill, NC.

OBJECTIVE: To investigate ethnic and racial disparities among outcomes of uterus-sparing endometriosis surgery.

MATERIALS AND METHODS: We performed a retrospective cohort study using the National Surgical Quality Improvement Program database. Patients were identified who had open or laparoscopic surgery by a gynecologist for endometriosis between January 1, 2006 and December 21, 2020. Hysterectomy and cancer diagnoses were excluded. Preoperative factors, surgical operative times, intra- and post-operative complications, and mortality were compared. Data analysis was performed using Chi-square, Fisher’s exact test, ANOVA, Kruskal Wallis test, and multivariable logistic regression (P<0.05). Analyses were completed in R version 4.1.0 (Vienna, Austria).
RESULTS: A total of 6,386 cases were identified. Patients were stratified by self-identified ethnicity and race; African American (AA), Caucasian (C), Asian or Pacific Islander (API), and Hispanic (H). The groups significantly differed in baseline characteristics and surgical approach (Table 1). Patients undergoing laparotomy had a 10.3% rate of sustaining a perioperative complication, compared to 3.3% for laparoscopic surgery (p<0.0001). After adjusting for preoperative factors, AA were more likely to undergo a laparotomy than any other group (adjusted OR, 2.73; CI, 1.98-3.74; p<0.0001). Rate of conversion from laparoscopic to laparotomy was 2.2% for AA vs. 1.3% for C (p=0.19). Additionally, AA were more likely to experience a major complication (adjusted OR, 2.66; CI, 1.53-4.54, p=0.0004). Mean (SD) postoperative length of stay was 0.67 (1.69) days for AA vs. 0.33 (0.97) for C (p<0.0001).

CONCLUSIONS: AA patients with endometriosis underwent laparotomy more frequently than other racial and ethnic groups and had higher rates of composite morbidity. Limitations of the study are inherent to the database which depends on CPT and ICD coding.

IMPACT STATEMENT: This study raises concerns about the existence of structural inequities regarding access to minimally invasive surgery, underplaying the importance of appropriate use of these surgical approaches.

P-265 6:45 AM Tuesday, October 25, 2022

CO-EXPRESSION OF ACTIVATING AND INHIBITORY RECEPTORS ON PERITONEAL FLUID NK CELLS DIFFERS BETWEEN DEEP ENDOMETRIOSIS AND PERITONEAL ENDOMETRIOSIS, Shinichiro Saeki, MD,1 Ayano Yamaya, MD, PhD,2 Ryu Takeyama, MD PhD,3 Atsushi Fukui, MD, PhD1 1Hyogo Medical University, Nishinomiya, Hyogo, Japan; 2Hyogo College of Medicine, Nishinomiya, Hyogo, Japan.

OBJECTIVE: Deep endometriosis causes severe dysmenorrhea and chronic pelvic pain. Deep endometriosis and peritoneal endometriosis are considered to have different histopathogenesis. Previously, we have reported that NKp46 expression, an active receptor for NK cells in ascites, is reduced in women with pelvic endometriosis. So, in this study, we aimed to investigate the differences in NK cell associations between deep endometriosis and peritoneal endometriosis, and the correlation between the degree of dysmenorrhea as a symptom of deep endometriosis and the expression of NK cell surface markers or intracellular cytokine production.

MATERIALS AND METHODS: We collected peritoneal fluid (pNK) cells from women who underwent a laparoscopic operation for pelvic endometriosis (n=32) and control women who underwent a laparoscopic procedure for benign gynecological diseases such as uterine myoma or ovarian cyst (n=30). The co-expression of activating receptors (CD16, NKp46, NKG2C and NKG2D) and inhibitory receptors (CD158a and NKG2A), and cytokines (TNF-α, IFN-γ, IL-4, IL-10 and TGF-β) in CD56+ NK cells were analyzed using six-color flow cytometry. In addition, the correlation between the degree of dysmenorrhea and the expression of NK cell surface markers or intracellular cytokine production.

RESULTS: CD16+/CD56dim NK cells and NKp46+/NKG2C+ NK cells significantly decreased in women with endometriosis compared to controls, while CD56+/NKp46− NK cells showed a predominant decrease (p<0.05, respectively). However, NKp46+/NKG2D+ NK cells significantly increased in women with endometriosis compared to controls (p<0.05). Moreover, there was a positive correlation between non-

Table 1. Baseline demographics, clinical characteristics, and surgical approach by ethnic and racial group.

<table>
<thead>
<tr>
<th>Perioperative factors</th>
<th>API C n=4244</th>
<th>API N=774</th>
<th>AA n=661</th>
<th>H n=707</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Years (median (IQR))</td>
<td>31.00 (26.00-37.00)</td>
<td>36.00 (32.00-40.00)</td>
<td>32.00 (27.00-38.00)</td>
<td>34.00 (29.00-40.00)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI ≥30 (%)</td>
<td>1266 (29.8)</td>
<td>140 (18.1)</td>
<td>298 (45.1)</td>
<td>252 (35.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>777 (18.3)</td>
<td>146 (1.9)</td>
<td>104 (15.6)</td>
<td>15 (2.1)</td>
<td>0.06</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>134 (3.2)</td>
<td>40 (5.2)</td>
<td>21 (3.2)</td>
<td>25 (3.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>245 (5.8)</td>
<td>37 (4.8)</td>
<td>20 (3.0)</td>
<td>36 (5.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Open approach (%)</td>
<td>218 (5.1)</td>
<td>24 (3.1)</td>
<td>74 (11.2)</td>
<td>42 (5.9)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Our study highlights the endometriosis-detrimental effect and the age enhancement effect of endometriosis on ovarian reserve. Given that many couples begin their family building at an older age and considering the decline in ovarian reserve with aging, exacerbated in the presence of endometriosis, it seems prudent to discuss fertility goals and options including fertility preservations with patients in general, and more importantly with women suffering from endometriosis. At the very least, close follow up and assessment of ovarian reserve should be considered in women with endometriosis.

IMPACT STATEMENT: Detrimental effect of endometriosis on ovarian reserve is further enhanced by increasing age.

SUPPORT: none
menstrual chronic pelvic pain and CD16+/NKp46+ NK cells (p=0.553, p<=0.05) in women with endometriosis. When examining the deep endometriosis and peritoneal endometriosis, CD16+/NKp46+ NK cells showed a significant increase in women with peritoneal endometriosis compared to women with deep endometriosis. (p<0.01), while these cells were significantly decreased in the peritoneal endometriosis compared to controls (p<0.01). In addition, activating NKp46+/NKG2D+ NK cells showed a significant increase in women with peritoneal endometriosis compared to control (p<0.01) and NKp46+/NKG2D+ NK cells and TNF-α/IFN-γ+ CD56bright NK cells showed a significant negative correlation (p=0.34, p<0.05).

CONCLUSIONS: An association with cytokines was observed for activating receptors. This may indicate that abnormal cytokine production may exist as a functional abnormality of NK cells in endometriosis. In addition, The results also suggest that peritoneal fluid NK cells from women with endometriosis have different functions in peritoneal and deep endometriosis.

IMPACT STATEMENT: It was speculated that reduced numbers of cytotoxic pNK cells allow for endometrial cell adherence and progression of endometriosis lesions.

P-266 6:45 AM Tuesday, October 25, 2022

A BAYESIAN NETWORK FOR COMPLEX PAIN-RELATED FEATURES OF ENDOMETRIOSIS. 
Amber C. Kiser, BS,1 Karen C. Schliep, PhD, MSPH,1 Mark Yandell, PhD,2 Karen Eilbeck, MSc, PhD3 University of Utah, Salt Lake City, UT; 2University of Utah, UT.

OBJECTIVE: To model the complex co-dependencies of pain-related features using a Bayesian network and to identify the relative risk of endometriosis.

MATERIALS AND METHODS: Data was collected from 473 women enrolled in the ENDO Study undergoing laparoscopy or laparotomy for a variety of surgical indications. Participants answered survey questions regarding pain experiences and indicated on an anatomical map where they felt pain regularly. Post-operative diagnoses included endometriosis (n=190), normal pelvis (n=122), uterine fibroids (n=59), benign ovarian cysts (n=52), and other gynecological pathology (pelvic adhesions [n=37], congenital Müllerian anomalies [n=10], and neoplasm [n=3]). Clustering grouped the 155 anatomical sites into 15 pain locations. A Bayesian network was developed to model the relationships between pain types, pain locations, and diagnoses. The network was queried for the relative risk of a diagnosis, given the presence of different pain types or locations. The network was bootstrapped for 1000 iterations to obtain the mean and 95% confidence intervals.

RESULTS: The presence of all 18 pain types and locations resulted in an increased relative risk for endometriosis (p-value < 0.001). In univariate analysis, chronic pelvic pain, subfertility, and dyspareunia resulted in the greatest increase in relative risk for endometriosis. The table demonstrates the ability of the Bayesian network to combine multiple pain-related features and quantify their combined effect on the relative risk of a diagnosis.

Table: Relative risk of a diagnosis given pain-related features. Mean estimates with 95% confidence intervals.

<table>
<thead>
<tr>
<th>Prior Condition(s)</th>
<th>Endometriosis</th>
<th>Uterine Fibroids</th>
<th>Benign Ovarian Cysts</th>
<th>Other Gynecological Pathology</th>
<th>Normal Pelvis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain in epigastrium</td>
<td>1.167 (1.160, 1.174)</td>
<td>0.794 (0.781, 0.806)</td>
<td>1.020 (1.012, 1.029)</td>
<td>0.899 (0.888, 0.910)</td>
<td>0.919 (0.910, 0.928)</td>
</tr>
<tr>
<td>Pain in epigastrium + Dyspareunia</td>
<td>1.460 (1.443, 1.476)</td>
<td>0.645 (0.632, 0.657)</td>
<td>0.994 (0.979, 1.009)</td>
<td>0.843 (0.829, 0.857)</td>
<td>0.794 (0.783, 0.805)</td>
</tr>
<tr>
<td>Pain in epigastrium + Dyspareunia + Subfertility</td>
<td>2.077 (2.033, 2.122)</td>
<td>0.530 (0.516, 0.543)</td>
<td>0.649 (0.624, 0.674)</td>
<td>0.769 (0.752, 0.787)</td>
<td>0.679 (0.667, 0.691)</td>
</tr>
</tbody>
</table>

IMPACT STATEMENT: Our study used novel techniques and features, including a Bayesian network with pain locations along with pain types, to investigate vague symptoms of pain. We sought to clarify distinct pain symptoms that could be indicative of endometriosis.

SUPPORT: AK is supported by training grant T15LM007124 from the National Library of Medicine. The ENDO (Endometriosis, Natural History, Diagnosis, and Outcomes) study was funded by the Intramural Research Program, Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), National Institutes of Health (contract numbers N01-DK-6-3428, N01-DK-6-3427, and 10001406-02).

P-267 6:45 AM Tuesday, October 25, 2022

VALIDATION OF TURKISH VERSION OF QUALITY OF LIFE QUESTIONNAIRE FOR WOMEN WITH ENDOMETRIOSIS: ENDOMETRIOSIS HEALTH PROFILE QUESTIONNAIRE – EHP-30. 
Pinar Yalcin Bahat, M.D.,1 Miray Nilufer Cimsit Kemahli, MD,2 Ergzi Durici, MD,3 Burak Yücel, MD,3 Engin Oral, MD, Prof1 University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, Istanbul, Turkey; 2University of Health Sciences, Istanbul Zeynep Kamil Women and Children’s Hospital, Istanbul, Turkey; 3Brussels IVF, Universitair Ziekenhuis Brussel, Brussels, Belgium; 4University of Health Sciences, Başakşehir Çam and Sakura City Hospital, Istanbul, Turkey; 5Bezmialem Vakif University, Istanbul, Turkey.

OBJECTIVE: University of Oxford has developed Endometriosis Health Profile questionnaire (EHP-30), 30-item quality of life questionnaire to obtain information about the impact of endometriosis on the daily living of endometriosis patients. This questionnaire has been translated into many languages and used in various countries. However, has not yet been validated or evaluated psychometrically for use with Turkish patients. The aim of the present study was therefore to evaluate the reliability and validity of the EHP-30 questionnaire.

MATERIALS AND METHODS: We conducted a cross-sectional study on 281 endometriosis patients randomly selected from Turkish Endometriosis Patient support groups. Psychometric evaluation included factor analysis, convergent validity, internal consistency, test-retest reliability, data completeness and the determination of floor and ceiling effects.

RESULTS: Two-hundred eighty-one completed questionnaires were included in the study and the return rate among patients was 91%. Overall, excellent data completeness was achieved on all subscales. In the modular questionnaire, floor effects were found in three modules: medical profession (37%), children (32%) and work (31%). No ceiling effects were found. Factor analysis confirmed the division of the core questionnaire into five subscales identical to the original EHP-30. Both predefined hypotheses were found to hold true between EHP-30 and EQ-5D-3L. Cronbach’s a for internal consistency across each scale ranged 0.822 to 0.914.

CONCLUSIONS: The validation of the questionnaire showed high data completeness, low floor and no ceiling effects, good internal consistency, excellent test-retest reliability concluding that Turkish version of the EHP-30 is a valid and reliable measure of HRQOL in patients with endometriosis.

IMPACT STATEMENT: Turkish version of the EHP-30 is a valid and reliable measure of HRQOL in patients with endometriosis.

SUPPORT: The authors received no specific funding for this work.
EVALUATION OF THE EFFECT OF RELUGOLIX COMBINATION THERAPY ON BONE MINERAL DENSITY (BMD) OVER TWO YEARS IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED PAIN: SPIRIT LONG-TERM EXTENSION (LTE) STUDY.

OBJECTIVE: Once-daily relugolix combination therapy (Rel-CT; relugolix 40 mg, estradiol [E2] 1 mg, norethindrone acetate [NETA] 0.5 mg) in women with endometriosis-associated pain was associated with maintained efficacy on dysmenorrhea (DYS) and non-menstrual pelvic pain (NMPP) through 104 weeks (Becker, ESHRE 2022). Here, the effect of Rel-CT on BMD was assessed for up to 104 weeks (wks) in the SPIRIT LTE study.

MATERIALS AND METHODS: In the pivotal SPIRIT 1/2 studies, premenopausal women with moderate-to-severe DYS and NMPP and selected baseline characteristics. Women who chose to enroll in the LTE received open-label Rel-CT for up to an additional 80 wks. BMD was assessed by dual-energy X-ray absorptiometry of the lumbar spine (L1–4), total hip, and femoral neck at Weeks 12 and 24 (SPIRIT 1/2), and Weeks 36, 52 and 104 (LTE). Percent change from baseline was summarized by anatomical location according to pivotal study treatment assignment using a mixed-effects model with repeated measures balanced when stratified by region, years since surgical diagnosis of endometriosis, visit and selected baseline characteristics.

RESULTS: Of 1261 women randomized in SPIRIT 1/2, 1251 included in the analyses, and 104 completed these studies. In the SPIRIT LTE study, of 280 (77%) entered the LTE and 501 (62%) completed Week 104. In the Rel-CT group (N=277), small decreases (<1%) in lumbar spine BMD were observed at Week 24, followed by stabilization of BMD up to Wk 104 (Table). For women treated initially with placebo who transitioned to Rel-CT at Week 24 (N=275), BMD did not change substantially over 104 wks. Women in the delayed Rel-CT group (N=247) who first received relugolix monotherapy had significant early BMD loss at Week 12, with a trend towards BMD recovery after transition to Rel-CT up to Week 104, supporting the value of adding E2 and NETA.

<table>
<thead>
<tr>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 36</th>
<th>Week 52</th>
<th>Week 104</th>
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<td>-0.11 (-0.48, 0.27)</td>
<td>0.07 (-0.32, 0.46)</td>
<td>0.09 (-0.33, 0.51)</td>
<td>-0.09 (-0.57, 0.39)</td>
<td>-0.09 (-0.67, 0.48)</td>
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<tr>
<td>-0.57 (-0.94, -0.19)</td>
<td>-0.92 (-1.31, -0.54)</td>
<td>-0.66 (-1.08, -0.24)</td>
<td>-0.69 (-1.16, -0.21)</td>
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<td>1.72 (-2.11, -1.33)</td>
<td>1.86 (-2.26, -1.45)</td>
<td>1.60 (-2.04, -1.16)</td>
<td>1.09 (-1.59, -0.59)</td>
<td>-0.56 (-1.17, 0.05)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Treatment with Rel-CT for 104 wks was associated with mean BMD loss < 1% at the lumbar spine that plateaued starting at Week 36 and was sustained for the treatment duration. Impact Statement: Rel-CT may offer a longer-term treatment option for women with endometriosis-associated pain, with minimal changes in BMD.

REFERENCES:

OBJECTIVE: To assess patient-reported pain relief in endometriosis (EM) for women receiving Elagolix (ELX), an oral gonadotrophin-releasing hormone ( GnRH) antagonist, versus other treatments (Tx).

MATERIALS AND METHODS: Interim data were drawn from the Adelphi EM Disease Specific Programme (DSP); a 201-point-in-time survey of physicians and patients, conducted in the United States (US).

Obstetrician-gynaecologists seeing ≥12 pre-menopausal women aged ≥18 years with a physician-confirmed diagnosis of EM a month, completed details for a consecutive sample of patients with EM regarding their demographic, clinical and Tx information. Patients were invited by the physician to complete a questionnaire on EM pain at different timepoints (from 0 to 10: no pain to worst pain imaginable) and days of pain/month prior to and since starting Tx. This interim analysis included patients who had received Ts for their EM for ≥3 months. T-test (TT) and Fishers Exact (FE) were used as appropriate.

RESULTS: 123 patients met inclusion criteria and completed the relevant pain questions; 80 prescribed ELX and 43 prescribed other Tx at survey date, most commonly the combined birth control pill (40%) and GnRH agonist injection (28%). Mean ± standard deviation (SD) patient age was 32.4 ± 7.1 years; BMI was 27.2 ± 4.2; 89% were white/Caucasian; and 25% were perceived by their physician as having moderate to severe (III-IV) EM staging.

Before starting current Tx, ELX (n=70) and other (n=37) patients reported experiencing a mean ± SD of 13.9 ± 8.1 and 11.8 ± 7.9 days of pain/month, compared with 4.2 ± 5.2 and 4.9 ± 6.6 days of pain/month on surgery date, respectively. ELX patients (9.7 ± 7.3) had significantly fewer pain days as assessed at survey date compared to prior to current Tx, than other patients (-6.8 ± 5.8) (TT, p = 0.0421). Over the last 30 days, no pain between menstrual periods was reported by 20% (n=16/80) of ELX patients and 5% (n=2/43) of other patients (FE, p = 0.0302). Numerical differences were also observed for more frequent absence of pain reported by ELX patients than other patients during menstrual periods and 9% vs. 3% had higher EM symptoms during sex intercourse prior to current Tx (FE, p = 0.0551) and during sexual intercourse [20% for ELX (n=1471) and 9% for other (n=353), FE, p = 0.1695].

CONCLUSIONS: Interim results suggest that patients who started ELX had significantly fewer pain days per month during current Tx compared to prior, than other patients. A significant difference was reported between Tx groups for absence of pain between menstrual periods. Numerical differences were observed for more frequent absence of pain reported by ELX patients during menstrual periods and sexual intercourse than other patients.

IMPROVE STATEMENT: EM can result in debilitating and chronic bodily pain. Following EM-targeted ELX Tx, we observe a greater reduction in patient-reported EM pain compared to other more generic hormonal and analgesic EM Tx. By reducing EM symptoms, novel Tx such as ELX demonstrated that EMTx can provide improved options for achieving EM pain relief. Please note study is still ongoing; we present interim data only. Final data to be provided end 2022.

SUPPORT: Data collection was undertaken by Adelphi Real World as part of an independent survey, entitled the Adelphi Endometriosis Disease Specific Programme (DSP). The DSP is a wholly-owned Adelphi product, all methodology, materials, data and data analysis that support the findings of this survey are the intellectual property of Adelphi Real World.

AbbVie, Inc. subscribed to this survey and participated in the analysis and interpretation of data, reviewing, and approval of the publication.

P-273 6:45 AM Tuesday, October 25, 2022

LAPAROSCOPIc PERITONEAL EXCISION OF ENDO- METRIOSIS IMPROVES IN VITRO FERTILIZATION (IVF) LIVE BIRTH RATES IN WOMEN <41 YEARS OF AGE WITH DIMINISHED OVARIAN RESERVE. Sophia I. Lipari Research, Student; Christopher W. Lipari, M.D.; Sarah E. Paschall, M.D.; Michael D. Fox, M.D.; Amy Hearne, M.D.; JCRC. Jacksonville, FL; 2JCRMC

OBJECTIVE: In vitro fertilization (IVF) has become the preferred treatment approach for women with diminished ovarian reserve (DOR). Although there is a high prevalence of endometriosis in this population, data is lacking as it relates to the potential benefits of laparoscopy prior to IVF. The aim of this study is to determine whether laparoscopic peritoneal excision of endometriosis improves IVF live birth rates in women under 41 years of age with DOR.

MATERIALS AND METHODS: Data submitted to the Society for Assisted Reproductive Technology (SART) from 2018-2021 at a single fertility clinic was utilized to identify patients that underwent ART with the diagnosis of DOR. Charts were reviewed for baseline characteristics, treatment(s), past surgical intervention, and cycle outcome data. IRB exempt status was obtained from Baptist Health.

The study groups were identified as surgical or non-surgical and the primary outcome was live birth rate (LBR) per embryo transfer (ET). Secondary outcomes included pregnancy rate per ET, average number of oocytes retrieved, ongoing pregnancy rate and cancellation rate. Baseline characteristics included: age, body mass index (BMI), follicle stimulating hormone (FSH) and antimullerian hormone (AMH) levels.

Groups were compared utilizing the unpaired t-test and differences in proportions were assessed with a z-test.

RESULTS: A total of 130 charts were reviewed. Of the total, 43 were excluded: 25 donor cycles, 1 cryopreservation cycle, 1 surgery performed at an outside facility and 16 patients that were >40 years of age. A total of 50 patients undergoing 66 ETs in the surgical group and 37 patients undergoing 49 ETs in the non-surgical group were compared. Of the patients that underwent surgery, 94.8% had pathology proven endometriosis. The mean age in the surgical group was 32.2 ± 0.5 yrs vs. 33.8 ± 0.7 yrs (p = 0.05). Baseline characteristics between the surgical and non-surgical groups did not differ significantly, (0.4-0.8 kg/m², 13.4 ± 4.2 vs. 13.6 ± 4.0 kg/m², 1.3 ± 0.2 vs. 1.3 ± 0.3 mg/mL, respectively). AMH (9.4 ± 0.7 IU/mL vs. 8.1 ± 0.6 IU/mL). The average number of oocytes retrieved (6.1 ± 0.7 vs. 5.6 ± 0.6) and the cancellation rate were similar. Although the pregnancy rate per ET between the two groups did not reach statistical significance (54.5% vs. 36.7%, p = 0.06), the ongoing pregnancy rate per ET and LBR per ET were significantly higher in the surgical group (53.0% vs. 30.6%; p = 0.02).

CONCLUSIONS: Laparoscopic peritoneal excision of endometriosis prior to ART in women under the age of 41 with DOR was associated with a significant increase in LBR per ET. The surgical group experienced a 22.4% higher LBR. Since operative intervention was not associated with an increase in the number of oocytes retrieved or cancellation rate, the benefit may be related to improvements in endometrial receptivity.

IMPACT STATEMENT: This study indicates that the aggressive management of endometriosis prior to IVF improves the LBR in women under the age of 41 diagnosed with DOR. This may potentially shorten the time of childlessness and reduce the number of ART cycles, and the financial and emotional cost to patients.
suture hemostasis was compared to barbed sutures and in another study bipolar coagulation was compared to bipolar vaporization. All included studies were deemed to be at high risk of bias due to blinding. AMH levels were reported for one month (n = 4), three months (n = 9), and six months post-surgery (n = 5), which showed a statistically significant difference and a sustained drop in AMH levels regardless of the hemostatic method used. No hemostatic method showed significantly better preservation of AMH levels compared to bipolar coagulation at any time point except for hemostatic agents (3 months post-surgery: 0.74 ng/mL higher, 95% CI: 0.33 to 1.16) but the finding was mainly driven by a small study, which was at high risk of bias. The ranking of treatments at the longest follow-up (six months) showed suture hemostasis was the best (MD: 0.85 ng/mL higher) followed by laser vaporization (MD: 0.49 ng/mL higher), and hemostatic agent use (MD: 0.20 ng/mL higher) when compared to bipolar coagulation. High statistical heterogeneity was observed in all analyses.

CONCLUSIONS: Laparoscopic endometrioma removal was associated with a sustained drop in AMH levels in all included trials. Statistically significant preservation of ovarian reserve could only be demonstrated for hemostatic agent use while suture hemostasis ranked first for preservation of AMH levels at the longest follow-up period (six months).

IMPACT STATEMENT: Suture hemostasis, laser vaporization, and hemostatic agents look promising as a way of preserving ovarian reserve compared to bipolar coagulation but included studies were small and at high risk of bias. High quality trials with larger sample sizes are needed.

P-275 6:45 AM Tuesday, October 25, 2022

BEHAVIORAL SYMPTOMS OF EATING DISORDERS AND RISK OF ENDOMETRIOSIS: A PROSPECTIVE COHORT STUDY. Sarah Thornburgh, MPH,1 Ariella R. Tabacca, MSc, PhD,2 Leslie V. Farland, ScD,3 Holly R. Harris, M.P.H., Sc.D.4 Kendrin R. Sonneville, ScD, RD,5 Alison E. Flick, PhD,6 Jorge E. Chavarro, MD, ScD,7 Stacey A. Missmer, ScD,8 Audrey Jane Gaskins, ScD9 Emory University Rollins School of Public Health, Atlanta, GA; 2Boston Children's Hospital, Boston, MA; 3University of Arizona, Tucson, AZ; 4Fred Hutchinson Cancer Center, Seattle, WA; 5University of Michigan School of Public Health; 6Brown University School of Public Health; 7Harvard T.H. Chan School of Public Health, Boston, MA; 8Michigan State University, Grand Rapids, MI; 9Emory University, Rollins School of Public Health, Atlanta, GA.

OBJECTIVE: Behavioral symptoms of eating disorders, such as restriction, purging, and binging, are likely to have an important impact on the gynecologic health of adolescents through impacts on body weight and menstrual cycle function. However, few prospective studies have evaluated these associations, particularly in regards to endometriosis. Therefore, our objective was to prospectively evaluate the association between behavioral symptoms of eating disorders in young adult females and risk of endometriosis.

MATERIALS AND METHODS: We included 12,463 female participants from The Growing Up Today Study (1996–present), a US based prospective cohort. Starting when the girls were 14 to 19 years, they began self-reporting binging and purging behaviors over the past year on each follow-up questionnaire. Girls were classified into four mutually exclusive categories, Binge Eating Disorder (BED), Purging Disorder (PD), Bulimia Nervosa (BN), and Other Specified Feeding and Eating Disorders (OSFED). Girls who did not meet the criteria for these four eating disorders served as the reference group. Self-reported endometriosis diagnoses were captured on consecutive follow-up questionnaires, with participants reporting a physician diagnosis and whether the diagnosis was laparoscopically confirmed. Multivariable logistic regression models with generalized estimating equations were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) adjusting for smoking history, final adult height, birthday, age at menarche, race, and childhood body size while accounting for sibling clusters.

RESULTS: Over 15 years of follow-up, we identified 239 incident cases of endometriosis (1.9%), 160 of which were laparoscopically confirmed (1.3%). A total of 1988 girls (16.0%) were classified as ever having OSFED (n = 1292, 10.4%) followed by BED (538, 4.3%), BN (n = 99, 0.8%), and PD (n = 59, 0.4%). Participants with behavioral symptoms of an eating disorder had a 79% (95% CI 59-89%) lower odds of endometriosis diagnosis compared to those who did not have behavioral symptoms. This association was similar with and without adjustment for childhood body size and when restricted to laparoscopically confirmed endometriosis. While the prevalence of BN and PD was too low to examine on their own, both OSFED and BED had strong inverse associations with odds of endometriosis (OR = 0.28 95% CI 0.14-0.56 and OR = 0.18 95% CI 0.04-0.71, respectively).

CONCLUSIONS: We observed that adolescent and young adult females with a history of disordered eating behaviors were at decreased risk of endometriosis diagnosis compared to those who did not exhibit disordered eating behaviors.

IMPACT STATEMENT: The strong inverse associations we observed between behavioral symptoms of eating disorders and risk of endometriosis diagnosis may provide unique insights into the potential biological mechanisms underlying the etiology of endometriosis or paths to diagnosis in young women.

CURRENT AND FUTURE MEDICAL, SURGICAL, AND INTERVENTIONAL APPROACHES TO MANAGE ASHERMAN'S SYNDROME. Hamid Sanjaghaz, D.O., Elham Neisani Samani, MD, Chadi Haddad, D.O., Alissa Walker, M.D., PSY.D. Michigan State University, Garden City Hospital, Garden City, MI.

OBJECTIVE: Intrauterine adhesions (IUAs), also known as Asherman’s syndrome, can impact both reproductive outcomes and gynecologic symptoms. This review aims to update on recent evidence in the etiology, diagnosis, and management of Asherman’s syndrome.

MATERIALS AND METHODS: The data research was conducted using MEDLINE, EMBASE, Ovid, Scopus, and Cochrane Library and querying for all the articles related to Asherman’s syndrome, including studies focused on risk factors, pathogenesis, diagnosis, and treatment that were published between January 1, 2000, to February 1, 2022. Seminal studies published before 2000 were included when relevant to the review and when more recent data were unavailable. The studies were identified using the following text words: intrauterine synechiae, intrauterine adhesion, Asherman’s syndrome, hysteroscopy. The selection criteria of this review included randomized clinical trials and non-randomized controlled studies (observational prospective, retrospective cohort studies, case-control studies, case series). A total of 541 studies were identified. We prioritized randomized clinical trials, meta-analyses, population-based studies, and observational studies.

RESULTS: Recurrent dilatation and curettage procedures were identified as the most common cause of intrauterine adhesion formation. Direct visualization of intrauterine adhesions with hysteroscopy is the gold standard for the diagnosis. Magnetic resonance imaging is required in cases with an obliterated uterine cavity. There are several classifications for the planning of surgery, information on prognosis, and scientific purposes. However, clinical studies have not validated the classification systems, and no one has used them uniformly when reporting reproductive outcomes after treatment of intrauterine adhesions. Hysteroscopic surgery uses scissors or a power instrument working from the central part of the uterus to the periphery. Hysteroscopy with fluoroscopy is preferred in severe cases. Intrauterine devices like balloon catheters or intrauterine contraceptive devices are recommended for preventing the reoccurrence of adhesions after treatment. Some studies suggest estrogen therapy after lysis of intrauterine adhesions, but its use has not been universally adopted. Prevention of reformation of adhesions remains challenging, and no single method for preventing recurrence has shown superiority. Cell-based therapies using endometrial stem cells hold promise for future use.

CONCLUSIONS: Treatment of moderate to severe Asherman syndrome remains a challenge. A comprehensive approach to intrauterine adhesion, including early diagnosis and surgical modalities to reduce scar reformation, has been demonstrated to optimize outcomes. Furthermore, close antenatal surveillance and monitoring are essential for women who conceive after treatment. Well-designed clinical trials are needed to determine the most appropriate preventive and therapeutic modalities.

IMPACT STATEMENT: This review have important practical points for clinicians caring for patients with intrauterine adhesion.

FERTILITY & STERILITY®
Hysteroscopic Myomectomy is not associated with intrauterine dissemination of myometrial cells.

OBJECTIVE: Hysteroscopic myomectomy is the surgical treatment of choice for women with submucosal fibroids. Although many studies have looked at the risk of intrauterine dissemination of myoma cells following laparoscopic myomectomy, only a few isolated case reports have shown the possible spread of leiomyosarcoma cells intraperitoneally following hysteroscopic myomectomy. The objective of this study is to determine whether myometrial cells can be detected intraperitoneally following hysteroscopic myomectomy.

MATERIALS AND METHODS: This is a pilot prospective cohort study which included premenopausal women over the age of 18 undergoing hysteroscopic myomectomy for uterine fibroids. Only women with fibroids >2 cm were included as determined by preoperative ultrasonography. Included patients had no prior tubal surgery or risk factors for tubal disease. Hysteroscopic myomectomy was performed with a bipolar resectoscope using saline for uterine distention. Washings of the peritoneal cavity were obtained via culdocentesis, collected at two times during surgery: (1) after performing diagnostic hysteroscopy but before hysteroscopic morcellation, and (2) after hysteroscopic resection of the fibroids was completed. The study pathologist was blinded to whether the samples were obtained pre- or post-myomectomy. One Papanicolaou stained ThinPrep slide (Hologic; Marlborough MA) and one hematoxylin and eosin stained cell block slide was reviewed for each washing. An immunohistochemical stain for desmin (Dako; Carpinteria, CA) was performed on each sample to assist with the identification of smooth muscle cells.

RESULTS: Five women undergoing hysteroscopic myomectomy were included for analysis. Four of the five women presented primarily for management of abnormal uterine bleeding. One woman presented for uterine cavity evaluation prior to a frozen embryo transfer. The mean patient age was 41 years [range: 31-48 years], The mean diameter of the largest intracavitary submucosal fibroid was 33 mm [range: 28-45 mm]. Across all participants, no muscle cells were identified in either the pre- or post-myomectomy cytology samples using routine and desmin immunohistochemical staining.

CONCLUSIONS: Hysteroscopic myomectomy utilizing a bipolar resectoscope was found to not be associated with the intraperitoneal dissemination of myometrial cells. This study provides reassuring data for both surgeons and patients undergoing hysteroscopic morcellation of submucosal fibroids although further study with a larger cohort must be performed.

IMPACT STATEMENT: This is the first prospective study evaluating the presence of intraperitoneal myometrial cells following hysteroscopic myomectomy. These data suggest hysteroscopic myomectomy is a safe option for women with submucosal leiomyomas and confers low risk for the dissemination of leiomyosarcoma.

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Reproductive outcomes and overall prognosis of patients with Asherman's syndrome undergoing IVF cycles.

OBJECTIVE: To assess the impact of Asherman’s Syndrome (AS) following hysteroscopic adhesiolysis on short term reproductive outcomes and the time to achieve pregnancy in infertile patients during IVF cycles.

MATERIALS AND METHODS: A retrospective case control study in a tertiary university affiliated medical center between January 2010 and October 2020 that included all infertile patients who were treated for AS and underwent IVF cycles (study group). Patients were matched with controls in a 1:1 ratio, according to their age and etiology of infertility. A Kaplan–Meier curve for time to conceive was used.

RESULTS: A total of 51 infertile patients who were treated for AS and underwent IVF cycles were included in the study group, of whom 75% had moderate to severe disease. There was no difference in the mean number of embryo transfer per patient between the two groups (4.9 ±4.6 vs. 6.22 ±4.3, p=0.78). The mean endometrial thickness before embryo transfer was significantly higher among women in the control group (6.95 ±1.7, respectively, p=0.001). Women with AS had significantly lower cumulative live birth rate and significantly higher miscarriage rate as compared to women in the control group (23.5% vs 56.8, p=0.001 and 41% vs. 15.6%, p=0.008 accordingly). Overall AS patients had longer time to conceive within the timeframe of surveillance. The mantel-Cox square R ank was 7.481 p=0.006 respectively. The Overall time to conception was significantly longer among with AS (407.962 ±74.7 Vs 785.6 ±110.4). The mean endometrial thickness was significantly higher among women with AS who had live birth (8.2 (±1.4) 6.9 (±1.2), p=0.001).

CONCLUSIONS: AS has an impact on the reproductive potential in infertile patients following hysteroscopic adhesiolysis. Endometrial thickness was shown to be an important predictor for live birth among women with AS that utilizing IVF.

IMPACT STATEMENT: The time interval to conceive is significantly longer among patients with AS so as patient dropout. Second, increased endometrial thickness after hysteroscopic adhesiolysis in the AS group was associated with a higher live birth rate.

Third, women with AS were characterized by lower cumulative live birth rate and significantly higher miscarriage rate.

SUPPORT: None

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Single euploid embryo transfer outcomes after uterine septum resection. Samantha Lauren Estevez, MD, Tamar Alkon-Meadows, MD; Natalie Cohen, MD; Ethan Nyein, MD; Keri Bergin, BS, M.D.; Carlos Hernandez-Nieto, MD; Dmitry Gounko, B.S., M.A.; Joseph A. Lee, BA; Erkan Buyuk, MD; Alan B. Copperman, MD 1 Icahn School of Medicine at Mount Sinai, New York, NY; 2 Reproductive Medicine Associates of New York, New York, NY; 3 Albany Medical Center, Albany, NY.

Objective: A septate uterus is the most common Müllerian anomaly. There is limited evidence supporting surgical versus expectant management of uterine septa. The objective of this study is to compare single euploid embryo transfer (SET) outcomes in patients who underwent prior uterine septum resection to those with uteri of normal contour without Müllerian anomaly and without a history of prior uterine surgeries.

Materials and Methods: Cycles of patients with prior hysteroscopic uterine septum resection and underwent autologous SET between 2012-2020 were included. A 3:1 ratio propensity score matched cycles without a history of uterine septa was used as the control group. Cycles were matched by age, anti-Müllerian hormone (AMH), and body mass index (BMI). Baseline demographics included age, BMI, gravity, parity, history of spontaneous abortions, duration of infertility, endometrial thickness at SET, embryo quality, and cycle outcomes. Patients with uterine factors other than septum patients were matched by age, pretransplant anatomic and hydrosalpinx grades were performed using chi-square and students t-test. A multivariate regression analysis fitted with a generalized estimating equation was conducted to evaluate the association of prior septum resection and pregnancy outcomes.

Results: Sixty cycles in 35 septum patients were compared to 180 cycles in 154 controls. Septum patients had longer infertility duration (18.2±16 vs 12.9±7.7, p<0.02) and higher gravidity (1.68±1.21 vs 1.11±1.24, p=0.002) but similar parity (0.33±0.57 vs 0.38±0.65, p=0.59) compared with controls. Septum patients had significantly lower rates of chemical pregnancy (58.33% vs 77.2%, p=0.004), implantation (41.67% vs 65.6%, p=0.001), and live birth (33.33% vs 57.8%, p=0.001) per transfer. No statistical difference in clinical pregnancy loss rates was found comparing septum patients with controls (8.33% vs 7.8%, p=0.89). Additionally, after adjusting for gravidity, number of prior spontaneous abortions, duration of infertility, endometrial thickness at transfer, and embryo quality, there was a significant association between having a prior hysteroscopic septum resection and lower odds of implantation (aOR=0.46, CI 95%; 0.24-0.91) and live birth (aOR=0.40, CI 95%; 0.20-0.79). With these adjustments, there was no significant association between septum resection and miscarriage (aOR=1.58, CI 95%; 0.51-4.8).

Conclusions: Patients with uterine septa and history of hysteroscopic resections are susceptible to suboptimal live birth outcomes. Uncorrected uterine septa are associated with a higher incidence of miscarriage. However, miscarriage rates after resection are similar to normal uteri. Patients born with septate uteri should assess the value of surgical intervention prior to SET to best optimize their reproductive outcomes.

Impact Statement: Uterine septa are the form of Müllerian anomaly most amenable to surgical correction. Despite corrective hysteroscopic septum resection, SET outcomes were suboptimal. The best treatment approach for women with septate uteri remains to be determined.

Support: None

References: N/A

P-281 6:45 AM Tuesday, October 25, 2022

P-282 6:45 AM Tuesday, October 25, 2022

The exception or the rule? Anatomicomotic vaginal stricture after uterus transplant: case series and systematic review. Leigh A. Humphries, MD; Margaret Rush, MD; Elliott G. Richards, MD; Liza Johannesson, MD, PhD; Kathleen O’Neill, MD 1 University of Pennsylvania, Philadelphia, PA; 2 Hospital of the University of Pennsylvania, Philadelphia, PA; 3 Cleveland Clinic, Cleveland, OH; 4 Baylor University Medical Center, Dallas, TX.

Objective: To report the incidence and management of vaginal stricture at the donor/recipient anastomosis in all uterus transplants performed in the United States between 2016 and 2021, and to review the literature on vaginal stricture in patients with uterus transplant.

Materials and Methods: Prospective data were collected on complications after uterus transplant in all patients at three sites: Baylor Scott & White Health, Cleveland Clinic, and University of Pennsylvania. Patients underwent regular vaginal biopsies to monitor for graft rejection. Strictures were diagnosed using pelvic exams and surgical procedures such as hysteroscopy. Pubmed search was performed with terms for uterus, transplant, and complication or stricture. Studies were included if they reported incidence of stricture in patients with uterus transplant.

Results: Of the 32 uterus transplant recipients (12 with deceased donor; 20 with living donor), 18 (56%) developed vaginal stricture at the donor/recipient anastomosis. Stricture diameter ranged from less than 1 cm to about 2 cm, with average diameter partially obscured in all cases. For 6 patients, stricture was noted within 30 days after transplant, and overall median time to stricture was 36 days. Interventions to treat stricture included surgical repair (9 patients) and self-dilation at home and/or provider-directed dilation in office or under anesthesia (9 patients). Manual dilation of up to 3 cm was achieved in most cases within 3 to 6 months. In some cases, anterior cervical stitch was placed to facilitate procedures or biopsies. The presence of stricture did not negatively impact pregnancy outcomes after frozen embryo transfer.

For systematic review, 791 titles/abstracts were screened, 55 full texts reviewed, and 9 studies included. The incidence of vaginal stricture in patients with uterus transplant was 40% (18/45 cases). Treatments for stricture included surgical excision of vaginal scar, placement of self-expanding vaginal stents, and/or manual dilation. Techniques and rationale for treatment approach were not consistently described. Early vaginal dilation and limiting the number of sutures at the anastomosis were proposed as ways to minimize stricture formation.

Conclusions: Vaginal stricture is a common problem among patients undergoing uterus transplantation. Early and consistent vaginal dilation is an important way to prevent and treat this condition.

Impact Statement: This is the first study to report overall incidence of vaginal strictures after uterine transplant and discuss identification and management approach in detail. Strictures require intensive dilation or surgical repair as they can complicate fertility procedures and limit access to monitor for graft rejection.

Racial disparities in abdominal and laparoscopic myomectomies. Audrey Garneau, M.D., Anthony Bui, M.D., M.S., Steven L. Young, M.D., Ph.D.; Genevieve S. Neal-Perry, M.D., Ph.D. 1 University of North Carolina, Chapel Hill, NC; 2 University of North Carolina School of Medicine, Chapel Hill, NC; 3 University of North Carolina, Chapel Hill, NC.

Objective: To investigate ethnic and racial disparities among outcomes of abdominal and laparoscopic myomectomies.

Materials and Methods: We performed a retrospective cohort study using the National Surgical Quality Improvement Program (NSQIP) database. We included patients who had open or laparoscopic myomectomies between January 1, 2016, and December 31, 2020. Racial and ethnic differences in preoperative factors, surgical operative times, intra- and postoperative complications, and mortality were compared. Cases with a cancer diagnosis were excluded. Data analysis was performed using Chi square, ANOVA, and multivariable logistic regression (P<0.05). Analyses were completed in R version 4.1.0 (Vienna, Austria).

Results: A total of 11,795 cases were identified. Patients were stratified by self-identified ethnicity and race; African American (AA), Caucasian (C), Asian or Pacific Islander (API), and Hispanic (H). The groups differed in baseline characteristics and surgical approach (Table 1). After adjusting for these factors, fibroid size and quantity, and surgical history, AA were more likely to undergo a laparotomy than any other group (adjusted OR 2.15; CI 1.96-2.37, p<0.0001). The rates of any complication and of major complication were higher in AA than C (16.7% and 15.1% versus 6.7% and 4.9% in C, P<0.0001) and other groups. Blood transfusions occurred more frequently in AA than C (14.0% vs 8.2%, P<0.0001). After adjusting for preoperative factors, AA patients were 1.21 more likely to sustain perioperative complications than C patients (95% CI 1.03-1.44, P=0.03). Mean (SD) postoperative length of stay was 5.89 (1.60) days for AA, versus 5.98 (1.92) days in C (P<0.0001).

Conclusions: After adjusting fibroid size and other modifiers, AA underwent laparotomy more frequently than other racial or ethnic group and had higher rates of composite morbidity.

Impact Statement: This study highlights inequality in provision of healthcare and highlights the need to improve access to minimally invasive myomectomies among AA patients.
INCIDENCE AND RISK FACTORS OF INTRAUTERINE ADHESIONS FOLLOWING MYOMECTOMY.

Pietro Bortolotto, MD, MSc.,1 Kimberly W. Keefe, MD,2 Emily Unger, MD,3 Eduardo Hariton, MD, MBA,4 Antonio R. Gargiulo, MD3 1NewYork-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY; 2Brigham and Women’s Hospital, Boston, MA; 3University of Washington, Seattle, WA; 4Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; 5Brigham and Women’s Hospital –Harvard Medical School, Boston, MA.

OBJECTIVE: To determine the incidence and risk factors for intrauterine adhesions (IUA) following minimally invasive, open and hysteroscopic myomectomy.

MATERIALS AND METHODS: This was a retrospective cohort study conducted at a single university-affiliated fertility center. Patients 18 and older undergoing robotic-assisted or conventional laparoscopic minimally invasive myomectomy (MIS), abdominal myomectomy (AM) or hysteroscopic myomectomy (HM) between January 2007 and January 2017. Only patients who underwent a uterine cavity evaluation within 12 months of surgery via hysteroscopy or hysterosalpingogram were included. Patients were excluded if they had a history of IUA prior to myomectomy. Severity of intrauterine adhesions were scored by two authors using a previously published grading system (March et al). The primary outcome(s) of this study were presence and severity of IUA. The secondary outcomes were identification of risk factors for IUA formation.

RESULTS: Of n = 1315 patients who underwent myomectomy, n = 173 (13.2%) met inclusion criteria. Intrauterine adhesions were identified in 9.3% of all patients, 75.0% of which were classified as minimal. The incidence of IUA did not vary by modality: 8.6% MIS, 7.8% AM, and 11.8% HM (p > 0.800). There were no differences in incidence of IUA by number or size of fibroids removed (p > 0.05). Of patients with IUA, 87.5% had submucosal fibroids resected compared to 58.6% without IUA (p = 0.029).

CONCLUSIONS: The incidence of post-operative IUA in women undergoing myomectomy of any modality is relatively low (9.3%) and does not vary by modality alone. Most IUA are of minimal degree. The presence of submucous fibroids is associated with increased risk of IUA in all modalities.

IMPACT STATEMENT: In summary, based on the 10-year experience of a single, large academic center’s with multi-modality myomectomy for patients desiring future childbearing, we report an incidence of post-operative intrauterine adhesions of 9.3% which did not vary significantly by the surgical modality utilized. Furthermore, aside from the presence of submucous fibroids, there were no readily identifiable risk factors associated with IUA formation.

SUPPORT: None
REFERENCES: None

P-286 6:45 AM Tuesday, October 25, 2022

EFFECT OF NON-CAVITY–DISTORTING INTRAMURAL MYOMAS ON PREGNANCY OUTCOMES IN EUPLOID FROZEN EMBRYO TRANSFER CYCLES. A PROSPECTIVE STUDY.

Antonio R. Gargiulo, MD 5 1NewYork-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY; 2Brigham and Women’s Hospital, Boston, MA; 3University of Washington, Seattle, WA; 4Brigham and Women’s Hospital –Harvard Medical School, Boston, MA; 5Brigham and Women’s Hospital –Harvard Medical School, Boston, MA.

OBJECTIVE: We sought to evaluate the impact of non-cavity–distorting intramural myomas on pregnancy outcomes in an ideal study group: patients undergoing frozen embryo transfer (FET) of a single euploid blastocyst.

MATERIALS AND METHODS: This is an interval analysis of a prospective cohort study at a single large university-affiliated institution from January 2018 to April 2022. There was a hiatus in recruitment from March 2020 to February 2022 due to the COVID-19 pandemic. All patients underwent an autologous natural or programmed FET with endometrial preparation and luteal support per a standardized protocol. Prior to transfer, patients were divided based on the presence (Group A) or absence (Group B) of non-cavity–distorting myomas. All ultrasounds (US) were performed by physicians. If myomas were detected, their number, size, location (FIGO classification system), and distance from the uterine cavity were recorded. The primary outcome was clinical intrauterine pregnancy (IUP). The secondary outcomes were positive chorionic gonadotropin (hCG) test, biochemical pregnancy, missed abortion, and ongoing pregnancy and live birth rates. A Fisher’s exact test was done to compare proportions. A p-value of <0.05 was deemed statistically significant.

RESULTS: Of the 122 enrolled patients, 19 (15.6%) had a non-cavity–distorting intramural myoma (Group A), while 103 (84.4%) did not have a myoma (Group B). No patients had a cavity-distorting myoma. The patients who had myomas tended to be older with a higher BMI, but otherwise had similar baseline characteristics including gravidity, parity, endometrial thickness, peak estradiol level, and AMH. There was no significant difference in the proportion of patients who achieved a clinical IUP in Group A (52.6%) and Group B (63.1%, p = 0.45). There was also no difference in the secondary outcomes (Table 1).

CONCLUSIONS: This prospective observational study has not demonstrated a significant impact of non-cavity–distorting intramural myomas on FET outcomes, although this study is ongoing and will continue to recruit patients.

IMPACT STATEMENT: Non-cavity–distorting myomas do not appear to affect positive hCG, biochemical, clinical IUP rate, miscarriage, or ongoing pregnancy or live birth rates in an ideal study population of single euploid FET transfer cycles.

Table 1. Baseline demographics, clinical characteristics, and surgical approach by ethnic and racial group.

<table>
<thead>
<tr>
<th>Perioperative factors</th>
<th>C n=3710</th>
<th>API N= 1210</th>
<th>AA n=5899</th>
<th>H n=976</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Years (mean (SD))</td>
<td>37.08 (7.33)</td>
<td>37.85 (6.14)</td>
<td>36.35 (5.93)</td>
<td>36.33 (6.33)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI &gt;30 (%)</td>
<td>1168 (31.5)</td>
<td>133 (11.0)</td>
<td>2985 (50.6)</td>
<td>372 (38.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>377 (10.2)</td>
<td>73 (6.0)</td>
<td>526 (8.9)</td>
<td>59 (6.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Preoperative Hematocrit (mean (SD))</td>
<td>38.98 (4.08)</td>
<td>38.21 (4.22)</td>
<td>36.45 (4.15)</td>
<td>38.06 (4.17)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>76 (2.0)</td>
<td>25 (2.1)</td>
<td>194 (3.3)</td>
<td>34 (3.5)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>209 (5.6)</td>
<td>53 (4.4)</td>
<td>817 (13.8)</td>
<td>65 (6.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Laparotomy (%)</td>
<td>1552 (41.8)</td>
<td>566 (46.3)</td>
<td>3862 (65.5)</td>
<td>540 (55.3)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 2. Baseline demographics, clinical characteristics, and surgical approach by ethnic and racial group.

<table>
<thead>
<tr>
<th>n (%)</th>
<th>Group A</th>
<th>Group B</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-cavity-distorting myoma</td>
<td>n = 19 (15.6)</td>
<td>n = 103 (84.4)</td>
<td></td>
</tr>
<tr>
<td>Positive hCG</td>
<td>13 (68.4)</td>
<td>73 (70.9)</td>
<td>0.79</td>
</tr>
<tr>
<td>If positive hCG</td>
<td>3 (15.8)</td>
<td>8 (7.8)</td>
<td>0.38</td>
</tr>
<tr>
<td>Biochemical</td>
<td>10 (52.6)</td>
<td>65 (63.1)</td>
<td>0.45</td>
</tr>
<tr>
<td>Clinical IUP</td>
<td>0 (0.0)</td>
<td>6 (5.8)</td>
<td>0.58</td>
</tr>
<tr>
<td>If Clinical IUP</td>
<td>1 (5.3)</td>
<td>4 (3.9)</td>
<td>0.58</td>
</tr>
<tr>
<td>Ongoing pregnancy / live birth</td>
<td>9 (47.4)</td>
<td>55 (53.4)</td>
<td>0.80</td>
</tr>
</tbody>
</table>
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TGF-B AND EARLY-LIFE EXPOSURE TO ENDOCRINE-DISRUPTING CHEMICALS IMPAIR NUCLEOTIDE EXCISION REPAIR IN EKER RAT MYOMETRIAL STEM CELLS. Maria Victoria Victoria Bariani, PhD,¹ Yanhong Cui, PhD,¹ Mohamed Ali, PhD,² Tao Bai, PhD,³ Yu-Ying He, PhD,¹ Qiwei Yang, Ph.D.,² Ayman Al-Hendy, MD, PhD,¹ University of Chicago, Chicago, IL; ²Clinical Pharmacy Department, Faculty of Pharmacy, Ain Shams University, Cairo, Egypt.

OBJECTIVE: Uterine fibroids (UFs) are the most common noncancerous tumors in women of reproductive age, and their prevalence is associated with environmental exposure to endocrine-disrupting chemicals (EDCs). Each UF is thought to arise from a single transformed myometrial stem cell (MMSC) that acquires a driver mutation in pivotal genes such as Tsc-2 in Eker rats. The Eker rat is a unique animal model of spontaneous development of UFs in adulthood, that are characteristically similar to human UFs. There is evidence that a deficient DNA repair capacity could be involved in the emergence of such mutations. We have previously shown that the TGF-b1 pathway is more active in Eker rat MMSCs exposed to EDCs compared to VEH. There is evidence that TGF-b links to the DNA damage response with implications for tumor origin and development. The objective of this work was to evaluate the role of TGF-b1 and EDCs exposure on nucleotide excision repair (NER, a DNA repair mechanism) capacity in MMSCs.

MATERIALS AND METHODS: Female Eker rats received subcutaneous injections of 10 µg of Diethylstilbestrol (DES, an EDCs) per rat per day or 50 μl of sesame seed oil (vehicle, VEH) on 10, 11, and 12 postnatal days. MMSCs were isolated from 5-months myometrial tissue (N=5 for each group) using Sca-1 and CD44 surface markers. In vitro, VEH-MMSCs cells were supplemented with TGF-b1 (10 ng/µl) for 48 h. NER pathway members’ mRNA levels in VEH- and DES-MMSCs were measured using qRT-PCR and the protein expression was evaluated by Western Blot. To evaluate NER capacity, we quantified the percentage of cyclobutane pyrimidine dimers (CPD) repair, a form of UVB-induced DNA damage, at 0, 6 and 12 h after UVB exposure (10 mJ/cm²) by blot assay. Two-tailed unpaired Student t-test was used to assess any statistically significant differences (p-value<0.05).

RESULTS: The mRNA levels of the NER pathway members XPA, XPB, XPC, and XPF showed a significant decrease in MMSCs from animals exposed neonatally to DES and we found the same results in their protein levels. No differences were found in XPD and DDB2 mRNA and protein levels. Besides, we observed that DES-MMSCs exhibited NER capacity deficiency compared to VEH-MMSCs (% of CPD repair at 12 h after UVB exposure: 76.3 % ± 4.1 vs. 7.6 % ± 15, respectively). Interestingly, when VEH-MMSCs were exposed to exogenous TGF-b1 we found that NER capacity was statistically decreased in comparison with the control group (% of CPD repair at 12 h after UVB exposure: 71.3 % ± 2 vs. 63 % ± 1.2, respectively).

CONCLUSIONS: Our results showed that early-life exposure to DES and TGF-b1 provoked changes in the NER pathway impacting the DNA damage repair capacity, which would lead to increased genetic instability, mutations, and tumorigenesis. 

IMPACT STATEMENT: This study demonstrates for the first time that EDCs exposure and TGF-b alter the DNA damage NER capacity of MMSCs, which contributes to an increased risk of developing UFs.

SUPPORT: This study was supported by National Institutes of Health grants R01 HD094378, RO1 ES028615, and U54 MD007602.

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THE FUNCTIONAL ROLE AND MECHANISM OF BRODOMAIN-CONTAINING PROTEIN 9 IN HUMAN UTERINE LEIOMYOSARCOMA. Qiwei Yang, Ph.D., Maria Victoria Victoria Bariani, PhD, Hiba Siblini, MD, Ayman Al-Hendy, MD, PhD University of Chicago, Chicago, IL.

OBJECTIVE: The aberrant functions of Bromodomain (BRD)-containing proteins have been shown to contribute to many diseases, including cancer. This study aims to determine the role and regulatory mechanism of Bromodomain (BRD)-containing protein 9 in uterine leiomyosarcoma (LMS) cancer.

MATERIALS AND METHODS: Normal myometrium (n=8) and uterine leiomyosarcoma tissues (n=9) were obtained from the University of Chicago tissue bank and stained with BRD9 antibody. Cell proliferation was measured using a trypan blue exclusion assay in LMS cell lines (SK-UT-1, MES-SA). Western blot and qPCR were performed to determine the levels of protein and RNA, respectively. To decode the mechanism underlying the inhibitory effect of BRD9 inhibition, the LMS SK-UT-1 cells were treated with BRD9 inhibitor TP-472 (5 µM) for 48 hr (n=4 for each group). The isolated RNA was subjected for RNA-seq using an Illumina NovaSEQ6000. Hallmark gene set enrichment analysis (GSEA) was performed to determine the enriched pathway, and Enrichr was used to characterize epigenome changes in response to TP-472 treatment. A comparison of 2 groups was carried out using a student t-test for parametric distribution and Mann Whitney test for nonparametric distribution. The significant difference was defined as p<0.05.

RESULTS: Immunohistochemistry analysis demonstrated that the levels of BRD9 are significantly higher in LMS compared to adjacent myometrium and myometrium without LMS. In addition, BRD9 expression was upregulated in LMS cell lines compared to uterine fibroids and myometrial cell lines. Inhibition of BRD9 using the specific inhibitor (TP-472) suppressed LMS cell proliferation concomitant with decreased protein levels of BCL-2 and increased RNA expression of p21, CDKN2C, and BAK. To further characterize the mechanistic basis for TP-472 inhibition of LMS cell growth, we performed a comparative RNA-seq analysis of vehicle-treated and TP-472-treated LMS cells. Bioinformatics analysis revealed that TP-472 treatment distinctly altered the LMS cell transcriptome. GSEA identified critical pathways altered by regular inhibition, including KRAS signaling, MYC targets, TNF-a signaling via NFkB, and MTORC1 signaling. Moreover, the ENCODE Histone Modifications gene set and TargetScan microRNA analysis in Enrichr suggested that TP-472-mediated BRD9 inhibition correlated with histone modifications (H3K4me3 and H3K27me3) and several miRNAs, suggesting that BRD9 inhibition may alter the LMS cell transcriptome by reprogramming the oncogenic epigenome and modulating miRNA-mediated gene regulation.

CONCLUSIONS: Our studies demonstrate a novel finding that BRD9 is dysregulated in LMS tissues and cell lines. Inhibition of BRD9 suppresses the LMS phenotype via altering key pathways and coordinating gene transcription, chromatin state and miRNAs network. Therefore, BRD9 may consider a promising candidate biomarker in LMS. 

IMPACT STATEMENT: Small-molecule inhibitors such as TP-472 attenuate the aberrant functions of BRD9 in LMS and may provide a promising and novel epigenetic strategy for treating patients with this aggressive uterine cancer.

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PREGNANCY OUTCOMES FOLLOWING IN-VITRO FERTILIZATION IN A POPULATION OF SUBFERTILE WOMEN TREATED FOR UTERINE ADHESIONS WITH Hysteroscopic ADHESIOlysis. Roisin Ryan, MB BCH BAO,¹ Ian Waldman, MD,² Šerene S. Strojzi, MD,³ Andrea Lanes, PhD,¹ Elizabeth S. Ginsburg, MD¹ ²Brigham and Women’s Hospital, Boston, MA; ³Brigham and Womens, Boston, OR.

OBJECTIVE: There are no published studies assessing the impact of hysteroscopy for adhesiolysis on reproductive and pregnancy outcomes amongst women who subsequently undergo in-vitro fertilization (IVF). Following treatment for Asherman’s syndrome and restoration of a normal cavity, risk for abnormal placentaion persists, IVF is also an independent risk factor for abnormal placentaion, and this combination of risk factors could increase pregnancy risks. This study aimed to explore the effect of hysteroscopy for adhesiolysis on pregnancy outcomes amongst patients who undergo IVF.

MATERIALS AND METHODS: Women who underwent hysteroscopic adhesiolysis at our tertiary referral center and subsequently underwent IVF with a resultant pregnancy were included. An age-matched control cohort in a 3:1 ratio of women who underwent IVF with a subsequent live birth for non-uterine factor infertility was selected for comparison. Adhesion severity was classified using the 1988 AFS classification system. Primary outcome was endometrial thickness prior to transfer. Secondary outcomes were differences in placental, maternal, and neonatal outcomes between groups, adjusted for prior cesarean section or uterine surgery, prior pregnancy. Frequencies and proportions were calculated for categorical variables;
INTER-OBSERVER VARIABILITY IN HYSTEROSCOPIC DIAGNOSIS OF CHRONIC ENDOMETRITIS.

Ahmed Halouani, MD,1 Anissa Ben Amor, MD,2 Rim Hamdaoui, Resident,3 Lazhar Halouani, MD 4 1Ariana, Ariana, Tunisia; 2Mongi Slim Hospital, Tunis, Tunis, Tunisia; 3Mongi Slim Hospital, tunis, Tunis, Tunisia; 4Jasmins Clinic, Tunis, Tunisia.

OBJECTIVE: To evaluate the inter-observer variability in the interpretation of hysteroscopic images for diagnosing of chronic endometritis (CE) using Cicinelli criteria.

To evaluate the performance of hysteroscopy in diagnosing CE using Cicinelli criteria.

RESULTS: 56 patients were included in this study. The average age of patients was 35 ±4.9. 11.5 % of patients were smokers. The Body Mass Index (BMI) average was 28.3 ±6.1. 34.6% of patients had a CE confirmed by histological examination.

Observer 1 : sensibility and specificity of hysteroscopy in the diagnosis of CE were 47% and 64%.

Observer 2 : sensibility and specificity of hysteroscopy in the diagnosis of CE were 56.3% and 69.2%.

There was a moderate agreement between the two observers: Cohen’s k: 0.56.

CONCLUSIONS: Even with the use of the unified diagnostic criteria for chronic endometritis at fluid hysteroscopy the inter observer agreement remains moderate.

Hysteroscopy can be interpreted differently between physicians. Hysteroscopy has a low sensibility and sensitivity in the diagnosis of CE.

IMPACT STATEMENT: Endometrial biopsy with a pipelle endometrial suction curette and anatomopathological examination with Immunohistochemistry (IHC) are probably more efficient in these cases before ART.

REFERENCES:
Unified diagnostic criteria for chronic endometritis at fluid hysteroscopy: proposal and reliability evaluation through an international randomized-controlled observer study
Etore Cicinelli and al. https://doi.org/10.1016/j.fertnstert.2019.03.004
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PRESENCE OF BRCA MUTATIONS AND A PRE-CHEMOTHERAPY AMH LEVEL OF < 2NG/Ml STRONGLY PREDICT RISK OF AMENORRHEA IN WOMEN WITH BREAST CANCER. Katthuk H. Oktay, M.D., Ph.D., Voletkan Turan, M.D., M.S., Giuliano Barcellos, M.D., Ph.D., Sharad Goldfarb, M.D., Heejung Bang, Ph.D. 1 Yale University School of Medicine, New Haven, CT; 2 Health and Technology University School of Medicine, Istanbul, Turkey; 3 University of São Paulo - Ribeirão Preto Medical School, Brazil; 4 Memorial Sloan Kettering Cancer Center, New York, NY; 5 University of California Davis, Davis, CA.

OBJECTIVE: The likelihood of post-chemotherapy (ChT) amenorrhea is still empirically determined. Breast cancer is the most prevalent malignancy among the women of reproductive age. Our aim was to determine the predictors of amenorrhea risk post-ChT in women with breast cancer (ca). As acute amenorrhea (<12mo post-ChT) can be temporary, we used amenorrhea status 12- and 18-months post-ChT as the primary endpoint.

MATERIALS AND METHODS: 102 women aged 18-44, with regular cycles and stage I breast ca were prospectively and longitudinally followed for their menstrual pattern changes at 6, 12, and 18mo after the completion of adjuvant ChT with an Anthracycline-Cyclophosphamide-based (AC) or Cyclophosphamide-Methotrexate-x5-Fluorouracil regimen. Prior ChT, ovarian surgery, pelvic RT, family history of POI, infertility diagnosis were the exclusion criteria. AMH was measured pre- and immediately post-ChT amenorrhea defined as no bleeding for 4 consecutive cycles. Pre- and/or post-ChT AMH levels, age and BMI at the onset of ChT, BMI tamoxifen use, regimen type (AC-based vs. not) and BRCA mutation (m) status (positive vs. not) were evaluated for the prediction of amenorrhea risk.

RESULTS: In multivariable-adjusted logistic regression models, age (p=0.03) and AMH (p=0.03) were significant predictors of amenorrhea at 12mo, and BRCAstatus (p=0.03) at 18mo; these models yielded areas under the ROC curve of 0.77 and 0.76, respectively. An undetectable AMH post-ChT was predictive of amenorrhea best with shorter follow-up, but not at 18mo. In longitudinal analysis (with data at 0, 6, 12, and 18 months) estimating ‘time-trends’, a baseline AMH <2.0 ng/ml (optimal cut-off from ROC curve) and BRCAstatus were associated with the risk of amenorrhea. The baseline AMH ≥2.0 group showed an attenuated time-trend in the odds ratio (OR) of amenorrhea vs. the AMH <2.0 ng/ml group (ratio of ORs=0.01, 95% CI=0.86-0.97, p=0.003), while the BRCAstatus group showed a steeper time-trend in the OR of amenorrhea, compared to the non-positive group (ratio of ORs=1.12, 95% CI=1.04-1.20, p=0.003). Sensitivity analyses demonstrated the robustness of these findings, for example, yielding an 8-10% increased risk of amenorrhea for BRCA carriers, with p-values of 0.008-0.04.

CONCLUSIONS: Age, pre- and post-ChT AMH levels, and BRCAstatus are potential predictors of amenorrhea at 12 and 18mo post-ChT. IMPACT STATEMENT: A pre-ChT serum AMH level of <2.0 ng/mL and BRCAstatus are strong predictors of post-ChT amenorrhea, and this information may help better guide fertility preservation decision making in women with breast ca. The higher likelihood of amenorrhea in women with BRCAstatus suggests that they may be more prone to lose their ovarian function post-ChT and should be accordingly counseled. This prospective longitudinal study with a uniform cancer population is the first to show the association between BRCAstatus and the post-ChT amenorrhea risk.

SUPPORT: NIH R01HD053112.

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FERTILITY PRESERVATION FOR NEWLY DIAGNOSED CANCER PATIENTS IN WEST AFRICA - A MULTI CENTERED OVERVIEW AMONG RELATED MEDICAL SPECIALISTS IN GHANA. Ellis Fleischner-Djolte, B.Sc., MSc.; 1 Promise E. Selofah, MD, MPH, DLSHTM, FWACS; 2 William Kudzi, PhD; 3 Divonne N. Bampahala, MFAW, PhD, LLB; 4 Finney Hospital and Fertility Centre, Accra, Ghana; 5 University of Ghana Medical School, Accra, Ghana; 6 University of Ghana, Accra, Ghana; 7 Medical and Dental Council, Ghana, Accra, Ghana.

BACKGROUND: Advances in medical oncology have improved cancer survival including childhood cancers. Fertility among cancer survivors is a major quality of life concern and potential fertility loss post cancer treatment has significant impact on patients’ psychosocial wellbeing. Availability and client referral for fertility preservation (FP) are key to giving cancer survivors some hope of future biological children. Data is scant on awareness and practice considerations among clinicians in developing countries.

OBJECTIVE: To study awareness, perspectives and practices of oncology specialists on fertility preservation for newly diagnosed reproductive-age cancer patients.

MATERIALS AND METHODS: A multicentered mixed method study using a cross sectional survey and qualitative exploratory phenomenological approach to examine fertility preservation for newly diagnosed cancer patients in two largest tertiary hospitals in Ghana among gynaecologists, urologists, general surgery and oncology specialists. A structured self-administered questionnaire was followed by semi-structured interview for data collection. Quantitative data analyzed with SPSS-22; interviews were recorded, transcribed and analyzed by coding to generate themes and subthemes, supported with verbatim quotes.

RESULTS: Overall, 78 specialists (34 gynaecologists, 22 general surgeons, 16 urologists, 6 oncologists) participated with 28 interviews. Majority (74%) had over 5years in specialty; 59% use surgery, chemotherapy, radiotherapy and cryoablation. All respondents are aware cancer treatment compromises fertility; 70% counsel patients on treatment’s impact; 77% expressed confidence in their knowledge of fertility preservation options; immature testicular cryopreservation and in vitro maturatation are least known.

A significant 68% of participants start cancer treatment without considering fertility preservation; 32% discuss fertility preservation if patient had fertility wishes; 46.2% offer fertility preservation before treatment but 53.8% start treatment without fertility preservation, in 23.1% of these due to late-stage disease.

Most medical specialists are conversant with ‘sperm cryopreservation’; ‘ovarian tissue cryopreservation’; and ‘oocyte cryopreservation’. Factors influencing fertility preservation consideration by specialists are: patient’s age, cancer stage, patient’s decision and the physician’s workload.

Specialists recommend fertility preservation technologies be made available in public health facilities, subsidized and integrated routinely in cancer management.

CONCLUSIONS: The medical specialists are aware of fertility preservation but only 32% refer younger cancer patients with early-stage disease and fertility wishes for FP. Integrating FP in cancer management is recommended.

IMPACT STATEMENT: This study emphasizes the need for fertility preservation consideration for cancer patients for improved quality of life post cancer treatment.

SUPPORT: No financial support was received for this study.

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CROWDFUNDING USE IN CANCER PATIENTS SEEKING INFERTILITY TREATMENT. Robin A. Frankel, M.D.; Victoria Timmel, B.S.; Alexandra Peser, M.D.; Baruch Abitan, M.D.; Christine Mullin, M.D.; Randi H. Goldman, M.D. 1 Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; 2 Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY; 3 Northwell Health Fertility, Zucker School of Medicine at Hofstra Northwell, Manhasset, NY; 4 Northwell Health Fertility, Northwell Health, Manhasset, NY.

OBJECTIVE: Cancer diagnoses are associated with high medical expense; the addition of infertility treatment adds great financial burden. A new diagnosis often requires immediate evaluation, preventing time to plan financially. This study explores the use of crowdfunding (CF) to offset the cost of fertility treatments in cancer patients.

MATERIALS AND METHODS: Cross-sectional analysis of campaigns launched on the CF website, GoFundMe®, for patients seeking infertility care as a result of cancer diagnoses. Campaigns were collected by searching the addition of infertility treatment adds great financial burden. A new diagnosis often requires immediate evaluation, preventing time to plan financially. This study explores the use of crowdfunding (CF) to offset the cost of fertility treatments in cancer patients.

OBJECTIVE: Cancer diagnoses are associated with high medical expense; the addition of infertility treatment adds great financial burden. A new diagnosis often requires immediate evaluation, preventing time to plan financially. This study explores the use of crowdfunding (CF) to offset the cost of fertility treatments in cancer patients.
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IMPACT STATEMENT: CF is an important tool for obtaining financial and social support in cancer patients seeking infertility treatment.

IMPACT OF FERTILITY PRESERVATION INSURANCE MANDATES ON UTILIZATION RATES. Khaila Ramsey-Collier, BS,1 Benjamin J. Peipert, MD,2 Tracy Truong, MS,3 Kelly S. Acharya, MD4 1Chapel Hill, NC; 2Duke University Medical Center, Durham, NC; 3Department of Biostatistics & Bioinformatics, Duke University Medical Center, Durham, NC; 4Duke Fertility Center, Morrisville, NC.

OBJECTIVE: To assess the impact of the 2017 fertility preservation (FP) insurance mandates in Rhode Island (RI) and Connecticut (CT) on FP utilization rates.

MATERIALS AND METHODS: FP cycle information was gathered from the 2016 and 2019 Assisted Reproductive Technology Fertility Clinic and Outcomes Reporting (ART FCOR) database of assisted reproductive technology (ART) procedures reported at the 2016 and 2019 ART cycles. National census data was acquired from the United States Census Bureau to calculate utilization rates per 100,000 reproductive-age women (ages 15-44). Change in FP cycle number from 2016-19 was compared to the non-FP autologous IVF growth seen over the same time frame. Chi-squared tests were performed to determine whether there were significant differences in percent change of FP utilization in RI and CT compared to other states (without FP mandates implemented in the time period of interest), accounting for overall increase in IVF utilization over time.

RESULTS: FP and autologous IVF utilization for the years 2016 and 2019 are reported in Table 1. Between 2016 and 2019, the FP cycle utilization increased by 108% and 86% in RI and CT, respectively, compared to 64% in all other states; however, this difference was not statistically significant (p=0.5 and p=0.2, respectively). Meanwhile, between 2016 and 2019, autologous non-FP IVF utilization increased by 63% and 79% in RI and CT, less than the growth seen in FP cycles in the same states.

CONCLUSIONS: Two states that implemented FP insurance mandates in 2017, RI and CT, demonstrate higher levels of post-mandate growth in fertility preservation cycles compared to all other states and compared with the non-FP autologous IVF growth seen over the same time frame.

IMPACT STATEMENT: Advocacy efforts have led to the passage of FP legislation in 10 states since 2017. State-mandated insurance coverage of FP for patients at risk for iatrogenic infertility results in increased FP cycle utilization relative to overall growth in IVF utilization. These findings have important implications for other states considering FP mandates.

Table 1: GoFundMe® Campaigns by US Geographic Region

<table>
<thead>
<tr>
<th>Region</th>
<th># of campaigns</th>
<th>$ amount requested (SD)</th>
<th>% that reached goal</th>
<th># of comments</th>
<th># of donors</th>
<th>Top $ donation (SD)</th>
<th>% of goal attained (SD)</th>
<th>% that reached goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>182</td>
<td>20,553 (22,426.7)</td>
<td>19.2 (6.61)</td>
<td>13.8 (22.1)</td>
<td>89.7 (78.3)</td>
<td>11,000</td>
<td>55.6 (0.61)</td>
<td>19.2</td>
</tr>
<tr>
<td>NE</td>
<td>196</td>
<td>24,753 (26,389.3)</td>
<td>30.6 (5.45)</td>
<td>23.0 (33.2)</td>
<td>146.3 (151.2)</td>
<td>15,000</td>
<td>69.7 (0.54)</td>
<td>30.6</td>
</tr>
<tr>
<td>W</td>
<td>305</td>
<td>10,770 (14,229.6)</td>
<td>17.0 (3.0)</td>
<td>17.3 (30.2)</td>
<td>111.0 (141.3)</td>
<td>11,847</td>
<td>55.2 (0.55)</td>
<td>17.0</td>
</tr>
<tr>
<td>Other</td>
<td>267</td>
<td>12,764 (16,236.1)</td>
<td>16.9 (2.4)</td>
<td>20.4 (43.4)</td>
<td>111.2 (139.8)</td>
<td>30,000</td>
<td>56.5 (0.60)</td>
<td>16.9</td>
</tr>
</tbody>
</table>

Note: *p-value < 0.05.

The table above shows the impact of fertility preservation insurance mandates on utilization rates across different regions in the US, highlighting the increased usage of FP cycles in regions where mandates have been implemented.

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IDENTIFYING BARRIERS TO FERTILITY PRESERVATION AND PATTERNS OF SELECTION AMONG INFANT ONCOLOGY PATIENTS. Virginia-Arlene Acosta Go, MD, Lindsay Hartup, M.D., Randal D. Robinson, MD UT Health San Antonio, San Antonio, TX.

OBJECTIVE: To identify missed opportunities and barriers in fertility preservation (FP) counseling and treatment in a pediatric/adolescent oncology patient population.

Table 1: FP and Autologous IVF Utilization in 2016 and 2019

<table>
<thead>
<tr>
<th>Year</th>
<th>FP Cycles</th>
<th>Cycles per 100,000*</th>
<th>% change</th>
<th>CT Cycles</th>
<th>Cycles per 100,000*</th>
<th>% change</th>
<th>Other States</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>13</td>
<td>6.2</td>
<td>108%</td>
<td>154</td>
<td>22.9</td>
<td>0.217</td>
<td>13765</td>
</tr>
<tr>
<td>2019</td>
<td>27</td>
<td>12.9</td>
<td>107%</td>
<td>286</td>
<td>42.7</td>
<td>0.86</td>
<td>22580</td>
</tr>
</tbody>
</table>

Autologous IVF Utilization

<table>
<thead>
<tr>
<th>Year</th>
<th>Cycles</th>
<th>Cycles per 100,000*</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>530</td>
<td>254.4</td>
<td>63%</td>
</tr>
<tr>
<td>2019</td>
<td>862</td>
<td>413.3</td>
<td>62%</td>
</tr>
</tbody>
</table>

Note: *p-value < 0.05.
RESULTS: A total of 58 patients met inclusion criteria, of which 19 (33%) received REI consultation. Females were more likely to receive a REI consult than males (OR 0.21, 95% CI 0.06-0.65, p-value < .006) and more likely to elect a FP option after consult (OR 0.04 95% CI 0.003 - 0.46, p-value <0.004). 11 of 12 (92%) female elections were ovarian suppression with GnRH agonists. Patients over age 16 were more likely to receive a REI consult than younger patients (OR 0.18 95% CI 0.04-0.80, p-value = 0.03); however all patients under 16 who did receive a consult, proceeded with a FP election. There was no difference in the number of patients receiving a REI consult between privately insured and Medicaid patients. However, after consultation, privately insured patients were more likely to elect FP than Medicaid patients (p-value < 0.001). There was no difference in race or language preference in those electing FP versus those who did not. Overall patients were more likely to proceed with FP if they received a REI consult than if there was no documented consult (OR 40.08, 95% CI T 3.72-192, p-value <.0001). The average time from diagnosis to REI consult was 1.9 days and the average time from REI consult to chemotherapy start was 3.8 days. CONCLUSIONS: In this study, REI consults were underutilized by the inpatient pediatric oncology service, though the majority of patients who received consults, elected a FP option. Female patients, older patients and privately insured patients were more likely to receive a consult and proceed with a FP consultation with GnRH agonist was the most common election, likely due to the inpatient setting and 3.8 day average from consult to chemotherapy start. There was no significant difference in REI consultation and ultimately FP election based on race or primary language. IMPACT STATEMENT: We have identified that younger patients, males and those without private insurance are particularly vulnerable to exclusion from the FP discussion and election. Despite national guidelines to recommend FP counseling prior to chemotherapy start, many patients in our center did not receive REI consultation, providing opportunity for improvement.

FERTILITY INTENTION AND RELATED FACTORS FOR HAVING A SECOND OR THIRD CHILD AMONG CHILDBEARING COUPLES IN SHANGHAI, CHINA. Chenfeng Zhu, BD, Li Yan, BD, Chuing He, BD, Jian Zhang, MD Shanghai, China; 2International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, China; 3Shanghai, China, Shanghai; 2International Peace Maternity and Child Health Hospital, School of Medicine.

OBJECTIVE: This study serves to evaluate fertility intention rates and related factors in couples intending to have a second or third child. MATERIALS AND METHODS: Couples who have had a first or second child were selected in the above prospective cohort to investigate the fertility intention of the second and third child and the related factors that may affect the fertility intention. The fertility intention rates of second and third births were analyzed, and the factors affecting fertility intention were analyzed using univariate and multivariate logistic regression.

RESULTS: Data was collected from a total of 1026 couples. Among couples with one child, 130 (16.2%) couples had the intention to have a second child. Additionally, only 9.4% of couples with two children desired to have third child. The study revealed large differences in socioeconomic and personal factors between the two groups. For couples with intentions for a second-child, a female age greater than 35 years (aOR 1.92[1.27-2.91]), a first child’s age range 3 to 6 years (aOR 3.12[1.9-8.17]), annual child spending as a percentage of household income greater than 30% (aOR 2.62[1.17-6.95]) were associated with lack of intent to have a second child. Similarly, among couples with two children, parents with family financial constraints (aOR 6.18[1.80-21.22]) and children’s educational barriers (aOR 4.93 [1.34-18.14]) are more likely to have lack of intent to have a third child.

Here, we report that government policies encouraging fertility (second child : aOR 1.69[1.06-2.70]; third child : aOR 37.34[7.86-177.36]) can effectively promote couples to pursue a second or third child. CONCLUSIONS: Overall, couples with one or two children in Shanghai had a low intention to give birth to a second or third child. In order to increase the birth rates, it is necessary to implement policies to reduce the burden of raising children and provide relief to parent’s pressure of rearing a child with increased free time. IMPACT STATEMENT: The decision of fertility intention is influenced by female age, the first child’s age, family economic conditions, children’s education and national fertility policies. It is necessary to take measures to reduce the burden of raising children and increase free time for couples to relieve parent’s pressure of rearing a child.

SUPPORT: This work was supported by National Key Research and Development Program (grant number 2018YFC1002102) and Shanghai Municipal Key Clinical Specialty, Shanghai, China (grant number shslczdzk1802).

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LIVE BIRTH FOLLOWING IVF PREGNANCY IN A TRANSGENDER MAN OF ADVANCED PATERNAL AGE WITH A HISTORY OF PROLONGED TESTOSTERONE USE. Austin Johnson, M.D., Janine Baldino, M.D., Mary Carolyn Peavey, B.S., M.D.1 University of North Carolina at Chapel Hill, Chapel Hill, NC; Durham, NC.

OBJECTIVE: Little is known about optimal IVF protocols and pregnancy outcomes in transgender men seeking fertility after long-term utilization of exogenous testosterone. Of limited studies reporting ART outcome, the majority study trans men with no or limited testosterone exposure and most culminate in reciprocal transfer to a cisgender female partner. Limited data exists on pregnancy outcomes in transgender men who carry a pregnancy derived from their own oocytes but existing studies suggest a higher risk of pregnancy-associated morbidity including preterm delivery. Our objective was to add to this important but limited body of evidence.

MATERIALS AND METHODS: We present a case of a 38 year old transgender man with a 16 year history of testosterone use who undergoes IVF to conceive and carry a pregnancy derived from his own oocytes with his cisgender male partner.

RESULTS: Following discontinuation of testosterone 8 months prior to seeking REI consultation, he underwent controlled ovarian hyperstimulation using a GnRH antagonist protocol, resulting in retrieval of 19 oocytes. 11 out of 14 mature oocytes were successfully fertilized (79% fertilization rate) via intracytoplasmic sperm injection using the partner’s sperm. 7 blastocysts resulted after embryo culture (64% blastulation rate). Following two prior failed double embryo transfers, a third frozen embryo transfer of two day 6 embryos resulted in conception of a diamniotic, dichorionic twin intrauterine pregnancy. He delivered boy-girl twins at 26 weeks via classical cesarean delivery, discharged to PPROM followed by preterm labor. Their infants were discharged from the NICU after 106 days (Twin A) and 115 days (Twin B) and are now healthy 6-month-olds.

CONCLUSIONS: This case supports retrospective data in transmen demonstrating comparable ovarian stimulation and embryological outcomes yet adverse pregnancy and obstetrical outcomes. Despite his much longer duration of testosterone exposure and advanced paternal age, ovarian stimulation and embryological outcomes were similar in our patient compared to previous reports of transgender men undergoing IVF. Autologous embryo transfer resulted in a viable twin pregnancy, complicated by PPROM and preterm birth at 26 weeks. Reproduction of findings in further study would lend credence to these implied associations.

IMPACT STATEMENT: Fertility outcomes in this transgender man support a small but growing body of literature that testosterone does not markedly impair ovarian reserve or response to stimulation. Of note, this case calls into question whether treatment guidelines, including those for embryo transfer, developed for cisgender females also confer optimal care to a growing population of transgender men.

REFERENCES:
CUMULATIVE LIVE BIRTH RATES (CLBRS) FROM FROZEN AUTOLOGOUS OOCYTES (AOS): LARGEST COHORT OF PLANNED OOCYTE CRYOPRESERVATION (OC) THAWS FROM A SINGLE CENTER IN THE UNITED STATES. Carlos M. Parra, MD,1 Sarah D. Cascante, MD,1 Jennifer K. Blakemore, MD, MSc,1 Shannon DeVore, MD,1 David H. McCullough, PhD,2 James A. Grifo, MD, PhD2 NYU Grossman School of Medicine, New York, NY;3 NYU Langone Fertility Center, New York, NY.

OBJECTIVE: Planned OC is increasing; yet, there is a lack of thaw data to provide an accurate estimate of CLBR. We reviewed our AO thaw outcomes to determine CLBR by age and #AOS.

MATERIALS AND METHODS: We reviewed AO thaws at our academic center from 2004-2021. Inclusion criteria: 1) ≥ 1 live birth (LB)/ongoing pregnancy (OP) >12 weeks, or 2) all AOs + embryos from OC consumed. Exclusion criteria: 1) OC for a medical reason, due to lack of sperm or a natural disaster, combined with embryos or for gestational carrier use, or 2) AO/embryos from OC transported out before a LB. Primary outcome was CLBR (LB + OP). Patients (pts) were stratified by age and #AOs or metaphase II oocytes (M2s) thawed. If pts had ≥ 1 OC cycle, we calculated a weighted age: [Σ (#AOS thawed × age at OC)] / [Σ (#AOS thawed)]. Statistics included multiple logistic regression (MLR), Fischer’s exact test, and chi-squared test (p < 0.05 significant).

RESULTS: 548 pts (median age at OC 38y, range 28-45y; 151 weighted ages used) underwent 767 OC (location: 90% our center, 9% elsewhere, 2% both; method: 77% vitrification, 4% slow cooling, 19% both), 604 thaw and 465 trans- fer cycles. 40% (n = 220) of AOs were thawed (p < 0.13) or M2s (p = 0.17). For pts with any # or > 20 AO/M2s thawed, CLBR was higher in pts <38y than ≥38y vs. pts ≥38y. If pts had ≥ 1 OC cycle, we calculated a weighted age: [Σ (#AOS thawed × age at OC)] / [Σ (#AOS thawed)]. Statistics included multiple logistic regression (MLR), Fischer’s exact test, and chi-squared test (p < 0.05 significant).

CONCLUSIONS: CLBR increases as more AO/M2s are thawed. OC at <38y has a CLBR of ~50%, a reasonable rate in younger pts at an ideal age for OC.

IMPACT STATEMENT: Pts who freeze >20 AOs at <38y can expect ≥ 70% CLBR based on actual outcomes. This is the largest report to date of AO thaw outcomes from a single U.S. center.

REFERENCES:
OBJECTIVE: Uterine transposition may be the only choice to preserve uterine function for a woman receiving pelvic irradiation. This study is aimed to report the short-term outcome of a rectal cancer patient who underwent uterine transposition before radiation and chemotherapy.

MATERIALS AND METHODS: We retrospectively evaluated a patient with rectal cancer. This patient had uterine transposition for fertility sparing prior to pelvic irradiation.

RESULTS: A 29-year old woman was diagnosed with stage 2 (cT3N0, pT3N0, resection margin positive, signet ring cell type) rectal cancer and had low anterior resection. Pelvic radiotherapy was planned because the anal side resection margin and pararectal fat was positive for cancer cells. The multidisciplinary oncology team decided to perform uterus and ovarian transposition before radiotherapy because the patient wanted to preserve both her uterine function and anal sphincter. Uterine and both ovary transposition were performed as follows. The left ovary was moved to the anterior left pelvic wall 4-centimeter(c) below the umbilicus level with the uterus. The right ovary was moved to high in the right paracolic gutter. Uterine fundus was fixed at just below umbilicus with the vaginal connection. From postoperative day 7, the patient received Intensity-modulated radiotherapy with simultaneous integrated boost (IMRT-SIB), 44 Gy at 2.2 Gy per fraction to the whole pelvis and 50 Gy at 2.5 Gy per fraction the tumor bed by integral boost. She undertook surgery to retrieve a part of the ovary to a normal position. She had a regular menstruation cycle during and after radiotherapy. Last vaginal bleeding was observed after GnRH agonist injection for ovarian protection from chemotherapy.

CONCLUSIONS: Uterine transposition may be a promising fertility preservation option for patients who require pelvic or abdominal radiotherapy.

IMPACT STATEMENT: This is the first case of preserving both uterine and anal sphincter function in stage 2 rectal cancer patient. Uterine transposition may provide better fertility sparing opportunities to cancer patient.

E-POSTER ABSTRACT SESSION: T9

P-301 6:45 AM Tuesday, October 25, 2022

INCIDENCE OF FERTILITY PRESERVATION PROCEDURES IN PREPUBERTAL INDIVIDUALS WITH CANCER. Joshua Theodore White, MD,1 Jesse Ory, MD,2 Ranjith Ramasamy, M.D.1 1Dalhousie University, Halifax, NS, Canada; 2Dalhousie University, Halifax, Canada; 3University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Fertility Preservation (FP) for children and adolescents with cancer is underutilized. In prepubertal individuals, ovarian and testicular tissue can be frozen; however, this is still considered largely experimental. Our objective was to identify trends of FP in prepubertal individuals.

MATERIALS AND METHODS: We performed a retrospective study of prepubertal children with cancer identified through the Pediatric Health Information System from 2011 to 2020. Children who underwent a testicular or ovarian biopsy were included. Any patients with testicular or ovarian malignancy, or other diagnoses which may have required a gonadal biopsy were excluded.

RESULTS: A total of 418 boys under 13 and 333 girls under 12 who underwent a gonadal biopsy were identified. There was a total of 66929 new cancer diagnoses in girls and 86001 new cancer diagnoses in boys during this time. The most common cancer diagnosis was hematologic in both boys (50.96%) and girls (36.64%). A concurrent procedure at time of gonadal biopsy was performed in 84% of boys and 62% of girls, with line insertion being the most common. The only predictive variable of receiving a gonadal biopsy was increasing year. Overall, only 0.04% of children had a gonadal biopsy for FP during this time period.

CONCLUSIONS: Gonadal biopsy rates have increased in prepubertal children with cancer, presumably for FP. While recent international guidelines support FP in this group, our findings highlight the need to establish protocols and tracking for FP procedures in the US.

IMPACT STATEMENT: This project addresses a large gap that exists in fertility preservation knowledge and practices in the US. This study helps build awareness of oncofertility and can help develop standardized protocols for oncofertility in pediatric patients.

Table 1: Descriptive Data of Males and Females Undergoing FP Procedure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Male &lt;13 (n=418)</th>
<th>Female &lt;12 (n=333)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>8.3 ± 4.7</td>
<td>8.8 ± 5.3</td>
</tr>
<tr>
<td>Cancer type, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematologic</td>
<td>213 (51.0)</td>
<td>122 (47.9)</td>
</tr>
<tr>
<td>Brain/Spinal Cord</td>
<td>57 (13.6)</td>
<td>29 (8.7)</td>
</tr>
<tr>
<td>Urologic</td>
<td>31 (7.4)</td>
<td>38 (11.4)</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>46 (11.0)</td>
<td>74 (22.2)</td>
</tr>
<tr>
<td>Non-neurologic solid abdominal tumor</td>
<td>0 (0.0)</td>
<td>65 (19.5)</td>
</tr>
<tr>
<td>Other</td>
<td>41 (9.8)</td>
<td>37 (11.1)</td>
</tr>
<tr>
<td>Chemotherapy, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conventional procedure, n (%)</td>
<td>363 (86.4)</td>
<td>322 (96.4)</td>
</tr>
<tr>
<td>Chemotherapy device insertion</td>
<td>351 (84.0)</td>
<td>208 (62.1)</td>
</tr>
<tr>
<td>Bone marrow biopsy, aspiration or extraction</td>
<td>231 (54.9)</td>
<td>134 (40.0)</td>
</tr>
<tr>
<td>Stem cell/bone marrow transfusion/ transplant</td>
<td>94 (22.3)</td>
<td>33 (9.8)</td>
</tr>
</tbody>
</table>

SUPPORT: This work was supported by the National Institutes of Health Grant R01 DK130991 and Clinician Scientist Development Grant from the American Cancer Society to RR.

P-302 6:45 AM Tuesday, October 25, 2022

RANDOM-START PROTOCOL IS EFFECTIVE IN ONCOFERTILITY PATIENTS. Nafisee Yilmaz, Prof Dr.,1 Banu Seven, MD,2 Mehmet Caner Ozer.1 1University of Health Science Turkey, Ankara City Hospital, Ankara, Turkey; 2Ankara City Hospital, Ankara, Turkey; 3Ankara City Hospital, Ankara, Ankara, Turkey.

OBJECTIVE: The aim of this study was to compare the success rates of random start controlled ovarian stimulation (RS-COS) and conventional start (CS-COS) for fertility preservation prior to gonodotoxic therapy in cancer patients in terms of oocyte output.

MATERIALS AND METHODS: This is a retrospective study planned between January 2020 and November 2021 in the ART Department of Ankara City Hospital. The study consisted of 21 newly diagnosed cancer patients who underwent emergent fertility preservation (FP) prior to gonodotoxic therapy. RS-COH was performed in 13 patients (group 1) and CS-COS was performed in 8 patients (group 2). Age, antral follicle count and hormone profile of all patients were recorded before treatment. Stimulation was performed with GnRH antagonist protocol to all patients. Final oocyte maturation was triggered with GnRH agonist when at least 1–2 follicles reached a mean diameter of ≥18 mm and 34–36 h later follicles were aspirated under sedation in all patients. The primary outcome measures were total oocyte count and mature oocyte rate (MOR), which are indicative of oocyte output. Independent sample t-test and Mann Whitney U Test was applied to compare the values between groups. A p value of <0.05 was considered statistically significant.

RESULTS: The most common cancer type was breast cancer with ten patients, followed by five patients with ovarian tumor, four patients with lymphoma, one patient with colon cancer and one patient with liposarcoma. Ages were similar between two groups [72.6 ± 8.27 (13-44) vs 77 ± 5.37 (18-35)]. Body mass index, AMH, basal FSH, estradiol, and antral follicle count were similar between groups. An aromatase inhibitor was administered to 10 patients in group 1, and 3 patients in group 2. Although the peak estradiol levels were similar between the groups, they were found to be statistically significantly lower in patients administered AI compared to patients who did not (297 vs 1124, p = 0.01). Stimulation duration and total oocyte count were similar between groups. The total gonadotropin dose used was higher in RS-COS than CS-COS, and the difference was statistically significant (2116.23 vs 1527.38, p = 0.026). Mean MII oocyte count was 9.31 ± 6.22 in group 1 and 7.25 ± 2.87 in group 2 and no statistically significant difference was found (p = 0.393). The mean MOR was found to be 79.87 ± 18.15 % in group 1 and 66.21 ± 18.91 % in group 2, and there was no statistically significant difference between the two groups.

CONCLUSIONS: According to our results, there was no difference between two groups in terms of stimulation time, number of retrieved oocytes and MOR. RS-COS resulted in a similar number of cryopreserved oocytes compared to CS-COS and should be considered a valid option for initiating ovarian stimulation in cancer patients.

IMPACT STATEMENT: This study contributes to other studies in the literature by confirming the effectiveness of RS-COS. Delays in the treatment of cancer patients can prevented by starting the stimulation at any phase of the cycle.
DOES BRCA 1/2 CARRIER STATUS EFFECT OOCYTE CRYOPRESERVATION OUTCOMES? Niral Jain, BA, MD, Jenna Reich, MD, Alison Pruzan, MD, Mary Elizabeth Fino, M.D., David H. McCallough, PhD, Jennifer K. Blakemore, MD, MS, NYU Langone Fertility Center, New York, NY; NYU Grossman School of Medicine, New York, NY.

OBJECTIVE: To evaluate differences in oocyte cryopreservation (OC) in BRCA 1/2 patients with and without cancer diagnoses compared to controls who underwent elective cryopreservation.

MATERIALS AND METHODS: This was a single-center retrospective cohort study of BRCA mutation carriers who presented for fertility preservation. A data query was performed to identify all patients who were referred to our academic center from 2006-2022 to discuss fertility preservation in the setting of known BRCA 1/2-carrier status with or without cancer diagnosis. BRCA 1/2 carriers without cancer (Group A), with cancer (Group B) and controls (Group C) were included in the study.

RESULTS: Of 242 BRCA 1/2 carriers who were referred to our center for fertility consultation, 103 underwent ART cycles, of which 38 completed at least one OC cycle (21 BRCA1, 17 BRCA2), with a total of 49 OC cycles within the study group. 7 BRCA 1/2 carriers had breast cancer at time of OC (2 BRCA1, 5 BRCA2).

There was no significant difference between median numbers of oocytes retrieved amongst groups (A: 18, B: 20, C: 16, p=0.93). Oocyte maturity also did not vary significantly between groups (A: 74.4 ± 13.5%, B: 57.3 ± 24.8%, C: 73.4 ± 18.1%; p=0.3). BRCA 1/2 carriers without cancer had a higher rate of M1 oocytes compared to cancer and control groups (A: 8.9 ± 10.4%, B: 4.5 ± 4.8%, C: 4.7 ± 8.9%; p=0.02). Furthermore, BRCA1/2 carriers with and without cancer had a significantly higher percent of GV oocytes (A: 8.6 ± 11.6%, B: 10.8 ± 11.4%, C: 0.2 ± 0.48%; p=0.001) compared to controls.

Mean AMH was significantly lower in BRCA 1/2 patients with cancer compared to those without and controls (A: 3.8 ± 2.4, B: 1.5 ± 1.9, C: 3.2 ± 2.6 ng/mL; p=0.04). There was no significant difference in median number of stimulation days and cumulative dose of exogenous FSH and hMG administered during stimulation. Data was analyzed using Kruskal-Wallis analysis and Mann Whitney test. A p-value < 0.05 was considered statistically significant.

CONCLUSIONS: BRCA1/2 carrier status does not compromise stimulation cycle characteristics or oocyte maturity rate. Although BRCA1/2 carriers with and without cancer at time of cycle had higher rates of M1 and GV oocytes per OC cycle, they had similar maturity rates overall compared to controls. IMPACT STATEMENT: BRCA1/2 carriers should be encouraged to pursue fertility preservation as they are interested. BRCA status and/or active breast cancer diagnosis do not negatively impact cycle characteristics or oocyte maturity potential.

ANXIETY AND DISTRESS IN YOUNG NEWLY DIAGNOSED CANCER PATIENTS DECREASE AFTER A FERTILITY PRESERVATION CONSULT. Ange Wang, MD, Flor Juarez-Hernandez, BA, Gabriela Gutierrez, BA, Mary Kathryn Kathryn Abel, AB, Joseph M. Letourneau, MD, Evelyn Mok-Lin, M.D., Mitchell P. Rosen, MD, HCLD, University of California, San Francisco, San Francisco, CA; UCSF, SAN FRANCISCO, CA; University of California San Francisco, San Francisco, CA; UC, San Francisco, CA; University of Utah, Salt Lake City, UT.

OBJECTIVE: To determine if a fertility preservation consultation is associated with anxiety and distress among an oncology cohort, and if these levels differ based on fertility preservation status.

MATERIALS AND METHODS: Oncofertility patients were followed as part of the Medical Decision Making (MDM) study at a single academic center. All participants had an initial fertility consultation, and some chose to pursue fertility preservation after their consultation. The surveys were administered at the following time points: Survey 1 (after diagnosis but prior to oncology consultation), Survey 2 (immediately after oncology consultation), and Survey 3 (approximately 2 years after oncology consultation). Anxiety and distress scores were reported on a scale of 0-60. A student t-test and Wilcoxon rank-sum test were used to compare scores before and after oncology consultation, as well as longitudinally from baseline to 2 years. These scores were also segmented by fertility preservation status.

RESULTS: A total of 348 oncology patients completed the initial survey prior to a fertility consultation. 180 completed a survey immediately after the consultation, and 106 have completed the survey at 2 years. In this cohort, 244 (56.6%) underwent fertility consultation. In our cohort, the average age was 33.9 (SD 5.9) years, with the majority of respondents reporting nulligravid and nulliparous status (65.2% and 63.3% respectively). 80.4% reported college degree or higher and 41.1% reported income greater than $100k. In regards to relationship status, 27.2% of respondents were single, 58.0% were partnered but not married, and 34.8% were married. Raw anxiety and distress scores over the 3 time points did not differ by fertility preservation status, with the only exception being baseline anxiety which was significantly higher in the group that underwent fertility preservation (65.7 vs 57.4; p=0.007). Anxiety and distress scores were significantly lower after fertility preservation consultation (62.8 vs 50.6 and 52.7 vs 44.2 respectively, p<0.001), regardless of whether or not patients chose to pursue fertility preservation. Anxiety and distress also decreased after two years compared to baseline (56.0 vs 40.9 and 49.5 vs 28.3 respectively, p<0.01), though sample size was limited to assess those who did not undergo fertility preservation.

CONCLUSIONS: Newly diagnosed cancer patients of reproductive age have a high level of anxiety which can be partially reduced after fertility preservation consultation. In our oncology cohort, anxiety and distress scores decreased after both fertility consultation (regardless of fertility preservation status) and 2 years post-consult compared to baseline.
IMPACT STATEMENT: Anxiety and distress is significantly lower among oncofertility patients after a fertility preservation consult, regardless of whether or not patients choose to pursue fertility preservation. Anxiety and distress were also significantly lower at year 2 compared to baseline. All oncofertility patients should be offered a consult to allow them the choice to pursue fertility preservation.

Table 1

<table>
<thead>
<tr>
<th>Centers by Specific Exclusion Criteria</th>
<th>Number of centers</th>
<th>Number of centers in states with FP insurance mandates</th>
<th>Centers by US Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncofertility Centers</td>
<td>370 (81.1%)</td>
<td>86 (18.9%)</td>
<td>Northeast</td>
</tr>
<tr>
<td>Non-Oncofertility Centers</td>
<td>147 (39.7%)</td>
<td>38 (44.2%)</td>
<td>Midwest</td>
</tr>
<tr>
<td>1: Zero FP cycles</td>
<td>62 (72.1%)</td>
<td>10 (11.6%)</td>
<td>South</td>
</tr>
<tr>
<td>2: No oocyte cryopreservation</td>
<td>26</td>
<td>6</td>
<td>West</td>
</tr>
<tr>
<td>3: No service for single women</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>4: No accredited lab</td>
<td>13</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*<p < .0001

OBJECTIVE: To compare the number of oocytes retrieved in oocyte/embryo banking cycles using Tamoxifen with traditional gonadotropins (Tam) vs. Aromatase Inhibitors with traditional gonadotropins (AI) vs. cycles with no adjuvant medications utilizing only traditional gonadotropins (NAM).

MATERIALS AND METHODS: Using the SART database, patients 18-43 years old with oocyte or embryo banking cycles who had a retrieval between 2016-2018 were analyzed. We compared the number of oocytes retrieved and cryopreserved in banking cycles utilizing either Tamoxifen (Tam), Aromatase Inhibitors (AI), or no adjuvant medications (NAM). A multivariable linear regression model with a generalized estimating equation (GEE) approach was used to test the association between adjuvant medications and number of oocytes retrieved while accounting for repeated cycles within a patient and adjusting for covariates (BMI, AMH, age, parity, smoking, ethnicity, history of infertility, and banking for gonadotoxic treatment).

A sensitivity analysis of banking cycles indicated due to gonadotoxic treatments and number of oocytes cryopreserved was similar.

CONCLUSIONS: Aromatase Inhibitor cycles had similar oocyte yield compared to that of NAM cycles. This is likely of minimal clinical significance as the number of oocytes cryopreserved was similar.

OBJECTIVE: To identify fertility centers capable of offering fertility preservation (FP) to patients with cancer and other fertility-threatening conditions within the United States (US) and compare practice characteristics and geographic distribution of fertility centers with and without the capacity to offer FP services.

MATERIALS AND METHODS: All centers reporting assisted reproductive technology (ART) cycles in the US were identified through the 2018 CDC Fertility Clinic Success Rates Report. “Oncofertility centers” were defined as those meeting 4 criteria: (1) offered embryo and oocyte cryopreservation; (2) performed >0 ART cycles for FP (“FP cycles”) in 2018; (3) offered services to single women; and (4) had an accredited laboratory. Baseline characteristics were compared between oncofertility centers and those not meeting criteria (“non-oncofertility centers”) using two-sample t-tests for continuous variables and chi-square tests for categorical variables at a two-tailed significance level of p < 0.05.

RESULTS: Among 456 centers, 370 (81.1%) met criteria as an oncofertility center. Practice characteristics of oncofertility centers are displayed in Table 1. Most non-oncofertility centers were excluded as they lacked an accredited laboratory and historical performance of FP cycles. Compared to non-oncofertility centers, oncofertility centers performed 5x as many ART cycles (p < .0001) and 12x more FP cycles per center (p < .0001). When evaluating geographic distribution, neither region of the US nor presence of a state FP insurance mandate was associated with designation as an oncofertility center.
CONCLUSIONS: Nearly one in five centers reporting ART cycles do not qualify as an oncofertility center, most due to lack of an accredited laboratory or experience performing FP cycles.

IMPACT STATEMENT: Identification of centers capable of offering FP is critical to expanding access. Additional incentives and support are needed for expansion of oncofertility services at existing centers and development of new oncofertility centers.

P-308 6:45 AM Tuesday, October 25, 2022

SUBSTANTIAL VARIABILITY IN OVARIAN CONSERVATION AT HYSTERECTOMY FOR ENDOMETRIAL HYPERPLASIA. Caroline Violette, MD,1 Koji Matsuo, MD, PhD,1 Rachel S. Mandelbaum, MD,2 Chelsey A. Harris, MD,3 Amin Tavakoli, MD,1 Maximilian Klär, MD,3 Donna Shoupe, MD,4 Lynda D. Roman, MD,5 University of Southern California, Los Angeles, CA; 4University of Freiburg; 5Keck School of Medicine.

OBJECTIVE: While ovarian conservation at hysterectomy for benign gynecologic disease has demonstrated mortality benefit in young patients, this benefit may be sustained up to age 65 years. There is a paucity of data regarding ovarian conservation in those with a diagnosis of endometrial hyperplasia, a premalignant uterine condition. The objective of the current study is to examine patient, hospital, treatment, and histology characteristics related to ovarian conservation at time of hysterectomy for endometrial hyperplasia.

MATERIALS AND METHODS: The National Inpatient Sample was retrospectively queried to examine patients aged ≤65 years with endometrial hyperplasia who had hysterectomy from January 2016 to December 2019. Exclusion criteria included concurrent gynecologic malignancy, adnexal pathology, or lymphadenectomy. Cases were grouped by adnexal surgery status (ovarian conservation or oophorectomy). A multivariable binary logistic regression model was used to identify independent characteristics for ovarian conservation. A classification-tree was constructed with recursive partitioning analysis to examine utilization patterns of ovarian conservation.

RESULTS: A total of 3,105 (31.1%) patients underwent ovarian conservation at hysterectomy among 9,975 patients. Utilization of ovarian conservation decreased in a gradual fashion until age 45 years, then earlier than in patients undergoing benign hysterectomy. There was substantial variability in ovarian conservation at hysterectomy for endometrial hyperplasia based on patient, hospital, surgical, and histology factors, suggesting the possible benefit of clinical practice guidelines for ovarian conservation in this population.

IMPACT STATEMENT: The decreased utilization of ovarian conservation in patients in their mid-40s is clinically relevant and suggests the need for updated treatment guidelines for patients undergoing surgical management of endometrial hyperplasia to determine appropriate candidates for ovarian conservation.

P-309 6:45 AM Tuesday, October 25, 2022

DO FERTILITY PRESERVATION OUTCOMES IN PATIENTS DIAGNOSED WITH LYMPHOMA DIFFER BASED ON CANCER AGE? B. S. ictoria Kocsuta, Shriya Shah, BA, Angela K. Lawson, Ph.D., Mary Ellen Pavone, MD Northwestern University Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: Conventional controlled ovarian hyperstimulation (COH) protocols for fertility preservation may take up to 4-6 weeks before cancer treatment. However, recently defined random-start COH protocols have been used successfully in urgent conditions. Given the increasing number of studies comparing outcomes between random-start COH and conventional COH, we conducted a meta-analysis reviewing the cycle outcome parameters, which mainly includes number of mature oocytes collected, number of frozen oocytes, and mature oocyte per antral follicle index (MII/AFC).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Stage 1 (n=8)</th>
<th>Stage 2 (n=21)</th>
<th>Stage 3 (n=5)</th>
<th>Stage 4 (n=9)</th>
<th>Unavailable (n=1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMH</td>
<td>1.72</td>
<td>2.81</td>
<td>0.94&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.00</td>
<td>2.40</td>
</tr>
<tr>
<td>Peak E&lt;sub&gt;2&lt;/sub&gt;</td>
<td>1278.76</td>
<td>1899.72</td>
<td>1244.00&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1848.01</td>
<td>1438.00</td>
</tr>
<tr>
<td>Total oocytes retrieved</td>
<td>14.13</td>
<td>16.76</td>
<td>13.00&lt;sup&gt;b&lt;/sup&gt;</td>
<td>17.00&lt;sup&gt;b&lt;/sup&gt;</td>
<td>17.00</td>
</tr>
<tr>
<td>Mature oocytes retrieved</td>
<td>8.88</td>
<td>12.10</td>
<td>9.20</td>
<td>17.44</td>
<td>15.00</td>
</tr>
<tr>
<td>Total oocytes frozen</td>
<td>6.88</td>
<td>8.29</td>
<td>11.00&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12.00&lt;sup&gt;a&lt;/sup&gt;</td>
<td>17.00</td>
</tr>
</tbody>
</table>

<sup>a</sup>median

CONCLUSIONS: We found no significant difference in number of retrieved, mature or vitrified oocytes between different cancer stages. There was also no difference in AMH levels in the different cancer stage groups. This suggests that even with advanced lymphoma, ovarian stimulation for freezing oocytes or embryos could still be a viable option.

IMPACT STATEMENT: This study suggests that even in higher stages of lymphoma, many patients respond to ovarian stimulation techniques and have a successful stimulation cycle. These findings in combination with improving cancer treatments make discussions about fertility preservation vital in patients of reproductive age.

P-310 6:45 AM Tuesday, October 25, 2022

RANDOM-START VERSUS CONVENTIONAL OVARIAN HYPERSTIMULATION FOR FERTILITY PRESERVATION IN FEMALE CANCER PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS. Murat Sonmezzer, M.D.,1 Yavuz Emre Sükür, M.D.,2 Can Ates, PhD,1 Koray Gökem Şançin, MD,1 Cem Demirel, Prof.,1 Meltem Sonmezzer, M.D.,1 Cem Somer Atabekoglu, M.D.2 1Ankara university school of medicine, Ankara, Turkey; 2Ankara University, University; 3Aksaray University; 4Ankara University, School of Medicine, Ankara, Turkey; 5Ateşhier Memorial IVF Center, Istanbul, Turkey; 6Private Clinic; 7TJOD, Turkey.

OBJECTIVE: Conventional controlled ovarian hyperstimulation (COH) protocols for fertility preservation may take up to 4-6 weeks before cancer treatment. However, recently defined random-start COH protocols have been used successfully in urgent conditions. Given the increasing number of studies comparing outcomes between random-start COH and conventional COH, we conducted a meta-analysis reviewing the cycle outcome parameters, which mainly includes number of mature oocytes collected, number of frozen oocytes, and mature oocyte per antral follicle index (MII/AFC).
MATERIALS AND METHODS: A literature search using MEDLINE, SCOPUS, EMBASE, Cochrane Library, and ClinicalTrials.gov was conducted for published research comparing cycle outcomes in random-start COH and conventional COH for fertility preservation in cancer patients. Primary outcomes of interest were numbers of oocytes and mature oocytes (MII) collected, and MII/AFC ratio. Studies were included if the following criteria were met: contained cohorts of random-start COH and conventional COH with outcome data regarding number of mature oocytes collected, number of oocytes frozen, or MII/AFC ratio. Data are presented as average number/percentage and standardized mean difference (SMD) with 95% confidence interval (CI) with fixed- or random-effects meta-analysis between cohorts of random-start COS and conventional COS protocols.

RESULTS: A total of 11 studies, including 1764 women, meeting the inclusion criteria were reviewed. Studies varied with respect to country of origin, and gonadotropin commencement time in random-start arm. Among all, nine were retrospective cohort studies and two were prospective observational studies. According to the data obtained from the studies included, age, body mass index, and antral follicle count were all similar between random-start and conventional COH cohorts. The duration of ovarian stimulation was significantly longer (SMD 0.35, 95% CI 0.09-0.61; P < 0.001), and total gonadotropin dose was significantly higher in random-start COH group compared to conventional COH group (SMD 0.23, 95% CI 0.06-0.40; P = 0.009). However, there were no differences in number of oocytes retrieved (SMD -0.02, 95% CI -0.25-0.20; P = 0.84), number of MII oocytes (SMD -0.17, 95% CI -0.55-0.20; P = 0.37), MII/AFC ratio (SMD -0.25, 95% CI -0.76-0.25; P = 0.33), and total number of frozen embryos (SMD 0.05, 95% CI -0.76-0.25 days; P = 0.67).

CONCLUSIONS: Data demonstrates that the duration of stimulation was longer and total gonadotropin consumption is higher in patients undergoing random-start COH compared to those undergoing conventional COH. However, total number of oocytes collected, MII oocyte yield, and MII/AFC ratio did not differ between random start COH and conventional COH protocols.

IMPACT STATEMENT: Random-start COH is a relatively quick procedure and successfully utilized in the setting of fertility preservation prior to gonadotoxic treatments. Random-start COH protocols are associated with similar IVF outcomes compared to conventional COH.

SUPPORT: None.

E-POSTER ABSTRACT SESSION: T10
P-311 6:45 AM Tuesday, October 25, 2022
CANCER PREDISPOSITION GENE MUTATIONS AND ONCOFERTILITY: PREVALENCE IN REPRODUCTIVE AGE CANCER PATIENTS AND EFFECTS ON OVARIAN RESERVE. Britanni Steinberg, BA,1 Wendy Kohlmann, MS, CGC,2 Douglas Fair, MD, MS,3 Anne Kirchhoff, PhD, MPH,4 Britton Trabert, PhD, MS,5 Corrine K. Welt, MD,6 Joseph M. Letourneau, MD7 Boca Raton, FL; 8 Huntsman Cancer Institute at the University of Utah, Salt Lake City, UT; 9 University of Utah, Salt Lake City, UT.

OBJECTIVE: Emerging evidence suggests pathogenic variants (PVs) in cancer risk genes may affect both oncofertility decision-making and ovarian reserve. However, the prevalence of PVs in the female oncofertility population is poorly understood. We assessed the prevalence of germline PVs in cancer risk genes among reproductive age females seeking oncofertility consultation, as well as the relationship between such PVs and pre-treatment ovarian reserve.

MATERIALS AND METHODS: We performed a retrospective chart review. We screened all patients who presented to a single academic REI clinic for female oncofertility consultation (years 2016-2022; n=236). Inclusion criteria included age <45 and new diagnosis of cancer. Patients with prior history of gonadotoxic cancer treatment were excluded. Charts were reviewed for age, cancer diagnosis; genetic testing (yes/no), results, and timing; and baseline serum anti-Mullerian hormone (AMH) levels. Descriptive statistics were used to evaluate the prevalence of PVs across cancer types. The association between PVs and AMH levels was assessed using an age-adjusted linear regression model.

RESULTS: A total of 172 patients met inclusion criteria (Table). Mean age was 28.1 ±7.1 years. Of these patients, 78 (45%) underwent germline genetic testing with 32 (41%) results available before oncofertility consultation. Seventeen PVs were found in 16 patients (20%). Fourteen patients (88%) had PVs associated with high or moderate cancer risk. There was no association between PVs and baseline AMH (3.43 vs 3.55 ng/mL, p = 0.81).

CONCLUSIONS: Half of reproductive age women with newly diagnosed cancer who seek oncofertility consultation underwent genetic testing for PVs. Of these patients, approximately 1 in 5 had a PV in a cancer risk gene. However, testing results were not available for majority of patients at the time of the oncofertility consult. There was no relationship between PV and AMH levels.

IMPACT STATEMENT: This is the first study to estimate the prevalence of PVs in cancer risk genes in a population of women with diverse cancer types in the oncofertility consult setting. Considering the high proportion of PVs in our population and the potential impacts of mutation status on oncofertility care, efforts should be made to improve access to genetic testing results prior to the consult.

Table 1.

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Number of patients</th>
<th>Patients tested</th>
<th>PV present</th>
<th>Gene name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>56</td>
<td>53</td>
<td>10</td>
<td>BRCA1 (3), BRCA2 (3), BRI1, RAD50*, RAD51D, TP53</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>13</td>
<td>3</td>
<td>1</td>
<td>CHEK2*, NF1*</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>6</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Gynecologic</td>
<td>31</td>
<td>10</td>
<td>3</td>
<td>BRCA1 (2), MSH2</td>
</tr>
<tr>
<td>Hodgkin’s lymphoma</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td>9</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>BRCA2, NTHL1*</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>15</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>11</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>172</td>
<td>78</td>
<td>16</td>
<td>17</td>
</tr>
</tbody>
</table>

*One patient with 2 PVs
Autosomal recessive cancer predisposition syndromes

FERTILITY & STERILITY®
RESULTS: RSCOH was initiated either in the late follicular (54%) or luteal phase (46%). The mean ages and serum AMH levels were similar between the groups (RSCOH vs SSCOH: 33.5 ± 4.8 vs. 33.1 ± 3.1 years; p = 0.65 and 2.7 ± 2.4 vs 2.4 ± 2.0 ng/ml; p = 0.63 respectively). Total dose of gonadotropins and but not the length of stimulation was significantly greater in the RSCOH group compared to SSCOH (3880 ± 159.7 IU vs 1956 ± 950.5 IU; p < 0.001 and 11.7 ± 2.5 days vs 10.6 ± 1.7 days; p = 0.07, respectively). The mean total oocytes 16.3 ± 7.3 vs 15.6 ± 7.9; p = 0.650), mature oocytes (11.0 ± 4.6 vs 10.1 ± 5.8; p = 0.479 respectively), maturity rate (72.5 ± 18.4 vs 67.8 ± 22.9; p = 0.333 respectively) and frozen embryos (7.2 ± 4.3 vs 7.7 ± 4.8; p = 0.708 respectively) were similar between RSCOH vs SSCOH, respectively.

CONCLUSIONS: Our data indicate that the fertility preservation cycle outcomes with RSCOH are comparable to those with SSCOH. Further follow up and larger prospective studies are required to determine the pregnancy success rates of RSCOH in comparison to SSCOH cycles.

IMPACT STATEMENT: RSCOH is a valuable strategy for fertility preservation in women with breast cancer and it appears to have similar outcomes to SSCOH.

SUPPORT: NONE.

P-313 6:45 AM Tuesday, October 25, 2022
RNASEQ ANALYSIS OF FACS SORTED SPERMATOGONIAL CELLS USED TO IDENTIFY MELANOCORTIN RECEPTOR 2 AS A NOVEL AND FUNCTIONAL MEMBRANE-ASSOCIATED SPERMATOGONIAL STEM CELL MARKER. Mahmoud Huleihil, PhD, 1 Ali Abumagedhem, MSc, 2 Eitan Rubin, PhD, 2 Eitan Lunenfeld, MD, 2 Ben-Gurion University of the Negev, Beer-Sheva, Israel; 3 Ben-Gurion University of the Negev, Beer Sheva, Israel; 4 Faculty of Medicine, Ariel, Israel.

OBJECTIVE: Spermatogonial stem cell (SSC) transplantation is successful to restore fertility in sterile animal models. It is not safe in human since there is no precise methodology to isolate pure SSCs from cancer cells. Therefore, the purpose of this study is to identify a functional membrane-associate specific SSC markers.

MATERIALS AND METHODS: Sexually immature mice (7-day-old) were intraperitoneally injected with busulfan (45 mg/kg) or DMSO (as control). Ten days later, testes were removed, cells were enzymatically isolated from the seminiferous tubules (STs) and spermatogonial cells (Thyl, alpha-6-intigren and C-KIT) were sorted by FACS. RNA was extracted and used for RNaseq analysis. Immunofluorescence staining was used to localize melanocortin receptor 2 (MC2R)-positive cells in testes of immature and adult human and mice. The effect of adrenocorticotropic hormone (ACTH) – the ligand of MC2R- on the capacity of spermatogonial cells to develop spermatogenesis was performed in vitro using methylcellulose culture system (MCS).

RESULTS: RNaseq analysis showed a high expression of MC2R in Thyl and alpha-6-intigren-positive cells sorted from busulfan and DMSO-treated mice. MC2R-positive cells were localized in the periphery of the STs of human and mice at immature and adult ages. MC2R was doubled stained with known SSC markers. Addition of ACTH to isolated cells from STs in MCS significantly increased the percentages and the expression levels of pre-meiotic and meiotic/post-meiotic cells after 4 weeks of culture.

CONCLUSIONS: We identified, for the first time, using RNaseq analysis of FACS sorted spermatogonial cells, MC2R as a novel membrane-associated and functional SSCs marker.

IMPACT STATEMENT: This marker (MC2R) may be used to isolate SSCs from cancer patients to be considered in future fertility preservation strategies for perpubertal cancer boys.

P-314 6:45 AM Tuesday, October 25, 2022
UTILIZATION OF EMBRYOS AND EGGS CRYOPRESERVED PRIOR TO GONADOTOXIC TREATMENT: WHY ARE SOME WOMEN NOT RETURNING TO USING THEIR FROZEN EMBRYOS OR EGGS? Megan E. Gornet, MD, 1 Bronwyn S. Bedrick, MD, MSCI, 2 Jacqueline Yano Maher, MD, MA, 3 Mindy S. Christianson, MD 1 John Hopkins University School of Medicine, Baltimore, MD; 2 Johns Hopkins University, Baltimore, MD; 3 National Institute of Child Health and Human Development, Bethesda, MD; 4 Johns Hopkins Medical Institutions, Lutheranville, MD.

OBJECTIVE: A growing number of patients are referred for fertility preservation treatment (FPT) prior to gonadotoxic therapy. FPT options include embryo (EC), oocyte (OC) and ovarian tissue cryopreservation. Our objective was to examine future utilization of cryopreserved embryos and eggs in females undergoing fertility preservation treatment prior to gonadotoxic therapy.

MATERIALS AND METHODS: This single center retrospective observational study and phone survey evaluated utilization of cryopreserved embryos and eggs between January 1, 2001 and December 31, 2021 among 629 female ages 6-42 years seen for FPT consultation prior to gonadotoxic treatment. Patients who underwent FPT were evaluated for utilization of cryopreserved embryos and eggs. Those with undocumented reasons for unused embryos and eggs were contacted by telephone and underwent a brief survey to identify factors impacting embryo or egg future use or reasons for disposition. Pearson chi-squared and Fisher’s exact tests were performed to test for associations.

RESULTS: Of a total of 629 females who received FPT counseling, 17.2% (n = 108) underwent EC, 23.8% (n = 150) underwent OC, and 9.1% (n = 57) cryopreserved ovarian tissue. Those who cryopreserved embryos were older than those who froze eggs (32.0 vs. 27.1 years, p < 0.01) with a longer mean duration of storage (6.7 vs. 4.8 years, p = 0.01). Those with frozen embryos returned more often to attempt pregnancy (34.3%, n = 37) than those with cryopreserved eggs (3.3%, n = 5). Of those with cryopreserved embryos, 12.9% (n = 14) passed away while 2.7% with cryopreserved eggs passed away (n = 4). Of the 108 patients who froze embryos, reasons reported for non-use were: 20.3% had spontaneous conception (n = 21), 11.1% (n = 12) had active disease or were not cleared for pregnancy, 10.2% (n = 11) had a change in relationship with the male partner embryos were created with, 7.4% (n = 8) plan to use embryos in the future and 1.9% (n = 2) no longer desired pregnancy. Of those who cryopreserved eggs (n = 150), 61.3% (n = 92) planned to use but were not ready for use in next year, while 21.3% (n = 32) were not medically cleared for pregnancy or undergoing discontinuation, and 2.6% (n = 4) had spontaneous pregnancies after treatment. Of note, 6% (n = 9) of patients were imminently planning egg thaw within the next year.

CONCLUSIONS: Women who pursued FPT more often returned for treatment when embryos versus eggs were cryopreserved. In those who underwent OC, most commonly cited reasons for non-use included plan for future use though not in next year, compared to women who froze embryos who most often had non-use due to spontaneous pregnancy. Interestingly, 10.2% of those who cryopreserved embryos did not use in the future as they were no longer in a relationship with the male partner embryos were created with.

IMPACT STATEMENT: This study demonstrates that understanding why women do not return to utilize their cryopreserved embryos or eggs in the future can vastly improve FPT counseling, and further work is needed in this area as fertility preservation prior to gonadotoxic treatment continues to become a priority in comprehensive care.

P-315 6:45 AM Tuesday, October 25, 2022
INFLUENCE OF FERTILITY PRESERVATION INDICATION ON OOCYTE AND EMBRYO CRYOPRESERVATION: A COMPARISON OF MEDICALLY INDICATED VS ELECTIVE CYCLES. Alexis K. Gadsen, MD, 1 Kathryn E. Anthony, MD, 1 Karine Matevensian, DO, 1 Christina Raker, ScD, 1 May-Tal Sauerbrun-Cutler, M.D. 1 Warren Alpert Medical School of Brown University; Women & Infants Hospital, Providence, RI. 2 Warren Alpert Medical School of Brown University; Women & Infants Hospital, Providence, RI.

OBJECTIVE: Cryopreservation of embryos/oocytes are feasible fertility preservation (FP) options in patients facing gonadotoxic treatments and age-related fertility decline. A paucity of data exists to guide patient counseling about cycle outcomes particularly ones pursuing FP for medical indications. The objective of this study is to compare expected oocyte/embryo yield and cycles between medically indicated and elective FP groups.

MATERIALS AND METHODS: This is a retrospective cohort study using data from the Women and Infants Hospital Fertility Center and includes all patients seen for FP consultation from January 2016 to February 2022. Cycles were grouped by indication for analysis. Variables collected included patient demographics, baseline ovarian reserve testing, and FP cycle data. Statistical analysis was performed using Wilcoxon rank sum test and chi-squared analysis.
RESULTS: Medically indicated FP patients were younger (28.1 yrs vs 35.4 yrs; p<0.001), less likely to be partnered (p=0.007), and nulliparous (p=0.005) than elective FP patients. There was no significant difference in the race or BMI between the two groups. Baseline fertility evaluations were similar except higher antral follicle count in the medically indicated FP patients (AFC 23 vs 16, p=0.02). This remained true when stratified by age and FP indication. Both groups favored antagonist cycle protocol, though more patients underwent estrogen priming cycles in the elective FP group (n=4, p=0.03). There was no significant difference in the number of stimulation days, total FSH dose, maximum E2, or oocytes/embryos frozen.

CONCLUSIONS: Many mature oocytes can be obtained from ovary tissue with simple media and no need for ovarian stimulation. The intact cumulus however is crucial. However, ovarian stimulation and indeed ovulation may only be necessary for removing the oocyte from the ovary, not for maturation, which can also be accomplished by simple ovarian dissection.

IMPACT STATEMENT: For fertility preservation in cancer patients, there is often a need for transplanting cancer cells when the thawed ovarian tissue is transplanted back to the patient. A robust IVM with simple culture media would solve this problem. From a basic science perspective, we know from in vitro gametogenesis that primordial follicles can be matured at low pressure to the GV stage with only 8 “core genes” (IVD) and then 11 days of FSH (IVG). GV oocytes dissected from ovary tissue have thus already become meiotically competent in vivo by what we term IVD and IVG. Also it is far easier to obtain many GV oocytes from tiny follicles using open cortical dissection than using a needle. In vitro gametogenesis and IVM thus reveal the limited role of the olfactory cycle and ovarian stimulation in oocyte development other than simply to exit the oocyte from the ovary.

Table 1: FP Cycle Outcomes

<table>
<thead>
<tr>
<th>Stimulaiton protocol</th>
<th>Medically Indicated</th>
<th>Elective</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antagonist</td>
<td>33 (100%)</td>
<td>14 (77.80%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Estrogen priming</td>
<td>0 (4.22%)</td>
<td>1 (22.2%)</td>
<td></td>
</tr>
<tr>
<td>Average days of stim</td>
<td>11 days ± 3</td>
<td>11 ± 2</td>
<td>0.53</td>
</tr>
<tr>
<td>Average total FSH Dose (IU)</td>
<td>2325 ± 1876</td>
<td>2661 ± 1003</td>
<td>0.06</td>
</tr>
<tr>
<td>Average max E2 (pg/mL)</td>
<td>1361 ± 1086</td>
<td>1817 ± 1255</td>
<td>0.51</td>
</tr>
<tr>
<td>Average Number Oocytes</td>
<td>18 ± 14</td>
<td>13 ± 9</td>
<td>0.32</td>
</tr>
<tr>
<td>Retrieved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Mature Oocytes Frozen</td>
<td>11 ± 9</td>
<td>10 ± 7</td>
<td>0.70</td>
</tr>
<tr>
<td>Embryo cryopreservation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Oocytes Fertilized</td>
<td>9 ± 11</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Average Embryos Frozen</td>
<td>5 ± 5</td>
<td>2</td>
<td>-</td>
</tr>
</tbody>
</table>

P-317 6:45 AM Tuesday, October 25, 2022

"SINGLE MOTHERS BY CHOICE" AFTER SOCIAL EGG FREEZING: OVERVIEW OF THE LAST 9 YEARS IN A PRIVATE ART SERVICE. Flávia Rocha Torelli, MD, MSc,1 Aline R. Lorenzon, PhD,2 Claudia Gomes, M.D.3 Huntington Medicina Reprodutiva - Eugin Group, Campinas, Brazil;3 Huntington Medicina Reprodutiva - Eugin Group, Sao Paulo, Brazil;3 Huntington Medicina Reprodutiva, Sao Paulo, Sp, Brazil.

OBJECTIVE: Social fertility preservation by egg freezing may benefit women who wish to delay childbearing, often because of the absence of a partner. This study aimed to analyze the use of autologous vitrified frozen/thawed oocytes with donor semen cycles for single woman treatment in a private ART center.

MATERIALS AND METHODS: Retrospective cohort study including patients that opted for oocyte freezing for social preservation reasons in a private IVF clinic in Brazil between 2013 and 2021. Patients that followed autologous frozen-thawed oocyte with donor semen for single motherhood were included in this study. Lesbian couples and patients with a male partner were excluded of this analysis. Clinical and laboratory parameters such as number of oocytes frozen and thawed, time between frozen and thawed, age at the time of freezing and thawing, blastocyst rate, number of embryos transferred and reproductive outcomes were considered for analysis. Mann-Whitney and Fisher exact’s tests were applied accordingly. A p value <0.05 was considered significant.

RESULTS: Between 2013 and 2021, our center performed 2173 cycles from patients that underwent social fertility preservation. From those, 86 (4%) performed autologous frozen-thawed oocyte cycles with donor sperm without a male or female partner. Mean age of these patients at the time the oocytes were frozen was 38,18±3,32 and 41,26±5,79 years old when oocytes were thawed (24,86±2,87 months apart). Mean number of oocytes retrieved was 10,49±8,28 and 7,42±5,22 were appropriate (metaphase II, MII) for freezing. At time of thawing, 6,90±4,16 oocytes were fertilized and 2,28±1,81 embryo achieved a blastocysts stage. Preimplantation genetic testing (PGT-A) was performed in 28 cycles (32%) in which 20 (71.4%) had at least 1 euploid embryo reported. Thirty-nine nine patients (45.3%) underwent embryo transfer (1,38±0,49 embryos per transfer), in which the majority underwent a fresh transfer (66.6%) and 43.6% transferred an euploid embryo (17,39). Age at the time of oocyte freezing and number of MII were significantly different between those patients that followed or not an embryo transfer (36,8±2,30 versus 39,3±3,2 years old, p=0.003 and 10,2±5,7 versus 5,2±3,4 MII, p<0.001, respectively). Positive pregnancy rate was 59.1% (13/22) and 58.8% (10/17) for non-biopsied and euploid embryo transfer respectively (p=1.0). Clinical pregnancy and live birth rates from those that underwent non-biopsied and euploid embryo transfer were 40.9% (9/22) and 35.3% (7/20) (p=0.75 and 1.0), respectively. In our cohort, there was no difference on age of oocyte freezing and the achievement of a clinical pregnancy (36,67±2,41 versus 37,38±3,40 years old).
CONCLUSIONS: The age at the time of oocyte freezing, as well the number of oocytes cryopreserved were detrimental for future embryo transfer option. Clinical pregnancy and livebirth rates were similar between non-biopsied and euploid embryo transfer.

IMPACT STATEMENT: Age is a key factor in the success of the treatment and women should be aware to consider fertility preservation earlier than 35 years old.

P-318 6:45 AM Tuesday, October 25, 2022

FERTILITY PRESERVATION IN ENDOMETRIOSIS: DOES PATIENT SYMPTOMATOLOGY AFFECTS THE EXTENT OF THE OVARIAN RESPONSE. Yuval Fouks, M.D., Yoni Cohen, M.D., Ph.D., Foad Azem, M.D., Aviad Cohen, M.D. Reproductive center - IVF unit. Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.

OBJECTIVE: This study was aimed to assess whether the extent of the disease and the individual symptomatology of patients with endometriosis seeking fertility preservation correlates with their ovarian response to cycle stimulation.

MATERIALS AND METHODS: An observational cross-sectional study was conducted from July 2017 to May 2020 in a tertiary university-affiliated medical center. We included patients who had been treated in the endometriosis clinic and undergone fertility preservation. The stage of endometriosis was determined according to the Revised ASRM Classification of Endometriosis and extracted from the endometriosis clinic report. The minimal and mild stages of endometriosis included in this study were surgically diagnosed, while the moderate to severe stages and the presence of deep infiltrative lesions were confirmed by either ultrasound or surgery.

All patients completed an online questionnaire that was crossed reference with electronic charts. An analysis related to patient data and fertility preservation cycles was performed. We have divided our cohort into subgroups based on the number of the reported symptoms and disease severity. A Mediation analysis was used to estimate whether any potential relationship between composite symptomatology and the number of oocytes vitrified is explained by surgical intervention as an intermediate factor. A mediation model with 2000 iterations using a Percentile Bootstrap resampling was used.

RESULTS: Eighty-one women were eligible for the analysis. The mean patients age at time of FP was 35.2 (±4.9) years. The diagnosis of endometriosis was confirmed by surgery in 47 (58%) of cases. The mean accumulated number of oocytes vitrified per patient through all cycles was 16.7(±2.1) oocytes. Seventeen patients reported a pregnancy after the procedure (either natural conception or via ART). The number of oocytes vitrified correlated significantly with number of reported symptoms and clinical characteristics (-0.479, p=0.0001) and -0.442, p=0.0001 respectively. In a mediation analysis, the potential causality of surgical intervention on the relation between the number of symptoms on the ovarian response was estimated to be 40% (p=0.04), a bootstrap analysis showed a similar relation: (-0.30, 95%CL (-1.60) to (-0.01) p=0.04).

CONCLUSIONS: We have observed an association between the number of clinical symptoms to the quantity vitrified oocytes. No association was found regarding the type of specific complain to the number of eventual vitrified oocytes.

IMPACT STATEMENT: A clinical questionnaire is a highly usable tool assessing the symptomatology of patients with endometriosis seeking fertility preservation as complementary information and otherwise was not taken by the fertility specialist. Second, a joint symptomatology reported by patients with endometriosis before FP significantly correlated with the number of oocytes vitrified. This relationship when referred to the number of oocytes vitrified was independent from surgical invention.

SUPPORT: None.

P-319 6:45 AM Tuesday, October 25, 2022

EMBRYO PLOIDY IN THAWED FROZEN VERSUS FRESH OOCYTES: IS THERE A DIFFERENCE? Shelun Tsai, MD, Jonas Malmsten, D.P.S., Steven D. Spandorfer, MD The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To evaluate embryo ploidy in a cohort of patients who underwent preimplantation genetic testing for aneuploidy (PGT-A) with thawed frozen oocytes compared to fresh oocytes.

MATERIALS AND METHODS: Patients who underwent their first autologous frozen oocyte thaw and subsequent in vitro fertilization (IVF) and trophodectoderm biopsy for PGT-A with next-generation sequencing at our center were included. Patients were excluded if they had a fresh or frozen transfer of an untested embryo or if they performed PGT to identify a specific genetic mutation or structural chromosomal rearrangement. Patients were also excluded if donor oocytes were used or if the oocytes were fertilized with surgically retrieved sperm. Subjects were compared to 3:1 age-matched controls who underwent their first IVF cycle with fresh oocytes and subsequent trophodectoderm biopsy for PGT-A during the same time period. The primary outcome was the proportion of euploid, mosaic, and aneuploid embryos between those using frozen versus fresh oocytes. Secondary outcomes included ovarian stimulation characteristics, fertilization rates, and blastulation rates. Student’s t-test or Chi-squared test were used to compare variables.

RESULTS: A total of 143 patients who cryopreserved a total of 1,571 oocytes were included in the study. The average age was 36.9 ± 2.7 years, and the median interval between oocyte cryopreservation and thaw was 40 months. When subjects using frozen oocytes were compared with the 429 controls using fresh oocytes, there were no statistically significant differences in rates of euploidy (41.3% vs. 41.9%), mosaicism (14.5% vs. 13.0%), or aneuploidy (44.2% vs. 45.1%, p=0.59). There were also no differences in the number of days of stimulation (9.7 ± 1.8 vs. 10.0 ± 1.8, p=0.37), peak estradiol levels (2245.0 ± 908.7 vs. 2212.6 ± 1013.9 pg/ml, p=0.73), total gonadotropin dose (2128.2 ± 1402.4 vs. 3262.6 ± 1345.3 IU, p=0.31), or baseline follicle size at trigger (17.6 ± 2.0 vs. 17.7 ± 2.2 mm, p=0.21). The numbers of mature oocytes were retrieved (12.2 ± 6.3 vs. 11.3 ± 6.4, p=0.15). In the frozen oocyte group, 91.2% of cryopreserved oocytes survived thawing, resulting in smaller proportions of fertilized oocytes per mature oocyte retrieved and usable blastocysts per mature oocyte retrieved (67.1% vs. 77.1%, p<0.01; 42.8% vs. 52.2%, p<0.01 respectively). As a result, the oocyte cryopreservation group had a slightly lower non-statistically significant mean number of fertilized oocytes per patient than the fresh oocyte group on 7.8 ± 4.1 vs. 8.7 ± 5.5, p=0.06) and a statistically significant lower mean number of total blastocysts per patient (5.0 ± 3.1 vs. 5.9 ± 4.3, p=0.04).

CONCLUSIONS: Oocyte cryopreservation with subsequent thaw, fertilization, and trophodectoderm biopsy for PGT-A was not associated with adverse chromosomal competence when compared to age-matched controls utilizing fresh oocytes. However, there may be slightly lower average blastocyst yield in embryos derived from cryopreserved oocytes.

IMPACT STATEMENT: Embryo ploidy remained the same for blastocysts created from fresh or frozen oocytes.

P-320 6:45 AM Tuesday, October 25, 2022

ICING ON THE CAKE: CAN OOCYTES "ON ICE" RESULT IN MORE THAN ONE LIVE BIRTH (LB)? Sarah D. Cascante, MD, Jennifer K. Blakemore, MD, M.S., Carlos M. Farrar, MD, Shannon DeVore, MD, Brooke Hodes-Wettz, M.D., M.P.H., Caroline McCaffrey, H.C.L.D., James A. Grifo, M.D, PhD 1NYU Langone Prelude Fertility Center, New York, NY; 2NYU Langone Fertility Center, New York, NY; 3NYU Grossman School of Medicine, New York, NY.

OBJECTIVE: Data regarding the chance of more than one LB from oocyte cryopreservation (OC) is lacking. We reviewed outcomes from patients (pts) with ≥1 LB from thawed autologous oocytes (AOs) to examine: 1) how many have inventory (AOs or resultant euploid/untested/no result embryos), and 2) embryo transfer (ET) outcomes after 1st LB.

MATERIALS AND METHODS: We reviewed all pts who thawed AOs at our center in 2006-2021 and had ≥1 resultant LB. Pts were excluded if OC was performed for a medical reason, as research, due to lack of sperm or a natural disaster, with embryo banking or for gestational carrier use.

RESULTS: 191 pts had ≥1 LB (median # OC cycles 1, median age at 1st OC 37 years (y), median # cryopreserved AOs 18, median # AOs thawed before 1st LB 15). After LB, 61% of pts (n=117) had inventory and 39% (n=74) did not; see table. Among pts with inventory, 12% (n=14) discarded or donated, 3% (n=4) transported out and 10% (n=12) consumed all inventory as of 1/2022. 22% of pts (n=42) had ≥1 LB after ET for LB. Among these pts, 21 thawed embryos (median # thawed, 1 range 1-2), 4 thawed AOs (median # thawed, 1 range 5-40) and 1 thawed both AOs + embryos (15 AOs + 4 embryos). Median time from the ET that led to 1st LB and next ET was 26 months (range 15-57) and median age at next ET was 44y (range 37-53). This ET resulted in: implantation rate of 63% (19/30), spontaneous abortion rate of 16% (3/19) and ongoing pregnancy (OP) + LB rate of 58% (15/26); 1 pregnancy was terminated for monochorionic twins. Among pts
who had a LB from this ET, 66% (10/15) had remaining inventory and 33% (5/15) did not. Among pts who did not have a LB from this ET, 45% (5/11) had remaining inventory and 54% (6/11) did not; 5 of these unsuccessful pts returned for another ET and 2 had a LB. In total, 16 pts had 2 ETs result in OP/LB and 1 pt had 3 ETs result in LB. 10 more pts had ≥2 children from a single ET (9 twins, 1 triplet); thus, we report 27 pts with ≥2 children from OC. Among pts with ≥2 children, median # OC cycles was 1 (range 1-8), median age at 1st OC was 37y (range 34-41), median # cryopreserved AOs was 20 (range 5-102) and median # thawed AOs was 19 (range 5-58).

CONCLUSIONS: Most pts (61%) had inventory after their 1st LB from OC, and most pts (65%) who returned for ET after LB achieved another OP/LB. Further research must explore pts’ thoughts regarding OC inventory after LB and its associated storage fees.

IMPACT STATEMENT: OC can help pts achieve their ideal family size, even if ≥1 child.

SUPPORT: None.

E-POSTER ABSTRACT SESSION: T11

P-321 6:45 AM Tuesday, October 25, 2022

HOW MANY EGGS WILL I GET AND HOW MUCH MEDICATION DO I NEED? A SART DATABASE PRE-DICTOR MODEL FOR EGG FREEZING. Bahar D. Yilmaz, MD,1 Chen Yeh, MS,2 Latifyya N. Muhammad, PhD, MPH,2 Eve C. Feinberg, MD1 Northwestern University, Chicago, IL;3Northwestern University Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: To develop a model for predicting individualized gonadotropin starting dose and estimating number of retrieved mature oocytes in planned oocyte cryopreservation (OC) cycles.

MATERIALS AND METHODS: Society for Assisted Reproductive Technology Clinic Outcome Reporting System Database was used to analyze 36,366 OC cycles between 2013-2018. Patients between ages 18-44, a BMI of 15-60 kg/m² were included when all variables were available. Seventy percent of the data was used as a training set to build the predictive model and 30% used for testing and internal validation. Bivariate copula additive models for location, scale and shape were performed. Candidate covariates for treatment dosage included age, race, BMI, smoking history, max D3 FSH, AMH, diminished ovarian reserve, ovulatory disorder. Models for each outcome are summarized by the coefficient for all covariates and the corresponding 95% confidence interval (CI). Candidate covariates for number of mature oocytes stayed the same with an addition of treatment dosage. Final model was determined by the smallest Akaike Information Criterion (AIC). Model performance was quantified by the percentage of observations falling within a pre-specified tolerance level, mean absolute error, and median absolute error.

RESULTS: There were 15,806 patients included without missing data. Average age was 35 years with 12 days of stimulation and 10 (0-89) mature oocytes. Gonadotropin dose increased with age, FSH, BMI≥35, smoking, and diagnosis of diminished ovarian reserve and dose decreased with increasing AMH, ovulatory disorder, and BMI<25. The number of mature oocytes retrieved was positively correlated with AMH and negatively correlated with age, FSH, Asian race, and diminished ovarian reserve. A tolerance level of 6 mature oocytes reached 70% accuracy with maximum gonadotropin dosage of 450 IU per day for 12+/ 3 days of stimulation in both data-sets. The mean absolute error for treatment dosage days and number of mature oocytes were 3 days and 5 mature oocytes, respectively. An online interactive calculator tool was created.

CONCLUSIONS: SART data was used to develop and internally validate a predictive model to estimate personalized treatment dose and number of mature oocytes. This calculator can be used to counsel patients on expectations from a planned OC cycle.

IMPACT STATEMENT: Creation of an online calculator tool can be used to help counsel patients and guide physicians for optimal gonadotropin dosing to maximize number of mature oocytes retrieved in a planned OC cycle.

SUPPORT: Northwestern University Biostatistical/EDW support FY22.

P-322 6:45 AM Tuesday, October 25, 2022

EVOLUTION OF KNOWLEDGE AND ATTITUDES REGARDING FERTILITY SERVICE UTILIZATION. Alexandra Grace Huttl, MD,1 Nathan C. Koelpel, MPH,2 Monica Ailawadi Mainini, MD,3 Clarisa Gracia, MD, MSCET,4 Suneeta Senapati, MD, MSCET1 University of Pennsylvania, University of Pennsylvania Health System, Philadelphia, PA;2UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, Philadelphia, PA;3University of Pennsylvania, Philadelphia, PA;4Hospital of the University of Pennsylvania, Philadelphia, PA;5University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: To evaluate the temporal evolution of knowledge and attitudes regarding fertility service utilization.

MATERIALS AND METHODS: 1000 women (21-45 years, stratified by age <= or > 35 years) were surveyed using an 82-item Internet-based questionnaire in April 2021. 50% had at least one child and 50% had interest in future childbearing. This cohort was compared to historical controls from a similar survey administered in 2016 (n=1000) using parametric tests. Multivariable linear regression was performed to evaluate differences in accepted costs.

RESULTS: Compared to historical controls, this cohort had a greater proportion of Hispanic and Black participants and those who reported lower-level education status, use of government-subsidized insurance, and being single. Despite consideration of the impact of the COVID-19 pandemic, likelihood to consider planned oocyte cryopreservation (OC) was similar between 2021 and 2016 (21.3% vs. 21.6%, p=0.87). In 2021, there was increased awareness of OC (92.3% vs. 87.2%), what the process entails (41.9% vs. 29.8%), and objectively assessed knowledge of associated costs (1.06/2 points vs. 0.68/2 points) despite decreased knowledge of OC efficacy (0.91/2 points vs. 0.99/2 points) and reproductive health (1.71/5 points vs. 2.40/5 points) (all p<0.01). Fewer participants cited relationship stability, completed education, and age as factors important in deciding when to pursue childbearing (82.1% vs. 91.7%; 56.8% vs. 70.7%; 69.2% vs. 79.6%; respectively; all p<0.01). If unable to conceive, women were less likely than previously reported to seek help from a specialist (74.2% vs. 82.0%) or adopt children (63.7% vs. 72.2%) and were more likely to use donor gametes (sperm: 32.7% vs. 25.4%; oocyte: 30.7% vs. 24.3%) (all p<0.01).

When asked about the minimum success rate of achieving a pregnancy if OC cost $10,000, 77.5% of the cohort accepted a minimum 50% chance of success compared to 91.1% in 2016, with 44.1% of the cohort accepting a minimum of 80% success compared to 55.9% in 2016 (both p<0.01). A success rate less than 80% was more likely to be acceptable to those likely to consider OC (COC) compared to those unlikely to consider (NOC) (65.9% vs. 53.0%, p<0.01). A success rate less than 50% was not considered more acceptable by COC compared to NOC (25.5% vs. 21.7%, p=0.25), despite this being the case in 2016. COC were overall accepting of a lower minimum success rate compared to NOC (p<0.01). In a model considering demographic and knowledge differences, participants in 2021 reported an acceptable minimum success rate that was on average 11.1% less than historical controls (p<0.01).
CONCLUSIONS: Likelihood to consider OC has remained constant, while third-party reproduction options have become more accepted. Despite improved awareness of the OC process, a disconnect exists between willingness to pay for OC and realistic success rates.

IMPACT STATEMENT: Understanding of and willingness to pay for OC has evolved in the decade since the experimental label on OC was removed, highlighting opportunities to provide more cost-effective and efficient fertility services.

SUPPORT: Financial support for survey distribution was provided by Pennsylvania Hospital Resident Research Funding.

### Table 1: Patient characteristics by season

<table>
<thead>
<tr>
<th>Season</th>
<th>Winter (n=378)</th>
<th>Spring (n=257)</th>
<th>Summer (n=364)</th>
<th>Fall (n=470)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oocytes retrieved</td>
<td>12.88</td>
<td>13.81</td>
<td>13.53</td>
<td>13.19</td>
<td>0.53</td>
</tr>
<tr>
<td>Age (years)</td>
<td>36.49</td>
<td>36.83</td>
<td>36.52</td>
<td>36.48</td>
<td>0.75</td>
</tr>
<tr>
<td>AMH (ng/mL)</td>
<td>2.83</td>
<td>3.27</td>
<td>3.28</td>
<td>2.99</td>
<td>0.18</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.25</td>
<td>26.86</td>
<td>26.89</td>
<td>26.24</td>
<td>0.068</td>
</tr>
</tbody>
</table>

### P-323 6:45 AM Tuesday, October 25, 2022

**SEASONAL VARIATION IMPACT ON OOCYTE RETRIEVAL OUTCOMES.** Miriam Tarrash, MD, 1 Alexandra Peyeser, M.D., 1 Randi H. Goldman, M.D., 1 Christine Mullin, M.D. 1 Northwell Health Fertility, Zucker School of Medicine at Hofstra Northwell, Manhasset, NY; 2 Northwell Health Fertility, Northwell Health, Manhasset, NY.

OBJECTIVE: To evaluate whether seasonal variability influences the number of oocytes retrieved in patients undergoing IVF and oocyte cryopreservation. Previous studies have been conducted evaluating the impact of seasonal variability on unassisted conception and birth rates. Seasonal patterns associated with assisted reproductive technology outcomes, including fertilization rates and embryo quality, have been studied in small cohorts of patients and with mixed results. Some studies have suggested higher odds of clinical pregnancy from IVF in warmer months, while others did not demonstrate a difference by season. The impact of seasonality on oocyte retrieval (OR) outcomes has not been specifically addressed to date.

MATERIALS AND METHODS: This was a retrospective cohort study of all patients who underwent an OR from November 2019 to January 2022 at a single academic institution located in the Northeast in the United States. Patients were stratified by the season their procedure occurred: Winter (December 21 – March 20), Spring (March 21 – June 20), Summer (June 21 – September 20), and Fall (September 21 – December 20). No cases were conducted in the Spring of 2020 secondary to the COVID-19 pandemic. The primary outcome was the average number of oocytes retrieved. ANOVA was used to compare the four seasons with \( p < 0.05 \) defining significance.

RESULTS: During the study period, 1469 patients underwent an egg retrieval, of which 378 occurred in the Winter, 257 in the Spring, 364 in the Summer and 470 in the Fall. According to the National Weather Service, the average temperature in the Winter is 36.1\(^{\circ}\)Fahrenheit, Summer is 75.8\(^{\circ}\)Fahrenheit, and Fall is 53.5\(^{\circ}\)Fahrenheit in New York City. There was no significant difference in the number of oocytes retrieved across all seasons (\( p = 0.53 \)). Additionally, patient characteristics were similar across seasons with no significant differences in age, AMH and BMI.

CONCLUSIONS: The average number of oocytes retrieved did not vary by season. Differences temperature, day length, precipitation, and humidity may not be associated with OR success.

IMPACT STATEMENT: Seasonal variation does not impact oocyte retrieval outcomes.

### P-324 6:45 AM Tuesday, October 25, 2022

**ACCEPTANCE OF GENETIC EDITING OF HUMAN EMBRYOS IN INFERTILITY PATIENTS: PRE- AND POST- COVID-19 ATTITUDES.** Yuval Fousk, MD, 1 Denis A. Vaughan, M.D., 1 Amiliz Macharia, MPH, 2 Insoo Hyun, PhD, 2 Eli Y. Adashi, MD, 3 Michele R. Hacker, Sc.D., 3 M.S.P.H., 4 Denny Sakkas, PhD, 5 Werner Neuhausser, M.D., PH.D. 6 Brookline, MA; 7 Boston IVF, Waltham, MA; 1 Beth Israel Deaconess Medical Center, Boston, MA; 4 Center for Bioethics, Harvard Medical School, Boston, MA 02115, U.S.A.; 8 Boston; 9 The Warren Alpert Medical School, Brown University, Providence, RI; 8 Harvard Medical School/Beth Israel Deaconess Medical Center, Boston, MA; 7 Boston IVF - The Eugin Group, Waltham, MA.

OBJECTIVE: To evaluate changes in the understanding and acceptance of heritable genome editing (HGE) pre- and post- COVID-19 amongst patients attending an infertility practice.

MATERIALS AND METHODS: A cross-sectional, written questionnaire conducted in two cohorts from April - June 2018 and from April - July - December 2021. Prior knowledge and acceptance of HGE for somatic mutations, HGE for germline mutations, patient demographics were assessed.

RESULTS: 587 and 200 patients were interviewed in 2018 and 2021 respectively (Table 1). Significantly more (\( p < 0.03 \)) participants in 2021 compared to 2018 would utilize HGE to have healthy children with their own gametes. In 2021, more respondents also stated that they would consider HGE to prevent genetic disease and reduce disease risk in adulthood than in 2018. More participants supported genetic enhancement to increase life expectancy, intelligence, creativity and alter physical characteristics of offspring in 2021 vs 2018, respectively. When specifically asked about the effect of the pandemic on their
attitude toward HGE, 15% of the 2021 cohort reported a positive effect of the pandemic, while only <1% reported a negative effect. In contrast, only 8% reported a positive and 5% a negative effect on their attitude towards HGE as a result of the transfer of gene edited human embryos in China in 2019, which resulted in two live births. However, only 48% of those questioned in 2021 had heard of this report.

CONCLUSIONS: We observed a significantly increased acceptance of HGE among infertility patients after the COVID-19 pandemic.

IMPACT STATEMENT: The acceptance of HGE has increased amongst patients attending an infertility clinic, where these technologies are likely to be first utilized.

The increased acceptance may be the result of the COVID-19 pandemic or other temporal trends.

SUPPORT: None

P-325 6:45 AM Tuesday, October 25, 2022

OPERATING CHARACTERISTICS OF SPERM CONCENTRATION AND FSH FOR PREDICTING CHROMOSOMAL ABNORMALITIES. Colin A. McLain, MD, 1 Eric D. Biwenga, MD, 1 Matt S. Christman, MD, 1 Donald S. Grun, MD 2 1Naval Medical Center San Diego, Department of Urology, San Diego, CA; 2Kaiser Permanente, Southern California Permanente Medical Group, Department of Urology, San Diego, CA.

OBJECTIVE: Current AUA/EUA guidelines recommend obtaining a genetic work-up in men with non-obstructive azoospermia or severe oligospermia (<5 mil/mL). A recent retrospective cohort study suggests that Yq microdeletions are primarily found at a sperm concentration <0.5 mil/mL, and that by lowering the concentration threshold for genetic testing, specificity could be increased and relative financial cost decreased without adversely affecting the sensitivity. Studies have shown that FSH is the best predictor of NOA in combination with testicular volume as well as a significant predictor of microdeleletion presence. We hypothesized that the combination of sperm concentration and FSH would better predict the presence of chromosomal abnormalities in infertile men.

MATERIALS AND METHODS: A retrospective cohort study was conducted with subjects who were referred to a military tertiary Urology clinic between 2010 to 2020 and who underwent an infertility evaluation to include genetic testing, hormone profile, and at least one semen analysis. Sperm density and FSH were analyzed as independent predictors of chromosomal abnormalities using logistic regression. Receiver operating characteristics were generated for each independent variable that achieved significance in regression.

RESULTS: 356 patients met inclusion criteria. Over the ten-year period, the prevalence of Y-chromosome microdeletions and karyotype abnormalities was 3.3% (n = 12) and 8.4% (n = 30), respectively. The ability to predict chromosomal abnormality based on logistic regression was statistically significant for each independent variable. The area under the curve for sperm concentration and FSH was found to be statistically better in combination than concentration alone (0.66 vs 0.57, p = 0.013). The best balance of sensitivity and specificity (i.e., for a diagnostic test) for concentration and FSH were found at cut-points of <0.215 mil/mL and >8.345 mIU/mL, respectively. To optimize performance as a screening test and maintain sensitivity >90%, the cut points for concentration and FSH were <1 mil/mL and >2.74 mIU/mL, respectively. There was no difference in sensitivity for concentration between 2-7 mil/mL and no abnormalities were found if concentration exceeded 7 mil/mL; thus a cutoff of 7 mil/mL would capture 100% of all chromosome abnormalities.

CONCLUSIONS: Based on receiver operating characteristics, lowering the threshold for chromosomal analysis to a sperm concentration of <1 mil/mL maintains acceptable performance as a screening test for genetic abnormality, with resulting cost savings expected. Incorporating FSH into this decision appears to improve both sensitivity and specificity in prediction of chromosomal abnormalities.

IMPACT STATEMENT: Our military single-institution ten-year cohort, exemplifies the potential improvement in patient selection and results that can be achieved if the sperm concentration is lowered from the current cutoff.
OBJECTIVE: Genetic diseases represent 20% of infant mortality, between 15-35% of pediatric hospitalizations and a large percentage of the main causes of disability. There are different ways to study the carrier of monogenic diseases, one of them is the CGT (CARRIER GENETIC TEST), which is blood samples and with no previous history of disease in order to have knowledge of the asymptomatic carrier status and to reduce the incidence of genetic abnormalities. We asked if is it possible to determine which are the most prevalent genetic diseases in our population to develop a regional genetic panel and carry out correct pre-reproductive counseling.

MATERIALS AND METHODS: Retrospective descriptive study. 586 blood samples were obtained in Nascentis (Cordoba) from December 2016 to November 2019 were analyzed. CGT® results of 586 patients of both sexes were analyzed. A blood sample was drawn from each patient and the kit was sent to Igenomix for the corresponding CGT analysis. A complete list of mutations obtained, was the most frequent were identified and the frequency of each one was calculated. We also created the ranking of the fifteen most frequent in the population. In addition, the percentage of individuals who did not present any alteration was calculated.

RESULTS: The 586 CGT analysis allowed us to compile a list of a total of 87 diseases present in the sample. Of all the patients, 61% presented one or more mutations. Among the positives, 46% were women and 54% men. The most common mutations observed were: cystic fibrosis (12,6%) central core congenital myopathy (5,04), Wilson disease (4,48%), Familial mediterranean Fever (4,48%) and glycine encaphalopathy (3,9%). Other common diseases were: Miyoshi myopathy, progressive external ophthalmoplegia, Usher syndrome type C, and autosomal recessive type 1a deafness.

CONCLUSIONS: An initial screening of the population was made to identify an extensive list of genetic recessive mutations in the Argentine population. Most frequent mutations were identified and we could lay the basis for future studies about genetic characteristics of the population under study. In the future, more detailed studies on these genetic patterns may allow the setting-up of a new panel of the region’s most frequent recessive genetic mutations.

IMPACT STATEMENT: Each fertility center should know the frequency of occurrence of the most common and/or serious genetic diseases in order to obtain safer results in each of their treatments.

P-329 6:45 AM Tuesday, October 25, 2022
SEGMENTAL AND SPECIFIC CHROMOSOMAL ANEUPLOIDIES ARE INCREASED IN EMBRYOS OF CONSAGNUOUS COUPLES AFTER IVF/ICSI WITH PREIMPLANTATION GENETIC TESTING FOR ANEUPLIOIDIES (PGT-A), Laura Melado, M.D., Ph.D.,1 Lawrenz Barbara, M.D., Ph.D.,2 Daniela Nogueira, Ph.D.,3 Rachana Patel, Ph.D.,4 Raquel Loja Vitorino, M.D.,5 Laura Marqueta, M.D.,6 Francisco Javier Ruiz, M.D.,6 Asina Bayram, M.Sc.,7 Ibrahim Elkhatib, M.Sc.,8 Human M. M. Fatemi, M.D., Ph.D Prof.,9 ART Fertility Clinics, Abu Dhabi, Abu Dhabi, United Arab Emirates;10 Abu Dhabi, United Arab Emirates;11 ART Fertility Clinics, Abu Dhabi, United Arab Emirates;12 ART Fertility Clinics, Gurgaon, India;13 ART Fertility Clinics,14 ART Fertility Clinics, United Arab Emirates.

OBJECTIVE: To evaluate the impact of couple consanguinity on embryo ploidy when PGT-A is performed during IVF/ICSI treatments.

MATERIALS AND METHODS: Single center observational study including data from 10556 blastocysts after PGT-A. Embryos were obtained from 2564 IVF/ICSI cycles of infertile couples, from November 2016 to December 2020. Consanguinity was defined as first-degree or second-degree cousins. Only blastocysts with ploidy information were included, 8164 blastocysts from 2564 IVF/ICSI cycles of infertile couples from November 2016 to December 2020. Consanguinity was defined as first-degree or second-degree cousins. Only blastocysts with ploidy information were included, 8164 blastocysts were classified in 106 groups with the same criteria. Ethical approval was obtained from the Research Ethics Committee (REFA023b).

RESULTS: CG was significantly younger (33.28±0.27 vs 35.11±0.13 years; p<0.001) and presented longer period of infertility (4.03±0.15 vs 3.27±0.08 years; p<0.001) when compared to non-CG. AMH was similar for both groups (2.55±0.12 vs 2.51±0.08 ng/mL; p=0.396), yet AFC was higher for the CG (12.48±4.80 kg/m2;p=0.08). There was a higher incidence of DOR in the CG (62% vs 57.3%;p=0.49), yet AFC was higher for the CG (12.48±4.80 kg/m2;p=0.08). A similar lower number of embryos were biopsied on day 5 in the CG compared to the non-CG (49.6% vs 51.7%; p<0.001). CG presented higher rates of segmental aneuploidies compared to non-CG (19% vs 16.7%; p=0.029) and significantly higher aneuploidy rates for chromosome 13 (7.71% vs 6.96%; p<0.001) and 14 (7.79% vs 5.85%; p=0.019). A total of 1660 frozen embryos were biopsied (PET cycles) were performed. 364 were classified as the CG and 1296 (78.07%) for the non-CG. Women from the CG were younger (32.5±5.60 vs 33.8±5.46 years; p<0.001) and with higher BMI (27.7±5.16 vs 26.9±4.80 kg/m²;p=0.0018). No differences were observed between groups regarding number of embryos transferred (CG1:5±0.5; non-CG:4.14±0.49;p=0.08). Live birth rate was 4.7% lower for the CG group, hence not reaching statistical significance (62% vs 57.3%; p=0.29).

CONCLUSIONS: Consanguine couples have an increased risk for embryos with segmental aneuploidies and aneuploidies for chromosome 13 and 14.

IMPACT STATEMENT: Consanguine couples and their progeny accounts for an estimated 10.4% of the world population (1 billion people). It is well known the increased risk for genetic diseases in consanguineous couples and worse obstetric outcomes. This robust study could be the first time point out the origin of their chromosomal abnormalities. Segmental aneuploidies are associated, as well, with complex clinical syndromes. Genetic counseling is mandatory, PGT should be considered for aneuploidy screening (PGT-A) together with monogenic diseases (PGT-M).

SUPPORT: None.

P-329 6:45 AM Tuesday, October 25, 2022
ATM AND INFERTILITY: ARE THERE ADDITIONAL BARRIERS TO PREGNANCY IN ATAXIA-TELANGIECTASIA MUTATION CARRIERS?1 Almalia Namath, M.D.,2 Samad Jahandideh, Ph.D.,1 D. Jason Bromer, M.D.,1 Kathleen Devine, M.D.,1 Jeanne E. O’Brien, M.D, MSc1 Rush University Medical Center, Chicago, IL;2 Shady Grove Fertility, Washington D.C., DC;3 Shady Grove Fertility Center, Rockville, MD.

OBJECTIVE: To investigate the clinical outcomes of female and male patients who are carriers of Ataxia-Telangiectasia (ATM) variants seeking fertility treatments.

MATERIALS AND METHODS: All patients found to be mutation carriers for Ataxia-Telangiectasia (ATM) during expanded carrier screening (ECS) by one provider (SEMA4) at a large fertility center from 2020-2021 were analyzed. All patients received focused genetic counseling about the increased cancer risk and option of pre-implantation genetic testing for monogenic disorders (PGT-M). Clinical outcomes, including diagnosis, type of fertility treatment, clinical pregnancy rates, and use of PGT were analyzed. For male patients with ATM mutations, semen analyses (SA) were analyzed. For females, their antral follicle count (AFC) and AMH levels were analyzed. Statistical analysis was performed with p<0.05 considered statistically significant.

RESULTS: We analyzed 126 patients in total, with 63 females and 63 males. This was 1.5% of all patients who underwent ECS. The most common affected sex ratio was female (56%) and least affected sex was male (45%). The average age was 34 years old for females and 37 for males at time of ECS, 66.7% had a family history of cancer and only one patient had a personal history. The most common variants were c.2250G>A (p.K750) and c.1402_1403delAA (p.K468EfsX18).

Overall, the most common infertility diagnosis was unexplained (24.6%) followed by diminished ovarian reserve (DOR) (22%). For affected males, the most common reason for infertility was female factor. For affected females, the most common diagnosis was unexplained (29%) followed by DOR (16%). Most patients underwent IVF (63%) and 37% underwent IUI. Only 24% of patients underwent PGT, with only 11 patients undergoing PGT-M (9% of all affected). 8 of those patients underwent PGT-M for ATM. Affected males had normal sperm analyses on average with no significant differences noted. Affected females had a mean AFC of 13.38 and mean AMH of 4.7. However, there was a higher incidence of DOR in the affected female population compared to the general clinic population with mean age of 14.3% (4.5% vs 5.1%, p=0.001). After a single IVF cycle, 37% of affected patients achieved pregnancy. From a single IUI treatment, 15% achieved pregnancy.

CONCLUSIONS: ECS identifies patients who are carriers for ATM variants, which has been associated with increased lifetime risk for cancer and has been found to be associated with premature ovarian insufficiency. Outcomes of ART from these patients have not been studied. Our study is the first of its kind to analyze clinical outcomes from fertility treatments in this population. There is a higher incidence of DOR in affected patients and low PGT-M utilization rates in our large cohort of patients with ATM variants.
ART OUTCOMES IN NIJMEGEN BREAKAGE SYNDROME CARRIERS. Amalia Namath, M.D.,1 Samad Jahandideh, Ph.D.,2 Jason Bromer, M.D.,3 Kathleen Devine, M.D.,2 Jeanne E. O’Brien, MD, MSc1 Rush University Medical Center, Chicago, IL;2Shady Grove Fertility, Washington D.C., DC;3Shady Grove Fertility Center, Rockville, MD.

OBJECTIVE: To investigate the ART outcomes of male and female carriers of Nijmegen Breakage Syndrome (NBN).

MATERIALS AND METHODS: All patients found to be mutation carriers for Nijmegen Breakage Syndrome (NBN) during expanded carrier screening (ECS) by one provider (SEMA4) at a large fertility center from 2020-2021 were analyzed. All patients received focused genetic counseling prior to starting fertility treatment about the increased cancer risk associated with this mutation and the option of pre-implantation genetic testing for monogenic disorders (PGT-M). Clinical outcomes, including diagnosis, type of fertility treatment, clinical pregnancy rates, and use of PGT were analyzed. For male patients with NBN mutation, semen analyses (SA) were analyzed. For female patients, their antral follicle count (AFC) and AMH were analyzed. Statistical analysis was performed with p<0.05 considered statistically significant.

RESULTS: We analyzed 43 patients in total, with 23 females and 20 males. This was 0.4% of all patients who underwent ECS. The most common ethnicity was White (58%) and least common was Hispanic/Latino (2%). The average age at time of ECS was 37 years old for males and 33 for females. 90% had a family history of cancer and only one patient had a personal history of breast cancer. The most common pathogenic mutation was c.657_661delACAAA (p.K219NfsX16) found in 11 patients. Overall, the most common reason for infertility was diminished ovarian reserve (DOR) (21%) and second most common were PCOS and unexplained (both 16.3%). Most patients underwent IUI (65%) and 35% underwent PGT and from those, two patients underwent PGT-M for non-NBN mutations. Affected males had normal sperm analyses on average with no significant differences noted. Affected females had a mean AFC of 16.3 and mean AMH of 4.08. In terms of outcomes, from a single IUI cycle, 30% of affected patients achieved pregnancy. From a single IUI treatment, 19% achieved pregnancy.

CONCLUSIONS: ECS identifies patients who are carriers for NBN, which puts them at increased risk for cancer. NBN has also been associated with premature ovarian insufficiency. Outcomes of ART from patients who are NBN mutation carriers have not been studied. Our study shows that these patients are similar to the general population and have comparable clinical outcomes. Aside from increased cancer risk, they should be counseled on all effective and increasing future cancer risk through IVF. Future studies are warranted.

Support: None

References:

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ARTOUTCOMESINNIJMEGENBREAKAGESYNDROME CARRIERS.

Amalia Namath, M.D.,1 Samad Jahandideh, Ph.D.,2 Jason Bromer, M.D.,3 Kathleen Devine, M.D.,2 Jeanne E. O’Brien, MD, MSc1 Rush University Medical Center, Chicago, IL;2Shady Grove Fertility, Washington D.C., DC;3Shady Grove Fertility Center, Rockville, MD.

OBJECTIVE: To investigate the ART outcomes of male and female carriers of Nijmegen Breakage Syndrome (NBN).

MATERIALS AND METHODS: All patients found to be mutation carriers for Nijmegen Breakage Syndrome (NBN) during expanded carrier screening (ECS) by one provider (SEMA4) at a large fertility center from 2020-2021 were analyzed. All patients received focused genetic counseling prior to starting fertility treatment about the increased cancer risk associated with this mutation and the option of pre-implantation genetic testing for monogenic disorders (PGT-M). Clinical outcomes, including diagnosis, type of fertility treatment, clinical pregnancy rates, and use of PGT were analyzed. For male patients with NBN mutation, semen analyses (SA) were analyzed. For female patients, their antral follicle count (AFC) and AMH were analyzed. Statistical analysis was performed with p<0.05 considered statistically significant.

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Support: None

References:

P-330 6:45 AM Tuesday, October 25, 2022

EVALUATION OF POTENTIAL FACTORS INVOLVED IN VARIABLE PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) RESULTING RATES BETWEEN IVF CLINICS. Kristine McWilliams, MD, PhD.1 Albulena Zogaj, BS, MS,2 Iris. TIENLYNN Lee, MD,3 Tara D. Berger, PhD,4 Perea Collins, Ph.D.1 CooperSurgical, Trumbull, CT;2CooperSurgical, Trumbull;3UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, Philadelphia, PA;4Penn Fertility Care, Philadelphia, PA.

OBJECTIVE: To identify factors associated with variable PGT-A outcomes, particularly failure to produce a result, between IVF clinics

MATERIALS AND METHODS: 20 North American clinics with high PGT-A volumes were selected for retrospective analysis. All samples were tested by the CooperSurgical PGTai 2.0 PGT-A platform, an NGS-based platform that incorporates AI-driven analysis, as well as automated result reporting. PGT-A and cycle data for these 20 clinics were collected from January of 2021 to January of 2022. The percentage of submitted samples that did not produce a result (“no result” rate) was recorded for each clinic. Clinics were stratified according to overall “no result” rates into categories of Low (<1%); Medium (1%-2.9%); High (3% or higher; 5 clinics). Differences between Low, Medium, and High clinics were assessed by one-way ANOVA with Tukey HSD analysis for averaged: patient age, samples per PGT-A referral, euploidy rate, aneuploidy rate, mosaicism rate, rate of lack of sample DNA amplification (“no amplification”), and rate of samples with insufficient quality to produce a result via NGS (“quality insufficient”). The total number of patients referred and distance from IVF clinic to PGT laboratory were also evaluated.

RESULTS: Clinic “no result” rates ranged from 0.64%-8.50%, averaging 2.16% (SD=1.79%). Of all parameters evaluated, only differences in the rates of no sample amplification and samples with insufficient quality reached significance between Low, Medium, and High “no result” clinics (Table 1).

Table 1: Average results between All clinics, as well as clinics with “Low”, “Medium”, or “High” average rates of PGT-A samples producing “no result”

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All</th>
<th>“Low”</th>
<th>“Medium”</th>
<th>“High”</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Age</td>
<td>38.5</td>
<td>39.3</td>
<td>38.2</td>
<td>38.0</td>
<td>0.058</td>
</tr>
<tr>
<td># Patients</td>
<td>629.3</td>
<td>817.4</td>
<td>569.5</td>
<td>461.6</td>
<td>0.378</td>
</tr>
<tr>
<td>Samples per patient</td>
<td>4.4</td>
<td>4.6</td>
<td>4.2</td>
<td>4.2</td>
<td>0.524</td>
</tr>
<tr>
<td>Clinic distance (miles)</td>
<td>902</td>
<td>518</td>
<td>1250</td>
<td>883</td>
<td>0.434</td>
</tr>
<tr>
<td>Euploidy rate (%)</td>
<td>44.7</td>
<td>43.3</td>
<td>45.4</td>
<td>45.6</td>
<td>0.727</td>
</tr>
<tr>
<td>Aneuploidy rate (%)</td>
<td>37.9</td>
<td>39.7</td>
<td>37.7</td>
<td>35.7</td>
<td>0.528</td>
</tr>
<tr>
<td>Mosaic rate (%)</td>
<td>15.0</td>
<td>15.7</td>
<td>14.9</td>
<td>14.23</td>
<td>0.258</td>
</tr>
<tr>
<td>No amplification rate (%)</td>
<td>0.3</td>
<td>0.1</td>
<td>0.4</td>
<td>0.8</td>
<td>0.00001</td>
</tr>
<tr>
<td>Quality insufficient rate (%)</td>
<td>1.6</td>
<td>0.7</td>
<td>1.5</td>
<td>3.7</td>
<td>0.0017</td>
</tr>
</tbody>
</table>

CONCLUSIONS: PGT-A no result rates vary across clinics, driven by significant differences in biopsy samples to both produce a DNA amplification signal, and for that DNA to be of significant quality to produce a clear PGT-A result. However, clinic differences in “no result” rates appear to be clearly driven by patient demographics, clinic volumes, location, or overall achieved PGT-A results.

IMPACT STATEMENT: PGT-A “no result” rates differ considerably between IVF clinics. High “no result” rates for a given clinic warrant partnership with the PGT laboratory to investigate and optimize associated procedures within the IVF laboratory.
MUTATIONS INHERITED CANCER GENE REPRODUCTIVE DECISIONS OF CARRIERS WITH 6:45 AM Tuesday, October 25, 2022

OBJECTIVE: Fumarase deficiency (FD) is an autosomal recessive condition characterized by severe neurologic abnormalities due to homozygous pathogenic variants in the fumarate hydratase (FH) gene. Heterozygous carriers of FH mutations have an increased risk of developing uterine leiomyomas. There is limited data regarding the incidence and treatment outcomes of patients with FH mutations. Therefore, the objective of our study was to characterize the incidence, infertility diagnoses, treatments, and outcomes of women presenting to our fertility center who were found to be carriers of FH mutations.

MATERIALS AND METHODS: This is a retrospective case series of women who were found to be carriers of FH mutations (c.1431_1433dup, p.K474dup and c.521C>G, p.P174R) on a carrier screening panel at a single academic fertility center from January 2018 to July 2021. Patient demographics, ultrasound findings, ovarian reserve markers, infertility diagnoses, treatments, and outcomes were obtained and analyzed using descriptive statistics.

RESULTS: Over the study period, 5,841 patients had genetic screening of which 10 (0.2%) were found to be carriers for FH. Eight patients were seen for infertility, 1 patient presented desiring planned oocyte cryopreservation, and 1 patient was seen from the study as she was lost to follow up. The mean age of FH carriers was 34.5 years (range: 32-39 years) with a mean AMH of 3.14 ng/ml (range: 0.44-5.56 ng/ml) and an average uterus length of 6.4 cm (range: 4.9-8.0 cm). Six patients identified as White, 1 Multiracial, 1 Black, and 1 unknown. Of the 9 FH carriers included, 2 (22%) had imaging consistent with uterine leiomyomas. One patient underwent a hysteroscopic myomectomy prior to initiating two cycles of ovulation induction (OI) followed by artificial insemination with subsequent successful frozen embryo transfer. Her pregnancy was complicated by intra-uterine growth restriction (IUGR) and she delivered a healthy live born at 37 weeks and 2 days via cesarean section due to breech presentation. The remaining 7 patients’ diagnoses included: recurrent pregnancy loss, polycystic ovary syndrome, tubal disease and male factor infertility, unexplained infertility (2), and encounter for procreative management (2). One patient conceived after 1 cycle of ovulation induction with intrauterine insemination (OI/UI) and the pregnancy was complicated by hypertensive disorder and IUGR, followed by an uncomplicated vaginal delivery at 37 weeks and 2 days. Other patients in the study only pursued OI/UI or timed intercourse and were unsuccessful.

CONCLUSIONS: Patients with infertility should be offered genetic carrier screening that includes FH mutations, as carriers are at risk for developing uterine leiomyomas, which are known to influence fertility, infertility diagnoses, treatments, and outcomes. Further research with a larger sample size is needed to investigate the impact of heterozygous FH mutations on infertility treatments and outcomes.

IMPACT STATEMENT: Heterozygous FH carriers are at increased risk for leiomyomas that may impact their fertility.

REFERENCES:

P-333 6:45 AM Tuesday, October 25, 2022

REPRODUCTIVE DECISIONS OF CARRIERS WITH INHERITED CANCER GENE MUTATIONS. Diane Klepacka, B.A., M.S., Annette M. Matts, MS,1 Alyssa Schickendanz, M.S., C.G.C.2 Rachel Swihart, MS,1 Lacey Armitage, BS,1 William B. Schoolcraft, MD,2 Mandy Katz-Jaffe, PhD1 CCRM Genetics, Lone Tree, CO; 2Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Carriers of an inherited cancer gene mutation have significantly increased risks of cancer during their lifetime. There is a 50% chance of passing on the cancer gene mutation due to autosomal dominant inheritance. One reproductive option for these carriers is IVF with preimplantation genetic testing for monogenic diseases (PGT-M) that allows for the selection of unaffected embryos for transfer, hence preventing transmission of the cancer gene mutation to the next generation. The aim of this study was to review treatment decisions by carriers of inherited cancer gene mutations to assist in future clinical management and counseling practices.

MATERIALS AND METHODS: Patients identified as carriers of inherited cancer gene mutations (n=141; mean 1.9 IVF cycles per patient) were counseled about reproductive options including PGT-M. Close to half (44.7%) of the cancer gene mutations belonged to either BRCA1 or 2 and the next most prevalent cancer gene was ATM at 20.6%. Statistical analysis was performed based on patient treatment decisions: PGT-M (n=67 patients; 47.5%; 136 cycles) and Declined PGT-M (n=74 patients; 52.5%; 126 cycles). Differences in group means between univariate dependent variables were assessed with an unpaired, two-sided T-test of base 10 log-transformed data. Significance determined at p<0.05.

RESULTS: Significant differences were observed between the groups, with patients who declined PGT-M being significantly older (37.0 vs 34.7 years PGT-M; p<0.001), having lower AMH (2.1 vs 4.3 PGT-M; p<0.001), lower antral follicle count (14.1 vs 22.5 PGT-M; p<0.001), fewer oocytes retrieved (13.5 vs 21.3 PGT-M; p<0.001) and fewer usable blastocysts (4.2 vs 6.4 PGT-M; p<0.001). Of the patients that elected PGT-M, 53 cycles (89.7%) resulted in the identification of ≥1 euploid, unaffected embryo for transfer. Across all carriers of inherited cancer gene mutations, a majority of IVF cycles (85.1%; 223 cycles) included PGT-A, and a comparable timely embryo rate of 44% was observed when compared to a 44% pregnancy rate of carriers with a poorer IVF prognosis were more likely to decline PGT-M highlighting that concern for fertility success may be more significant in patient treatment decisions. For those carriers of inherited cancer gene mutations that did elect to pursue PGT-M, close to 90% had at least one euploid, unaffected embryo for transfer. This encouraging data will be useful during patient genetic counseling and future clinical practice.

IMPACT STATEMENT: Carriers of inherited cancer gene mutations who elect PGT-M as a reproductive choice most likely will result in a transfer with an unaffected, euploid embryo.

SUPPORT: None.

P-334 6:45 AM Tuesday, October 25, 2022

MOSAIC EMBRYOS: DESCRIPTIVE ANALYSIS AND CLINICAL OUTCOMES AFTER PREIMPLANTATION GENETIC TESTING - ANEUPLOIDIES (PGT-A). Josep Pla-Victori, CGC, Maria Cruz, PhD,2 Judith Reina-Castillo, CGC,3 Andrea Otero Gonzalez, GC,4 Nicolas Prados, PhD MSc,5 Antonio Requena, MD6 1IVI, Barcelona, Barcelona, Spain; 2IVIRMA Global Headquarters, Madrid, Spain; 3IVIRMA, Valencia, Spain; 4IVIRMA Global Headquarters, Seville, Spain; 5IVI RMA Spain, Madrid, NJ, Spain.

OBJECTIVE: Descriptive analysis of mosaic embryos (ME) and their clinical outcomes (COs).

MATERIALS AND METHODS: Observational retrospective analysis of 538 PGT-M cycles at a preimplantation genetic testing - aneuploidy (PGT-A), and COs after embryo transfer. Inclusion criteria: PGT-A cycles between January 2020 and March 2022, from 171IVF clinics. Data was anonymised prior to analysis. Descriptive variables included type of ME (whole chromosome (WCM), segmental (SM)), type of aneuploidy (monosomy, trisomy), number of chromosomes in ME (simple (SA), dual (DA), complex(CA)), transferability based on current criteria, frequency per chromosome. COs included percentage of transferable ME that were transferred, pregnancy rate (PR), miscarriage rate (MR), ongoing pregnancy rate (OPR). MEs were stratified by the descriptive variables. ME rate per embryologist was evaluated. Statistical differences were assessed with a Chi-square analysis with SPSS (IBM Corporation, Armonk, NY, USA).

RESULTS: 55.44% ME involved WCM, 39.04% had SM and 5.51% were mixed. 88.19% of ME were classified as non-transferable. 46.03% of ME were classified as non-transferable.
Chromosomes 9, 14 and 1 were the most frequent, and chromosomes 15, 22 and Y were the least frequent. 18.72% of transferable ME were transferred. Clinical results are presented in Table 1. ME rate per embryologist was significantly different (n=96; p<.001).

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>PR (%)</th>
<th>MR (%)</th>
<th>OPR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ME</td>
<td>43.20a</td>
<td>19.10b</td>
<td>33.51a</td>
</tr>
<tr>
<td>WCM</td>
<td>43.88a</td>
<td>20.90a</td>
<td>34.48a</td>
</tr>
<tr>
<td>SM</td>
<td>43.56a</td>
<td>15.90a</td>
<td>34.07a</td>
</tr>
<tr>
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<td>CA</td>
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</tbody>
</table>

a p<.001 compared to euploid embryos
b p<.05 compared to euploid embryos
c p<.05 between groups

CONCLUSIONS: Aneuploid frequencies were consistent with previous studies. Almost half of ME were classified as non-transferable. A minority of couples with a transferable ME opted to transfer it. Clinical outcomes showed reduction in the PR and OPR; however, differences in MR were not significant. ME transfer should be considered after extensive genetic counselling. Prioritisation based on WCM vs SM, monosomies vs trisomies, or number of chromosomes in the ME was not supported. We suggest that ME transfer criteria may be revised as couples may benefit from more flexible criteria. ME rate per embryologist varied significantly, suggesting the biopsy process could impact the labelling of embryos.

IMPACT STATEMENT: This study provides further evidence regarding ME, which is a highly debated practice. Further research on biopsy impact on mosaicism or decisions to transfer or not ME could provide further evidence in this field.

P-336 6:45 AM Tuesday, October 25, 2022

THE EMBRYO HEALTH STUDY: RATE OF PATIENTS ELECTING POLYGENIC RISK SCORES IN PREIMPLANTATION GENETIC TESTING. Jennifer Eccles, LCGC;1 Deirdre Leathy, LCGC;2 Kelsey Reynolds, MS;2 Bhavini Rana, BA;1 Diego Marin, PhD;1 Nathan R. Treff, PhD, HCLD;1 Genomic Prediction, Inc., North Brunswick, NJ;2 Rutgers University.

OBJECTIVE: Embryo selection after PGT-A is limited to morphological grading. However, PGT for polygenic disease risk (PGT-P) has emerged as an additional method for selection. This study investigates the rate at which patients elect to include PGT-P in their IVF plan.

MATERIALS AND METHODS: Patients electing PGT-A at a single IVF center were recruited for an IRB approved “Embryo Health Study,” starting late 2020. Patients had pre-test genetic counseling to review benefits and limitations of PGT-P. Pre or post-embryo grading. However, PGT for polygenic disease risk (PGT-P) has emerged as an additional method for selection. This study investigates the rate at which patients elect to include PGT-P in their IVF plan.

RESULTS: In total, 113 patients were counseled about the Embryo Health Study. Sixty-three (55.8%) elected to participate, 43 (38.0%) declined and 7 (6.2%) patients remained undecided. Of the 63 patients, 43 (68.2%) preferred simultaneous reporting and 20 (31.7%) opted for sequential reporting. All participants who elected to report available disease. The total number of embryos tested was 253 with an average of 4 per patient. Mean maternal age was 36.4 years for participating and non-participating patients. Eleven participants have responded to the post-test survey, of which 90% ranked embryo health score as the highest importance compared to morphology or sex based selection. Success rates following PGT-P based embryo selection were 71%, compared to 62% using PGT-A and morphology based selection.

CONCLUSIONS: A significant percentage of patients have an interest in obtaining PGT-P to aid embryo selection. Most patients elected to obtain PGT-P results at the same time as PGT-A and all elected the maximum number of transferable conditions. No significant age difference between patients who elected to report available disease and those who did not. A non-significant number of euploid embryos may not significantly influence patient decision-making. In addition, embryo selection based on PGT-P did not reduce success rates when compared to morphology based selection. Preliminary data from the post-test survey indicates most respondents value PGT-P.

IMPACT STATEMENT: These data represent the first experience with informing patients of the option to include PGT-P in their IVF plan. Over half of patients utilizing PGT consented to the study, allowing PGT-P to be available to them. Efforts to reduce barriers to access are indicated.

P-336 6:45 AM Tuesday, October 25, 2022

MATERIAL FIBROID IMPACT ON CELL FREE DNA (CFDNA) SCREENING. Samantha Caldwell, MS;1 Brittany Dyr, MS; Vanessa Nithiboon, M.SC.;2 Laura Kline, MS; Juan-Sebastian Saldivar,1 LabCorp, Winston Salem, NC;3 St Johns, FL;1 Labcorp, Portland, OR;2 Morrissville, NC;3 Labcorp, NC.

OBJECTIVE: In cell free DNA (cfDNA) screening, a proportion of the circulating cfDNA is placental and serves as a proxy for fetal aneuploidy status. As the remaining cfDNA originates from maternal tissue, identification of unexpected maternal findings is possible. Like other tissues, fibroids can contribute cfDNA to maternal plasma. Unlike other tissues, fibroids are heterogeneous and have abnormal chromosomal complements which may confound fetal aneuploidy screening. Here we investigate cfDNA data and results from 57 patients with known fibroids.

MATERIALS AND METHODS: Samples submitted to Sequenom Laboratories for MaterniT®21 PLUS or MaterniT®GENOME testing between Jan 2016 - Aug 2021 with confirmed fibroids per clinician reporting were included. Diagnostic testing was elicited from the clinical provider or via diagnostic samples submitted to Laboratory Corporation of America. Genome wide data, which is available on all samples regardless of ordered test type, was reviewed for detected abnormalities.

RESULTS: 57 patients with fibroids were identified and sequencing data reviewed. The majority of samples (n=35, 61%) in this cohort resulted in a non-reportable (NR) cfDNA result and 19 (33%) resulted in a positive result. 90% (n=17) of positives were positive for findings outside traditional cfDNA screening with 7q deletions being most common (n=5). Pre or postnatal diagnosis was performed in 18 pregnancies, 15/18 with positive and 3/18 with NR results. 89% (n=16) had normal diagnostics, one case was discordant trisomy 21, and one case had monosomy X (NR cfDNA).

In all samples, (n=57) cfDNA data was reviewed for detected copy number variants (CNVs) and aneuploidies. CNVs were detected on all autosomes except chr 20, and most frequently observed on chrs 1, 7, and 3, respectively. Deletions (79%) were more common than duplications. The mean CNV size was 41.7Mb (median 33.15Mb). Trisomy 12 and 4 were the most frequently observed aneuploidies. The mean number of abnormalities detected per sample was 3 (range 0-12).

CONCLUSIONS: It is not unexpected that a fibroid, dependent on maternal and fibroid physiology, could also contribute cfDNA and potentially confound aneuploidy screening, depending on individual fibroid cytogenetics. Detected CNVs are consistent with fibroid cytogenetic literature. As the largely normal fetal diagnostic testing supports fibroid cfDNA contribution as the likely explanation for this subset of false positive and NR results. Upon receipt of a NR or positive cfDNA result in a patient with fibroids, fibroid interference should be considered in the differential.

Importantly, fibroids are not a contraindication to screening and are relatively common in the obstetrical population. This retrospectively ascertained cohort is likely enriched for NRs and positives, as fibroid status is not routinely recorded.

IMPACT STATEMENT: Maternal fibroids can be associated with abnormal sequencing data and may confound fetal aneuploidy screening. Close communication with the performing laboratory and additional counseling considerations may be important for patients with known fibroids and positive or NR cfDNA.

REFERENCES:

ANALYSIS OF PREFERENCES FOR ALLELE SEGREGATION ACCORDING TO THE GENDER OF AFFECTED PARENT IN PREIMPLANTATION EMBRYOS WITH MYOTONIC DYSTROPHY TYPE 1, HUNTINGTON DISEASE AND SPINOCEREBELLAR ATAXIA.

Sun Ok Park, MS,1 Min Jee Kim, MS,2 Ye Seul Hong, MS,3 Gaeul Han, MS,3 kyoung Hee Choi, Ph.D.,4 Eun A Park, MS,4 Eun Jeong Yu, MD,1 Inn Soo Kang, MD, Ph.D,1 1CHA Biotech, Seoul, Korea, Republic of (South); 2CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South); 3CHA Seoul Fertility Center, Seoul, Korea, Republic of (South); 4CHA Seoul Fertility Center, OB&GY, Seoul, Korea, Republic of (South).

OBJECTIVE: A previous study reported in 2020 suggested that in trinucleotide repeat disorder of autosomal dominant inheritance, there is a preferential allele segregation pattern according to the gender of the parent. We assessed the segregation pattern of preferential alleles in preimplantation embryos in Korean couple.

MATERIALS AND METHODS: A total of 185 embryos from 31 cycles of PGT-M in 14 couples of Myotonic dystrophy type 1 (DM1), 4 couples of Huntington disease (HD), and 3 couples of Spinocerebellar ataxia (SCA) that underwent PGT-M from 2016 to 2021 were analyzed. The female affected group consisted of 9 couples in DM1, 2 couples in HD, and 1 couple in SCA. The male affected group consisted of 5 couples in DM1, 2 couples in HD, and 2 couples in SCA. The embryo was analyzed using karyomapping and PCR-based STR marker. Karyomapping was performed by HumanKaryomap-12 BeadChip protocol (Illumina, USA), analyzed using BlueFuse Multi software (Illumina). Linkage analysis using STR marker was performed by multiplex PCR and 3500 capillary electrophoreses.

RESULTS: In this study, we evaluated a total of 185 embryos from 31 cycles in 14 DM1, 4 HD, and 3 SCA couples. For each disease, the percentage of affected embryos in the female affected group was 47.4% (37/78) in DM1, 42.9% (7/16) in HD, and 42.9% (7/16) in SCA. The percentage of affected embryos in the male affected group was 56.1% (32/58) in DM1, 64.1% (11/17) in HD, and 54.5% (6/11) in SCA. In total, the percentage of affected embryo was 48.4% (46/95) in female affected group and 59.8% (49/82) in the male affected group (Fisher’s exact test p = 0.17).

The affected embryos did not show a significant difference among these trinucleotide repeat disorders. Eight (4.3%) out of 185 embryos could not be determined due to ADO or amplification failure.

CONCLUSIONS: Unlike the previous report, our data shows no significant difference in segregation of the preferential allele of trinucleotide repeat expansion in preimplantation embryos for DM1, HD, and SCA. In this study, it cannot be concluded that the preferential allele can be distinguished according to parental ancestry, unlike previously reported papers, but additional analysis is needed to confirm more data in the future.

IMPACT STATEMENT: Our findings provide evidence that trinucleotide repeat disorders are frequent in fresh oocyte donation cycles and need to be considered when counseling patients, and indirectly suggests the potential benefit of PGT-M in the management of these embryos.

SUPPORT: CReAte Fertility Centre.
testing: 38% (5/13) had 0 AGG, 38% (5/13) had 1 AGG, and 23% (3/13) had 2 AGGs. 8% (4/49) additional patients were offered but declined AGG testing. 18% (9/49) of PGT-M patients had terminated an affected pregnancy prior to PGT-M. 10% (5/50) had documented family members affected or PGT-M. Between the treatment cycles, we sought to study the association between the blastulation rate, the presence of 1PN fertilized oocytes and a high blastulation rate is associated with a higher rate of aneuploidy. Further study into the mechanisms governing embryo development and the different check- points is warranted.

IMPACT STATEMENT: A cohort of embryos ploidy rate is negatively associated with the presence of 1PN fertilized oocytes and with the blastulation rate.

E-PAPER ABSTRACT SESSION: T13

P-341 6:45 AM Tuesday, October 25, 2022

AMH INDEPENDENTLY PREDICTS ANEUPLOIDY BUT NOT LIVE BIRTH PER TRANSFER IN IVF PGT- A CYCLES. Howard J. Li, MD, David B. Seifer, MD, Reshef Tal, MD, PhD Yale School of Medicine.

OBJECTIVE: To determine whether AMH predicts aneuploidy or live birth in IVF PGT-A cycles.

MATERIALS AND METHODS: Analysis of SART-CORS database (2014-2016) for autologous index cycles utilizing PGT-A for all embryos, resulting in either primary FET (of a presumed euploid embryo) or canceled transfer due to lack of normal embryos following PGT-A. Cycles without AMH reported within 1 yr were excluded. Likelihood of ≥1 euploid embryo for transfer and live birth following PGT-A were modeled with multivariate logistic regression using age, AMH, and number of embryos biopsied as independent variables.

RESULTS: Of 51,273 cycles utilizing PGT-A for all embryos, 2,100 cycles resulting in canceled transfer due to lack of normal embryos and 8,778 cycles resulting in primary FET were analyzed. There were 4,893 live births (55.8% of transfers).

Cycles with no normal embryos had a mean patient age of 40.0 ± 3.2 yrs (mean ± SD), mean serum AMH of 1.9 ± 2.4 ng/mL, and mean of 2.5 ± 1.7 embryos biopsied. Cycles resulting in ≥1 euploid embryo for transfer had a mean age of 37.0 ± 3.7 yrs, mean AMH of 3.5 ± 3.5 ng/mL, and mean of 5.1 ± 2.9 embryos biopsied.

AMH levels of cycles with ≥1 euploid embryo were greater than those of cycles with no normal embryos, stratifying by number of embryos biopsied (1-2, 3-4, 5-6, ≥ 7), P < 0.017 for each stratum.

Multivariate logistic models for likelihood of ≥1 euploid embryo were fitted for each of 3 age groups: < 35, 35-37, and ≥ 38 yrs. Adjusting for achieved number of embryos biopsied, AMH was a predictor of ≥1 euploid embryo for patients 35-37 yrs (OR 1.09; 95% CI 1.02–1.17) and ≥38 yrs (OR 1.06; 95% CI 1.02–1.09), with borderline significance for <35 yrs (OR 1.07; 95% CI 1.00–1.16). Age was a predictor of ≥1 euploid embryo for 35-37 yrs (OR 0.81; 95% CI 0.68–0.97) and ≥38 yrs (OR 0.71; 95% CI 0.69–0.74), but not for <35 yrs (OR 1.04; 95% CI 0.95–1.13).

In comparative model analysis, models including AMH were preferred over models without AMH, P < 0.03 in Likelihood Ratio testing for all 3 age groups. In Akaike information criterion scoring, AMH was superior to age as a predictor of ≥1 euploid embryo for age groups <35 yrs and 35-37 yrs, but not ≥38 yrs. Across all cycles, age (OR 0.95, 95% CI 0.94–0.96) and number of embryos biopsied (OR 1.14, 95% CI 1.13 – 1.15) predicted live birth, but not AMH (OR 1.00, 95% CI 0.98 – 1.01). Among the subset of cycles resulting in ≥ 1 euploid embryo, neither age nor AMH were predictors of live birth per transfer. The fitted model was not predictive of live birth (AUC 0.52, 95% CI 0.50 – 0.53).

CONCLUSIONS: Adjusting for age and number of embryos biopsied, AMH independently predicts likelihood of obtaining ≥ 1 euploid embryo in IVF PGT-A cycles. However, in contrast to prior findings in non-PGT IVF cycles, neither age nor AMH are predictive of live birth once a euploid embryo is identified by PGT-A for transfer.

IMPACT STATEMENT: While AMH is a predictor of live birth for non-PGT IVF cycles, it is unknown if this is due solely to quantitative factors or if qualitative factors contribute. These results suggest a predictive role for AMH on oocyte quality (aneuploidy), but not live birth once a euploid embryo is identified following PGT-A.

FERTILITY & STERILITY®
NON-INVASIVE PLOIDY EVALUATION BY ANALYSIS OF EMBRYO CULTURE MEDIUM

Hiroyuki Watanabe, M.S.,1 Hiroya Kitasaka, Ph.D.,2 Yuta Kida, M.S.,3 Fumiyu Kondo, M.S.,1 Sho Takeeda, B.S.,4 Noritaka Fukunaga, Ph.D.,4 Yoshimasa Asada, M.D., Ph.D.,1,3 Asada Ladies Clinic, Nagoya, Japan; 2Nagoya, Japan; 3Asada Ladies NAGOYA Clinic, Nagoya, Japan; 4Asada Ladies NAGOYA Clinic, Nagoya-Shi, Aichi, Japan.

OBJECTIVE: Currently TE -Biopsy is indispensable for PGT analysis. The technique has to be carefully carried out so as to not to jeopardise embryo viability. Other alternatives such as non-invasive PGT (niPGT) by Cell free DNA released from embryos into culture medium has been reported, and found to be highly correlated with the analysis results of TE-biopsy (Rubio et al., 2020). We started preliminary studies for clinical application of niPGT in 2021, and the concordance rate between the culture medium after embryo culture and the analysis results of whole blastocysts was about 90% (Fukunaga et al., 2021). In this updated study, we report on a larger data set the concordance rate between the culture medium and the analysis of blastocysts that were euploid or aneuploid.

MATERIALS AND METHODS: A total of 200 pronuclear-stage frozen embryos for which consent was obtained for research use, were thawed and co-cultured until Day 4 and then individually cultured in a new dish after Day 4. For 103 embryos that reached the morula stage on Day 4 or Day 5 and reached the blastocyst on Day 6 or Day 7, the blastocyst and the culture medium after individual culturing of the target blastocyst were collected.

RESULTS: The concordance rate of the ploidy results between the culture medium and blastocyst was 71.8% (74/103). For embryos whose blastocyst analysis results were euploid, the concordance rate with the culture medium was 81.3% (52/64), and for embryos whose blastocyst analysis results were euploid, the concordance rate with the culture medium was 56.4% (22/39).

CONCLUSIONS: From the results, in the embryos whose blastocyst analysis results were euploid, the concordance rate was about the same as previously reported. On the other hand, embryos that were euploid had a lower concordance rate than previously reported. The factors behind the low concordance rate in positive ploidy embryos may be linked to embryo morphology, culture days, patient background, etc., and detailed verification is still ongoing.

IMPACT STATEMENT: Compared to conventional TE biopsy PGT-A analysis of cell free DNA, has various advantages for example such as no invasion to embryos, technical ease, and shortened working time etc. Therefore, it would be very beneficial in the field of assisted reproductive technology if we could optimize the method of this technology, achieve further improvement in test accuracy, and break away from the current mainstream PGT-A with TE biopsy.

SUPPORT: None.

REFERENCES:

Blastocyst Ploidy is not correlated with the choice of ovulatory trigger agent after controlling for age and cohort size.

Bruce S. Shapiro, M.D., Ph.D.,1 Kajal Verma, MD,2 Melody A. Rasouli, MD, MBA,1 Leah A. Kaye, B.A., M.D.,M.S.,1 Forest C. Garner, MS,1 Carrie E. Bedient, MD1 Fertility Center of Las Vegas, Las Vegas, NV;2 University of Nevada, Las Vegas, Las Vegas, NV; University of Connecticut Health Center, Las Vegas, NV.

OBJECTIVE: To identify maternal and embryonic factors that correlate with and potentially influence embryo aneuploidy.

MATERIALS AND METHODS: This is an IRB-approved retrospective study. Patients underwent conventional ovarian stimulation with exogenous gonadotropins. Embryos were group-cultured to the blastocyst stage. Trophectoderm biopsies were followed by pre-implantation genetic testing for aneuploidy (PGT-A) using next-generation sequencing. Multiple logistic regression was used to determine if patient age, the ovulatory trigger agent (leuprolide acetate alone, hCG alone, or both in combination), biopsy, or both in combination, biopsy, or both in combination, biopsy, or both in combination, biopsy, or both in combination, total number of eggs collected, delayed (day 6 or 7) blastocyst formation, or blastocyst morphology correlated with ploidy. P<0.05 was considered significant.

RESULTS: A total of 1,411 blastocysts were biopsied in the 2.5-year study period. Patient age at retrieval ranged from 20.8 to 45.5 years. A logistic regression model was developed predicting PGT-A test results. The significant predictors of abnormal (aneuploidy) test results in this model were: patient age at retrieval (P<0.0001), trophectoderm quality (P=0.0001), delayed blastulation (P<0.0001), and the number of eggs collected (P=0.0419). Specifically, increased risk of an abnormal PGT-A result was associated with increasing patient age, poorer trophectoderm quality, delayed blastulation, and fewer collected oocytes. The ovulatory trigger agent was not significantly correlated with embryo ploidy (P=0.1966).

CONCLUSIONS: The ovulatory trigger agent was not significantly correlated with embryo ploidy among these 1,411 biopsied blastocysts. This suggests the trigger may be adjusted for safety reasons with little or no impact on the ploidy of resulting blastocysts.

SUPPORT: None.
P-346 6:45 AM Tuesday, October 25, 2022

THE CHROMOSOME ERRORS OF HUMAN BLASTOCYST IN AGE OF 44 YEARS OLD AND BEYOND. Hui Liu, MD, MS, Jiage Song, M.A., John J. Zhang, MD, PhD New Hope Fertility Center, New York City, NY.

OBJECTIVE: Female fertility decreases as matenal age increases in connection with chromosome errors. However, the evidence in age of 44 years old and beyond is limited - this study is to explore the characteristics of individual and overall chromosome errors with regards to aneuploidy (trisomy and monosomy) and sub-aneuploidy (partial aneuploidy, mosaic, and partial mosaic) in blastocyst of old age.

MATERIALS AND METHODS: Retrospective analysis of clinical lab data involved biopsy of 2305 trophectoderm samples from 2305 blastocyst at day 5 to day 7, fresh or frozen. Specifically, 850 samples came from 44-50 years old women (old age), 1455 samples came from 19-32 years old women (young age). Age is defined as the first date of blastocyst cryopreservation. Data excluded samples from cells of cleavage, morula, and cavity embryos, as well as samples tested with polyploidy, inconclusive, and degenerate DNA. PGT-A applied Next Generation Sequencing (NGS) and Array Comparative Genomic Hybridization (aCGH). Fisher’s exact test, two-tailed P value were applied to statistical analysis. In our analysis, blastocysts were categorized into three types: Type 1 blastocyst (aneuploidy), Type 2 blastocyst (sub-aneuploidy), and Type 3 blastocyst (affected concurrently by both aneuploidy and sub-aneuploidy). Individual chromosome errors cover only aneuploidy from Type 1 and Type 3 blastocyst.

RESULTS: In comparison with young age, overall rate of chromosome errors in blastocyst from old age is much higher (95.1% vs 44.6%, p<0.001), and the rate of chromosome errors at the age of 44, 45 and 46 were 94.1%, 94.5%, and 95.8% respectively. Noticeably, none was euploid followed by a testing of 130 blastocysts from age older than 46. In further comparisons, we found that the rates of chromosome errors in both Type 1 and Type 3 blastocyst from old age are extremely higher (82.5% vs. 21%, and 9.3% vs. 4% respectively, with p<0.001), however, the rate of chromosome errors in Type 2 blastocyst from old age is lower by 16 percentage point (p<0.001). In additional comparison with young age, the rates of individual chromosome errors with respect to aneuploidy in Type 1 and 3 blastocyst of old age are significantly higher in all chromosomes except Chromosome 1. In old age, the percentages of individual chromosome errors on Chromosome 21, 15, and 22 are 20 percentage points higher (21.2%, 20.9%, and 20.5% respectively), and the percentages on Chromosome 16, 19, 20, 18, 13, 11, and 9 are higher for more than 10 percentages point.

CONCLUSIONS: The aneuploidy instead of sub-aneuploidy are relevant with old age regarding the higher percentages of chromosome errors in blastocyst. The higher rate of individual chromosome errors in old age involve all chromosomes except Chromosome 1. Chromosome 21, 15, and 22 are most vulnerable to the age factor.

IMPACT STATEMENT: This study provides a comprehensive profile of chromosome errors relevant with old age and a discernment of individual chromosomes. Both of them should assist further exploration of the mechanism of old age aneuploidy.

SUPPORT: N/A

REFERENCES: N/A

P-347 6:45 AM Tuesday, October 25, 2022

THAWING BLASTOCYSTS FOR REPEAT OR DE NOVO PRE-IMPLANTATION GENETIC TESTING FOR ANEUPLOIDY WITH RE-VITRIFICATION: RESULTS AND OUTCOMES. Anna Vanderhoff, M.D., Andrea Lanes, PhD, Kathryn J. Go, PhD, Elizabeth S. Ginsburg, MD, Jay Patel, MS, Serene S. Srouji, MD Brigham and Women’s Hospital, Boston, MA.

OBJECTIVE: Many patients opt for pre-implantation genetic testing for aneuploidy (PGT-A) via trophectoderm biopsy and next generation sequencing (NGS) after completion of fresh IVF cycles (fresh-bx). A thaw-biopsy and refreeze of embryos that were not previously biopsied (single-bx TBR) or with no result after initial fresh biopsy (double-bx TBR) may also be indicated. Our study seeks to determine clinical pregnancy rates after cryopreserved embryo transfer (CET) of fresh-bx vs. single-bx TBR vs. double-bx TBR embryos.

MATERIALS AND METHODS: Retrospective cohort study of biopsy results and CET outcomes for patients who underwent fresh-bx or TBR for PGT-A at an academic center between March 4, 2013, and December 28, 2021. Donor egg and gestational carrier cycles were excluded.

OBJECTIVE: We aimed to determine pregnancy outcomes by biopsy group. Generalized estimating equations were used to account for patients contributing more than one record. Biopsy results were adjusted for egg age and embryo quality.

RESULTS: 1202 patients contributed 1769 fresh cycles. Of the fresh-bx embryos, 2929 (42.7%) were euploid and 169 (2.5%) had no signal. Among the single-bx TBR embryos, 162 (47.5%) were euploid (aRR: 0.99, 0.88-1.11) and 16 (4.7%) had no signal (aRR: 1.87, 1.11-3.15). For the double-bx TBR embryos, 73 (50.3%) were euploid (aRR:0.99, 0.80-1.21) and 8 (5.5%) had no signal (aRR:2.17, 0.62-7.57).

There were 1062 fresh-bx, 68 single-bx TBR and 19 double-bx TBR euploid SETs. After adjusting, though not statistically significant, our data showed a decreased implantation rate for the double-bx TBR group when compared to the fresh-bx group (9/19 47.4% vs. 663/1062 62.4%, RR 0.76 [95% CI 0.47-1.22]) and an almost two fold decrease in ongoing pregnancy >8 weeks for the double-bx TBR group as compared to the fresh-bx group (6/19 31.6% vs. 650/1062 61.2%, aRR 0.52 [95% CI 0.26-1.03]). In addition, there was a significant increase in the miscarriage rate for the double-bx TBR group compared to the fresh-bx group (4/19 21.2% vs. 660/1062 62.4%, RR 3.39 [1.38-8.31]). These differences were not seen when the single-bx TBR embryos outcomes were compared to those of fresh-bx groups.

CONCLUSIONS: Embryos that undergo TBR before CET is an equivalent euploidy rate to fresh biopsied embryos. Our results suggest possible impaired CET outcomes for double-bx TBR embryos when compared to fresh-bx embryos, though additional data are needed.

IMPACT STATEMENT: Patients with no-result embryos after initial PGT-A should consider CET without TBR, as over 50% were found to be euploid. Patients who do opt for TBR should be counseled that the extra embryo manipulation may impair CET outcomes.

SUPPORT: No financial support.

P-348 6:45 AM Tuesday, October 25, 2022

PGT-M STRATEGY USING GENOME-WIDE HAPLOTYPE KARYOMAPPING ANALYSIS FOR PATIENTS WITH DE NOVO MUTATIONS. Min Je Kim, MD, MS, Sun Ok Park, MS, Ye Seul Hong, MS, Gaeul Han, MS, Eun A. Park, MS, Kyung Ah Lee, PH.D., Eun Jeong Yu, M.D., In Soo Kang, MD, PhD, CHA Biotech, Seoul, Korea, Republic of (South); Chaibiotech, Seoul; Chaibiotech, Seoul, South Korea; Chaibiotech, Seoul, Korea, Republic of (South); Cha Seoul Fertility Center, Seoul, Korea, Republic of (South); Cha University, Sungnam-Si, Korea, Republic of (South); CHA Seoul Fertility Center, OB&GY, Seoul, Korea, Republic of (South); Department of OB&GY, CHA Fertility Center Daegu, CHA University, Daegu, Korea, Republic of (South).

OBJECTIVE: Wide application of genome-wide SNP analysis (karyomapping) in PGT-M has made it possible to eliminate laborious painstaking customized design for each family with monogenic diseases. Karyomapping requires a reference in the family. However, there are couples who cannot undergo karyomapping due to de novo mutation or couples who do not have (absence of) appropriate reference family member. In order to overcome limitation of karyomapping, we investigated whether alternate material can be used for reference in karyomapping for preimplantation genetic testing (PGT) in patients with de novo mutations lead to successful diagnosis and pregnancy.

MATERIALS AND METHODS: Four couples with de novo point mutation ( Ehlers-Danlos syndrome, Noonan syndrome, autosomal recessive polycystic kidney disease, Wiskott-Aldrich syndrome) underwent haplotype analysis by Karyomapping at CHA Fertility Center, Seoul Station from October 2020 to October 2021. Reference DNA samples were obtained from demised affected sibling tissue such as abortus for haplotype analysis. Customized design for each family with monogenic diseases. Karyomapping due to de novo mutation or couples who do not have (absence of) appropriate reference family member. In order to overcome limitation of karyomapping, we investigated whether alternate material can be used for reference in karyomapping for preimplantation genetic testing (PGT) in patients with de novo mutations lead to successful diagnosis and pregnancy.

SUPPORT: No financial support.

P-346 6:45 AM Tuesday, October 25, 2022

THAWING BLASTOCYSTS FOR REPEAT OR DE NOVO PRE-IMPLANTATION GENETIC TESTING FOR ANEUPLOIDY WITH RE-VITRIFICATION: RESULTS AND OUTCOMES. Anna Vanderhoff, M.D., Andrea Lanes, PhD, Kathryn J. Go, PhD, Elizabeth S. Ginsburg, MD, Jay Patel, MS, Serene S. Srouji, MD Brigham and Women’s Hospital, Boston, MA.

OBJECTIVE: Many patients opt for pre-implantation genetic testing for aneuploidy (PGT-A) via trophectoderm biopsy and next generation sequencing (NGS) after completion of fresh IVF cycles (fresh-bx). A thaw-biopsy and refreeze of embryos that were not previously biopsied (single-bx TBR) or with no result after initial fresh biopsy (double-bx TBR) may also be indicated. Our study seeks to determine clinical pregnancy rates after cryopreserved embryo transfer (CET) of fresh-bx vs. single-bx TBR vs. double-bx TBR embryos.
RESULTS: The preclinical karyomapping test showed sufficient number of informative SNPs ranging from 82 to 148 in four couples, which is a considerably larger than that of STR-linked markers using conventional PCR. A total of 39 blastocysts from four couples were biopsied and 37 embryos were successfully diagnosed. Of these, 95% (36/39) of the embryos, 22 unaffected embryos (10 normal, 12 carrier) were diagnosed (56%). Single embryo transfer was done in six frozen-thawed embryo transfer cycles, and four clinical pregnancies were achieved (67%). The prenatal diagnosis by amniocentesis for all four women confirmed the result of PGT-M. Three women delivered a healthy baby without complications and one pregnancy is currently ongoing beyond 20 weeks of gestation.

CONCLUSIONS: Karyomapping can still be applied and successful outcome can be achieved even in the absence of reference family member, if other source of DNA sample serving as a reference is available, such as abortus or demised fetal/baby tissues. This approach makes use of the advantage of karyomapping over conventional PCR methods.

IMPACT STATEMENT: This study provides a new approach of utilizing karyomapping for PGT-M in couples with de novo mutations and in couples who do not have reference member in the family. This approach can, at least in part, overcome the limitation of usage of karyomapping.

P-349 6:45 AM Tuesday, October 25, 2022
DETECT CRYPTIC CHROMOSOMAL REARRANGEMENT BY OPTICAL GENOME MAPPING (OGM) IN INFERTILE POPULATION. Yunxiu Li, M.D.,1 Yanz, Ph.D.,2 Jinghui Yang, Dr., M.D.,3 Yonggang Li, M.S.,4 Yanwen Xu, Dr., M.D.,5 Ze Wu, Ph.D.,6 Xiangong Yan, Ph.D.,7 Reproductive Medicine, Kunming, China;8 Reproductive Medical Center, First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; 9 The First People’s Hospital of Yunnan Province, Kunming, China; 10 Department of Reproductive Medicine, First People’s Hospital of Yunnan Province, Kunming, China; 11 Kunming, China.

OBJECTIVE: To evaluate diagnosis value of optical genome mapping (OGM) for potential PGT-SR patient with cryptic chromosomal rearrangement.

MATERIALS AND METHODS: From 2019—2022, 12 couples with unexplained recurrent miscarriage or repeatedly deletion or duplications in same location in embryos from previous PGT cycles were included for diagnosis or re-analysis. Peripheral blood lymphocytes from these patients were collected and detected by karyotype analysis (G-400 banding). FISH, CNV-seq, third generation sequencing (Nanopore) or OGM.

RESULTS: In the 11 couples with normal karyotype (46,XX or 46,XY by G-banding) bearing adverse pregnancy and childbirth, OGM discovered novel chromosome translocation or inversion in 10 couples (90.91%). In the known couple with t(4;17)(q12;p13), OGM detect an additional t(17;19)(p13;q13), which explained the repeated emerging CNV in chromosome observed in embryos from two previous PGT cycles. For small fragment comparison, terminal translocation and inversion resolution of OGM reached <1M. The OGM results were confirmed by FISH or third generation sequencing (Nanopore). The differences in breaking position reported by OGM and Nanopore were less than 500kb. However, OGM reported 6216 structure variants per sample in average and brought 1 false positive pathogenic CNV (90.1%).

CONCLUSIONS: Our result suggest OGM is a potential choice for cryptic chromosomal rearrangement detection, particularly in certain sicario traditional karyotype reported normal but with highly suspicious rearrangement. The accuracy and precision of OGM detecting reached 500kb. However, OGM hardly detect mutations near telomere and centromere regions.

IMPACT STATEMENT: PGT can be used to help carriers of balanced translocations or inversions avoid recurrent miscarriage, to give birth to healthy offspring. For cryptic rearrangement, conventional cytogenetic methods show great limitation in diagnosis. Conventional CNV-seq/aCGH/ SNP array could not detect the balanced SVs in general. G-banding is influenced by the laboratory, the operator or other factors which showed about 16M accuracy. Currently not all affiliate afford all the FISH probes and the throughput is quite low. In the previous report, low-pass genome sequencing was adopted for cryptic translocation detection in ART population and about 0.5% of embryos, 22 unaffected embryos (10 normal, 12 carrier) were diagnosed (56%). Single embryo transfer was done in six frozen-thawed embryo transfer cycles, and four clinical pregnancies were achieved (67%). The prenatal diagnosis by amniocentesis for all four women confirmed the result of PGT-M. Three women delivered a healthy baby without complications and one pregnancy is currently ongoing beyond 20 weeks of gestation.

CONCLUSIONS: Karyomapping can still be applied and successful outcome can be achieved even in the absence of reference family member, if other source of DNA sample serving as a reference is available, such as abortus or demised fetal/baby tissues. This approach makes use of the advantage of karyomapping over conventional PCR methods.

IMPACT STATEMENT: This study provides a new approach of utilizing karyomapping for PGT-M in couples with de novo mutations and in couples who do not have reference member in the family. This approach can, at least in part, overcome the limitation of usage of karyomapping.
VERIFICATION OF THE CONTENT OF EMBRYONIC CULTURE MEDIUM BY GENOTYPING USING STR MARKER. Hanen Elloumi Dr,1 Madhia Trabelsi, MD,1 Sonia Mnallah, Embryologist,1 Sana Bensailem, Technician,1 Fethi Zhioua, Dr,1 Mohamed Khrouf, Associate, Professor,1 Ridha Mrad, MD,1 Khalid Mahmoud, Dr,2 Centre d’aide médicale à la procréation FERTILLIA, Tunis, QC, Tunisia;2Genetic Department;3FERTILLIA, Tunisia;2FERTILLIA center, Tunis, Tunisia;3clinique la rose, centre FERTILLIA, Tunis, Tunisia;3clinique La Rose, Centre FERTILLIA, jardins du lac 2, Tunis, Tunisia.

OBJECTIVE: The success of assisted reproduction treatments is based on the selection for transfer of the best embryo. The most reliable method to assess the chromosomal status of embryos for transfer is preimplantation genetic testing (PGT).

However performing an invasive procedure like embryo biopsy (EB) could affect viability. To avoid the risk associated with cell removal, non-invasive methods based on the analysis of the cell-free DNA released by the embryo during the latest stages of preimplantation development have been proposed.

Our objective is to determine if non-invasive PGT may be possible to determine the embryo’s cyogenetic constitution in spent blastocyst media without the need of invasive EB. For this, we try to assess the origin of DNA present in spent blastocyst media.

MATERIALS AND METHODS: Our study was done on 12 blastocysts media sample from 3 different couples. The embryo culture was extended to day 6 for all blastocysts. We analysed all samples using AmpFLSTR Identifier Kit. We used also parental DNA to define the origin of detected DNA from blastocyst media sample.

Embryo culture media was collected from single embryo culture droplets, then stored at -20°C. Spent embryo culture media samples from 10ul-30ul culture droplets were whole genome amplified using SurePlex. The quantification and the quality of DNA yield was assessed by gel electrophoresis and high sensitivity Qubit instrument (ThermoFisher).

For PGT application, we used STR (short tandem repeat) loci. Data analysis and allele calling was performed with GeneMapper and the correspondent analysis software IDv3.2.1

RESULTS: For the studied STR loci, we found many discordances between parents DNA, and embryo drops DNA. Also, maternal DNA exceeded the paternal one.

CONCLUSIONS: Our result is due to significantly different allele dropout rates between maternal and paternal loci. We showed that maternal DNA exceeded the paternal one, suggesting DNA contamination from cumulus cells.

IMPACT STATEMENT: Current study suggest that spent culture media is unreliable for embryo’s genetic assessment, and the non-invasive methods need rigorous validation prior to clinical applications.

FERTILITY & STERILITY®

P-351 6:45 AM Tuesday, October 25, 2022

RECURRENT MONOZYGOTIC LIVE BIRTH IN OVER 65,000 SINGLE EMBRYO TRANSFERS. Cheryl Chu, M.D.,1 Dongmei Li, Ph.D.,1 Courtney Olson-Chen, M.D.,2 Jennifer F. Kawwass, M.D.,2 Manuel G. Torres-Velez, M.D.,3 Jorge E. Novo, M.D.,3 Francesca E. Duncan, Ph.D.,3 Kara N. Goldman, M.D.3 Feinberg School of Medicine, Northwestern University;3Northwestern University Feinberg School of Medicine, Chicago, IL;3Center for Reproductive Science, Northwestern University, Chicago, IL.

OBJECTIVE: To determine the recurrence risk and risk factors for monozygotic splitting after elective single embryo transfers (eSET).

MATERIALS AND METHODS: A retrospective cohort study was performed investigating 65,664 eSET cycles that resulted in a clinical pregnancy as reported in the Society for Assisted Reproductive Technology (SART) Clinical Outcomes Reporting System (CORS) between 2004 and 2017. Monozygosity was defined as more than one fetal heart tone by first trimester ultrasound and concordant sex at live birth. The primary outcome was recurrence risk, with recurrence defined as one patient having two or more cycles of eSET resulting in monozygotic multiples. The secondary objective was to identify factors associated with an increased risk of monozygotic splitting. Risk factors were identified using a multivariable logistic regression model and a stepwise purposeful model selection.

RESULTS: There were 1,355 (2.05%) pregnancies that resulted in two or more fetal heart tones after eSET, including 840 monozygotic twins and triplets at birth. Recurrence of monozygotic multiples occurred in 0.001% of patients with multiple eSET cycles. Two patients were identified to have had recurrence out of 13,488 patients who underwent multiple eSET cycles. One case resulted from embryos created from a single cohort with intracytoplasmic sperm injection (ICSI), assisted hatching (AH) and blastocyst transfers. The second case of recurrence resulted from donor egg embryos with ICSI and blastocyst transfers. Risk factors associated with monozygotic live birth were blastocyst transfer (OR 1.23, 95% CI 1.04-1.47, P = 0.0176) and AH (OR 1.23, 95% CI 1.05-1.44, P < 0.05), and preimplantation genetic testing (PGT), frozen embryo transfer (FET), or ICSI.

CONCLUSIONS: Recurrence of monozygotic live births in eSET was very rare. Blastocyst transfer and AH were confirmed to be risk factors for monozygotic live births, while persive and newer techniques such as ICSI, PGT and FET do not appear to be associated.
ABNORMAL PLACENTATION IN ART PREGNANCIES: PREDICTORS. Ecem Esencan, M.D.,1 Lubna Pal, MBBS 2 Yale School of Medicine, New Haven, CT; 2Yale University, Orange.

OBJECTIVE: Contributions of placenta abnormalities to maternal and fetal morbidity and mortality are well recognized. In pregnancies conceived with assisted reproductive technology (ART) use, we aimed to identify 1) magnitude of burden and abnormal placenta (AP) phenotypes, 2) patient and IVF cycle characteristics that may prognosticate eventual resolution of 1st trimester ultrasound (US) diagnosed placenta previa (PP), and 3) identify risks for placenta accreta (PA).

MATERIALS AND METHODS: In a retrospective cohort study, ART pregnancies that were conceived, received antenatal care and delivered within YNHH system between 2013-2019 were identified through query of EMR. Individual patient records were reviewed for 1st trimester US evidence of PP; course of pregnancy, US evidence of resolution vs persistence of PP at time of delivery were examined. Information on patient characteristics (age, race, infertility etiology, prior uterine surgery, BMI) & ART cycle (oocyte source, donor vs fresh embryo transfer [ET], endometrial thickness [EMT] prior to ET, day & number of ET, luteal support with vaginal vs intramuscular progesterone [IMP]), & outcome (gestational age at delivery & evidence of PA at delivery) were collected and examined in relation to PP. Multivariable logistic regression & propensity score analyses examined predictors of PP resolution & PA risk respectively.

RESULTS: 43 ART conceptions had PP in 1st trimester, 33/43 (77%) resolved with advancing gestation. Greater EMT on day of ET predicted significantly higher likelihood of resolution (OR 1.5, 95% CI 1.07-2.2); conversely, older age & donor egg use were associated with significantly reduced likelihood for PP resolution (OR 0.8 95% CI 0.64-0.98; OR 0.07 95% CI 0.01-0.8). Prior uterine surgery was unrelated to likelihood for resolution. Adjusting for EMT and donor egg, age>38 was an independent predictor of reduced PP resolution (OR 0.11 95% CI 0.01-0.69). PA was identified in 8/69 pregnancies (11.6%). Older age at ET (OR 1.3 95% CI 1.05-1.6), black race (OR 11.6% 95% CI 1.05-10.5), uterine factor (UF, OR 12.9, 95% CI 1.9-95.6) & donor egg use (OR 0.72 95% CI 1.2-5.67) significantly increased likelihood for PA. Use of IMP was noted in 6/8 cases of PA. Propensity score analysis including age, donor egg use, black race, UF & surgery affirmed that collectively, these covariates nearly doubled risk of PA (OR 1.9 95% CI 1.3-2.7).

CONCLUSIONS: Our study is informative regarding prevalence and type of AP in ART pregnancies. Demographic and clinical indices are identified that relate 1) to likelihood of subsequent resolution of 1st trimester diagnosed PP, and 2) to risk of PA. Expanding our sample size in the future will allow us to examine these associations with the goal of creating prognostic algorithms, for better preparedness for patient counseling and surveillance.

IMPACT STATEMENT: This study identifies specific risk factors for PA and parameters for prediction for resolution of PP as a clinical tool to better counsel patients with ART pregnancies who are at increased risk of potential adverse pregnancy outcomes related to AP.

REFERENCES:


DNA METHYLATION CHANGES IN EARLY PLACENTA FROM ASSISTED REPRODUCTIVE TECHNOLOGIES ARE NOT ASSOCIATED WITH SIGNIFICANT GENE EXPRESSION CHANGES. Amelia M. Schaub, MD,1 Tania L. Gonzalez, PhD,2 Jinrui Cui, MS,2 Mark O. Goodarzi, MD, PhD,2 Kent D. Taylor, MD,2 Erica T. Wang, MD, MAS,2 Jerome Rotter, MD,3 Yid-De Ida Chen,3 Allynson Novoa, BS,2 Rimsha Hussaini, B.S.,2 Puige Harakuni,3 Myaaf Khan, B.S.,2 John Williams, III, MD,3 Margareta D, Pisarska, MD 1Cedars-Sinai Medical Center; 3Cedars-Sinai Medical Center, Los Angeles, CA; 2Institute for Translational Genomics and Population Sciences, Lundquist Institute at Harbor-UCLA Medical Center, Torrence, CA; 3Cedars Sinai Medical Center.

OBJECTIVE: Studies suggest assisted reproductive technologies (ART) cause term placenta methylation differences when compared to spontaneous conceptions. However, 1st trimester placenta, closer to the utilization of fertility treatments has not been well studied. We aimed to determine whether methylation differences affecting gene expression exist in 1st trimester placenta between ART and spontaneous pregnancies and whether ART or infertility are causal. We compared differentially methylated probes (DMPs) in 1st trimester placenta from spontaneous, non in vitro fertilization treatment (NIFT), and in vitro fertilization (IVF) conceptions to corresponding differences in gene expression in these cohorts.

MATERIALS AND METHODS: Discorded chorionic villi was processed and DNA extracted using the AllPrep DNA/RNA Mini Kit. Global DNA methylation differences were analyzed with the Illumina Infinium MethylationEPIC kit. Sites were excluded if they were masked (unreliable), not on autosomal chromosomes, or overlapped single nucleotide polymorphisms, leaving 741,145 CpG sites. P values were calculated using a generalized linear model adjusted for fetal sex, with significance set at Bonferroni-adjusted P<0.05. DNA methylation was compared to our previous RNA-seq data using largely the same cohort of patients, with differentially expressed genes significant at Wald’s test P<0.05 using the DESeq2 R package. Data was compared for significant probes located in genes with overlapping significant gene expression between the cohorts.

RESULTS: There were 138 subjects, 56 conceived spontaneously, 38 with NIFT, and 44 with IVF. Between the infertility and spontaneous cohorts, there were 185 DMPs. Hierarchical clustering of DMPs between the infertility and spontaneous cohorts did not demonstrate segregation based on fertility treatment type (NIFT vs IVF). Of the DMPs, 15 had corresponding differences in gene expression. Between the NIFT and spontaneous cohorts, there were 28 DMPs, 2 with differences in corresponding gene expression. Between IVF and spontaneous cohorts, there were 195 DMPs, 18 with differences in corresponding gene expression. Thirteen DMPs were identified between NIFT and IVF, none correlated with differences in gene expression.

CONCLUSIONS: There are minimal differences in 1st trimester placenta methylation between spontaneous, NIFT, and IVF conceptions; even fewer DMPs with differences in corresponding gene expression. Hierarchical clustering did not demonstrate segregation of the infertility cohort based on fertility treatment type and zero DMPs also showed significant gene expression between IVF vs NIFT, suggesting that differences between infertile and spontaneous 1st trimester placenta are driven by underlying infertility, not treatments utilized.

IMPACT STATEMENT: Minimal differences exist in 1st trimester placenta gene expression secondary to methylation differences between spontaneous conceptions and those conceived with infertility treatments. Differences that do exist are likely due to the underlying infertility, not the treatments utilized.

SUPPORT: We gratefully acknowledge the support from the National Institutes of Health for funding: R01-HD074368 and T32-DK007770.
trigger type and each outcome, logistic and linear regression models were used to obtain odds ratios (OR) and beta coefficients with 95% confidence intervals (CI) adjusting for participant and cycle characteristics.

RESULTS: A total of 62,832 fresh embryo transfers were included (9% GnRHa, 15% hCG, and 76% trigger group). The GnRHa group had a significantly lower maternal age (32.8 ± 3.49 years), higher BMI (27.5 vs. 27.1 kg/m²), higher AMH (3.1 vs. 2.0 ng/mL), and less likely diagnosed with ovulatory dysfunction (31.0% vs. 39.0%) or diminished ovarian reserve (6.5% vs. 26.8%) than the hCG group. They were also more likely to have had 16 or more oocytes retrieved (GnRHa 50.1% vs. hCG 21.1%). Generally, the co-trigger group had characteristics intermediate between the other groups (e.g., ≥16 oocytes retrieved for 42.7%).

After adjustment, there were increased odds of CP and LB in both hCG (OR 1.19, CI 1.11-1.27; OR 1.20, CI 1.12-1.29, respectively) and co-trigger (OR 1.19, CI 1.10-1.29; OR 1.21, CI 1.11-1.31, respectively) groups compared to GnRHa. Further, there were increased odds of LBW (OR 1.26, CI 1.03-1.52) and PTB (OR 1.19, CI 1.01-1.42) in singleton pregnancies following hCG compared to GnRHa. hCG trigger was negatively associated with birthweight in singletons compared to GnRHa (Δ75.85g, CI -105.64, -41.52). There were no differences in neonatal outcomes between GnRHa and co-trigger.

CONCLUSIONS: As expected, CP and LB were more likely in fresh transfer cycles with hCG trigger, either alone or as a co-trigger, compared to GnRHa. However, the use of hCG only as a trigger was significantly associated with increased odds of LBW and PTB, and an overall decrease in birthweight compared to GnRHa trigger in fresh transfer. Neonatal outcomes were similar in co-trigger compared to GnRHa trigger.

IMPACT STATEMENT: IVF with fresh embryo transfer, particularly in high responders, has been associated with higher rates of adverse neonatal outcomes including LBW and PTB. GnRHa trigger has been utilized to decrease ovarian hyperstimulation syndrome in high responders. This study suggests that GnRHa or co-trigger may also decrease the likelihood of adverse neonatal outcomes associated with superovulation in fresh embryo transfer. If confirmed by further clinical and mechanistic study, this could improve the safety of fresh transfer in IVF.
success rates relative to couples in the lowest ADI category (ADI 1-2, highest SES) (OR: 0.57, 95% CI: 0.33-1.00, p = 0.049). Mothers with Hispanic ethnicity demonstrated significantly lower rates of successful IVF compared to mothers with non-Hispanic ethnicity (OR: 0.62, 95% CI: 0.44-0.98, p = 0.042).

CONCLUSIONS: Our results showed lower IVF success rates in couples with low SES and ethnic minority mothers.

IMPACT STATEMENT: These findings suggest that couples with low SES and ethnic minority mothers outcomes in IVF may require further investigation.

SUPPORT: None.

P-359 6:45 AM Tuesday, October 25, 2022
FERTILITY SERVICES IN GERMANY AND THE IMPACT OF COVID-19. Elena Brachimi Medical, Stunting,1 Piotr S. Gromski, PhD,2 Scott M. Nelson, MD, PhD2
1University of Glasgow, Glasgow, Glasgow City, United Kingdom; 2University of Glasgow, Glasgow, Glasgow, United Kingdom.

OBJECTIVE: To estimate the effect of the pandemic-induced short-term interruption of fertility services on pregnancies and births achieved through Assisted Reproduction Technology (ART), and to estimate longer-term trends in the German in vitro fertilisation (IVF) sector.

MATERIALS AND METHODS: Annual natality data and the German IVF Registry data for 2008-2019 encompassing 1,085,683 treatment cycles and 171,423 ART births was used to predict future population level data for 2020 to 2024. For 2020, predicted cycle activity and nationally reported outcome data were compared to assess the effect of the pandemic.

RESULTS: In 2020 despite temporary regulatory closure of IVF units for 21 days, 116,306 treatment cycles were undertaken (an increase of 4,519 treatment cycles compared to predicted, equivalent to 4.0% (95%CI -0.5% to 9.1%) more cycles), and a 3-fold increase in annual growth during 2020 over the preceding 5 years. 2,332 more frozen embryo transfers were undertaken in 2020 than predicted (5.16% more, 95%CI -1.67% to 12.9%), while compared to predictions, 2,674 fewer stimulation cycles were commenced, and 1,274 more stimulation cycles were cancelled. The observed clinical pregnancy rate per embryo transfer in fresh (31.6%) and frozen cycles (29.2%) for 2020 showed no significant change compared to the pre-pandemic trends in the German in vitro fertilisation (IVF) sector.

CONCLUSIONS: The temporary cessation of IVF activity in Germany had a limited impact on the number of pregnancies, due to an upsurge in demand, increased uptake of frozen embryo transfers and maintenance of pregnancy rates.

IMPACT STATEMENT: The COVID-19 pandemic appears to have had minimal effect on the German IVF sector due to continuously increasing demand for IVF treatment driven by high infertility rates. There is an urgent need for multiple pregnancy risk minimising strategies.

SUPPORT: European Society of Human Reproduction and Embryology (ESHRE) grant number 2021-1.

P-360 6:45 AM Tuesday, October 25, 2022
DIFFERENCES IN REPRODUCTIVE AND NEONATAL OUTCOMES BASED ON TIME INTERVAL FROM CESAREAN DELIVERY TO FROZEN EMBRYO TRANSFER. Laura X. Zalles, M.D.,1 Samad Jahandideh, PhD,2 Jiarui Wang, MS,3 Michael Vance Homer, M.D.,4 Meike L. Uhler, M.D.,2 Luis R. Hoyos, M.D.,6 Kathleen Devine, MD,7 Janet Bruno-Gaston, M.D.,8 Mount Sinai Hospital, New York, NY; 2Shady Grove Fertility, Washington D.C., DC; 3US Fertility; 4Reproductive Science Center; 5Fertility Centers of Illinois; 7IVF Florida Reproductive, Margate, FL; 8Shady Grove Fertility, Rockville, MD; 6Shady Grove Fertility, Houston, TX.

OBJECTIVE: To determine if the interval between prior cesarean delivery (CD) and subsequent freeze-thawed embryo transfer (FET) impacts reproductive and neonatal outcomes following the use of assisted reproductive technologies.

MATERIALS AND METHODS: This was a multi-center retrospective cohort study including all patients who underwent CD followed by autologous FET between January 2008 and September 2021. Age at time of FET, body mass index (BMI), preimplantation genetic testing, and infertility diagnosis were extracted. Implantation rate (IR), spontaneous abortion (SAB), live birth rate (LBR), gestational age (GA) at delivery, and neonatal birth weight were noted and differences by time (in months) from CD to day of FET were determined by ANOVA and Chi-Squared tests.

RESULTS: We identified 6,545 autologous FET cycles and grouped them by three-month intervals between CD and subsequent FET. There were no significant differences in IR, SAB, or LBR. GA at delivery and birth weight were lowest when FET occurred within 9 months of CD.

CONCLUSIONS: There were no differences in IR, SAB, or FET based on interval time from CD to FET. Shorter interval between CD and FET was associated with significantly decreased GA at delivery and birth weight. However, the differences were small and may not have clinical significance.

IMPACT STATEMENT: Short interpregnancy intervals have been associated with adverse perinatal outcomes. When counseling patients, timing of FET following CD must be balanced against increasing maternal age and reproductive outcomes. While large, this sample cannot address rarer outcomes associated with short interval between CDs, such as uterine rupture.

SUPPORT: None.

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<th>15-18</th>
<th>18-21</th>
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<td>n</td>
<td>74</td>
<td>260</td>
<td>598</td>
<td>969</td>
<td>914</td>
<td>759</td>
<td>578</td>
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<tr>
<td>Age at transfer (years)</td>
<td>36.5 ± 1.1</td>
<td>36.7 ± 1.2</td>
<td>36.5 ± 1.1</td>
<td>36.2 ± 1.2</td>
<td>36.2 ± 1.1</td>
<td>36.3 ± 1.2</td>
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<td>BMI (kg/m²)</td>
<td>26.6 ± 0.5</td>
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<td>Embryos transferred</td>
<td>1.31 (0.52)</td>
<td>1.36 (0.57)</td>
<td>1.29 (0.60)</td>
<td>1.25 (0.5)</td>
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<td>10 (3.8)</td>
<td>21 (3.5)</td>
<td>29 (2.7)</td>
<td>28 (3.1)</td>
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<td>40 (5.1)</td>
<td>113 (43.5)</td>
<td>284 (47.5)</td>
<td>482 (49.7)</td>
<td>467 (51.1)</td>
<td>395 (52.0)</td>
<td>277 (47.9)</td>
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<td>SAB (%)</td>
<td>11 (14.9)</td>
<td>28 (10.8)</td>
<td>49 (8.2)</td>
<td>93 (9.6)</td>
<td>83 (9.1)</td>
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<td>LBR (%)</td>
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<td>95 (36.5)</td>
<td>233 (39)</td>
<td>377 (38.9)</td>
<td>372 (40.7)</td>
<td>294 (38.7)</td>
<td>215 (37.2)</td>
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<td>Multiple Gestation (%)</td>
<td>5 (4.5)</td>
<td>24 (9.2)</td>
<td>30 (5.0)</td>
<td>49 (5.1)</td>
<td>39 (4.3)</td>
<td>29 (3.8)</td>
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<tr>
<td>Gestational age at delivery (%)</td>
<td>37.3 ± 3.3</td>
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<td>37.9 ± 2.4</td>
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<td>Birth weight (g)</td>
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<td>3185 ± 781</td>
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THE ASSOCIATIONS BETWEEN BODY MASS INDEX AND LIVE BIRTH OUTCOMES AMONG PATIENTS WITH AND WITHOUT OVULATORY DYSFUNCTION UNDERGOING INTRAUTERINE INSEMINATION CYCLES. Dorris DM, L. Jarshaw, B.S.,1 Parvin Hosseinizadeh, MD,2 LaTasha B. Craig, MD,3 Jennifer D. Peck, PhD.1 University of Oklahoma Health Sciences Center, Oklahoma City, OK; 2University of Oklahoma College of Medicine, Oklahoma City, OK.

OBJECTIVE: To determine whether body mass index (BMI) affects intrauterine insemination (IUI) treatment success in anovulatory versus ovulatory women, particularly with BMI ≥ 30 kg/m².

MATERIALS AND METHODS: This was a retrospective cohort study of all patients who underwent IUI between July 2007 and May 2012 at a university-affiliated infertility clinic. Cycles were excluded if two IUI procedures were performed in the same treatment cycle, two samples combined for IUI, lack of IUI procedure documentation, retrograde ejaculation, partner reported sample spill during collection or transportation of the sample, pregnancy outcome unknown, and/or missing covariate data including BMI. The primary outcome was live birth, with secondary outcomes of positive pregnancy test (serum quantitative hCG > 10 mIU/ml) and clinical pregnancy rate (intrauterine gestational sac with positive fetal heart beat; CPR). A cluster-weighted generalized estimating equation method was used to estimate modified Poisson regression models with robust standard errors. Multivariable models were adjusted for age, race/ethnicity, total motile sperm count, infertility duration, infertility diagnosis, sperm source and medications.

RESULTS: A total of 1959 cycles were performed on 661 women: 689 cycles among 237 anovulatory patients (mean age 30.5±4.3) and 1270 cycles among 424 ovulatory patients (mean age 32.7±5.1). Anovulatory patients were younger with shorter duration of infertility, higher BMI, and more likely to undergo a medicated cycle. Ovulatory women with BMI ≥ 30 had a higher CPR [RR 1.99 (95% CI 1.21-2.27)] and live birth rate [1.56 (0.76-3.21)] than ovulatory women with normal BMI, although confidence intervals for live birth did not exclude the null value. Anovulatory patients with obesity, however, exhibited a lower CPR [0.54 (0.29-1.01)] and live birth rate [0.73 (0.32-1.66)] compared to the normal BMI group although the estimate for live birth was less precise. Modest increases in CPR [anovulatory 1.50 (0.86-2.63); ovulatory 1.46 (0.94-2.26)] and live birth rates [anovulatory 1.63 (0.72-3.68); ovulatory 1.26 (0.71-2.25)] in overweight patients (BMI 25.0-29.9) compared with normal BMI did not differ by ovulatory status.

CONCLUSIONS: In our sample of anovulatory and ovulatory infertile patients, being overweight did not appear to negatively affect the outcome of live birth with IUI treatment, contrary to results found in assisted reproductive technology (ART) treatments. However, IUI outcomes may be less favorable in obese patients with anovulation. Future studies with a larger sample size are needed to better elucidate possible differences between these groups.

IMPACT STATEMENT: Although patients should be counseled that higher BMI has multiple adverse effects on reproduction and pregnancy, our data suggests it may not adversely impact delivery rates in obese patients, especially those that are ovulatory.
OBJECTIVE: Lower maternal education level is a well described predictor of obstetric morbidity. Our objective was to examine the association between maternal education and adverse maternal and neonatal outcomes in women who conceived using assisted conception (AC), which included fertility medications, intrauterine insemination, or in vitro fertilization.

MATERIALS AND METHODS: We conducted a retrospective cohort study utilizing the U.S. vital statistics data set on national birth certificates from 2016-2020. Women with live, non-anomalous singletontons who conceived using AC and had education status recorded were included. Patients were stratified into two groups: bachelor’s degree or higher, or less than a bachelor’s degree. The primary outcome was a composite of maternal adverse outcomes: intensive care unit (ICU) admission, unplanned hysterectomy, or blood transfusion. The secondary outcome was a composite of neonatal adverse outcomes: neonatal ICU admission, ventilator support, or seizure. Multivariable modified Poisson regression models with robust error variance adjusted for maternal age, race, marital status, prenatal care, smoking during pregnancy, neonatal sex, and birth year estimated the relative risk (RR) of outcomes with a 95% confidence interval (CI).

RESULTS: 190,444 patients met the inclusion criteria: 142,943 had a bachelor’s degree or higher and 47,501 were without a bachelor’s degree. Composite maternal adverse outcomes were similar among patients with a bachelor’s degree and those without (Table 1). However, composite adverse neonatal outcomes were significantly higher in women without a bachelor’s degree.

CONCLUSIONS: Our study demonstrated that lower maternal education level was not associated with maternal adverse outcomes in patients who conceived using AC but was associated with increased rates of neonatal adverse outcomes.

IMPACT STATEMENT: As access to infertility care increases, patients who conceive with AC may be counseled that education level is not associated with maternal morbidity. Further research into the association between maternal education level and neonatal morbidity is indicated.

SUPPORT: There was no funding received for conducting this project.

Table 1: Composite Maternal and Neonatal Morbidity Among Pregnancies from Assisted Conception Stratified by Education Level

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Total Births</th>
<th>Rate/1,000 Live Births</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite maternal morbidity</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>190,444</td>
<td>1,893</td>
<td>9.9</td>
</tr>
<tr>
<td>Bachelor’s or higher</td>
<td>142,943</td>
<td>1,448</td>
<td>10.1</td>
</tr>
<tr>
<td></td>
<td>47,501</td>
<td>445</td>
<td>9.4 Ref</td>
</tr>
<tr>
<td>Composite neonatal morbidity</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>190,517</td>
<td>18,480</td>
<td>97.0</td>
</tr>
<tr>
<td>Bachelor’s or higher</td>
<td>143,998</td>
<td>13,449</td>
<td>94.1</td>
</tr>
<tr>
<td></td>
<td>47,519</td>
<td>5,031</td>
<td>105.9 Ref</td>
</tr>
</tbody>
</table>

P-366 6:45 AM Tuesday, October 25, 2022

RECIPIENT AGE IS NOT ASSOCIATED WITH OUTCOMES IN DONOR EGG IVF CYCLES. Elizabeth Clain, M.D.,1 Samad Jahandideh, PhD,2 Anthony N. Imudia, MD,3 Papi Sarkar, MD,4 Kathleen Devine, MD,5 Cassandra Roeca, M.D.5 1Shady Grove Fertility, Colorado, Greenwood Village, CO; 2Shady Grove Fertility, Washington D.C., DC; 3University of South Florida/Tampa General Hospital, Tampa, FL; 4University of South Florida/Tampa General Hospital, Tampa, FL; 5University of Colorado School of Medicine, Aurora, CO.

OBJECTIVE: The use of donor oocytes is increasingly prevalent. A study using the SART database reported poorer outcomes for recipients over age 45. However, this study is over 10 years old and includes data from clinics with different protocols. Using data from our clinical network, we compare outcomes of donor oocyte IVF cycles based on recipient age.

MATERIALS AND METHODS: We performed a retrospective cohort study from January 2017 to March 2021 of patients who underwent fresh transfer of embryos created using fresh donor egg IVF at a multicenter fertility clinic. Cycles were categorized according to recipient age. Gestational carriers and donor embryo cycles were excluded. The primary outcome...
was live birth per embryo transfer. Secondary outcomes included clinical pregnancy and miscarriage rates. Generalized estimating equation analysis was performed to account for prior embryo transfer attempts, prior miscarriages, and recipient BMI.

RESULTS: A total of 11,119 cycles in which recipients underwent fresh transfer of donor egg embryos were identified, of which 369 (32.4%) were in patients aged 45 years or older. There were no significant differences in number of prior term or preterm births, BMI, or prior embryo transfer attempts. There were no significant differences in live birth rate per transfer, with live birth rates of 63.6% for patients <34 years old, 51.9% for patients 35-39, 52.1% for patients 40-44, 48.0% for patients 45-49, and 50.0% for patients 50 years or older (p < 0.117). Similarly, there was no significant difference in clinical pregnancy rate or miscarriage rate by recipient age. After further adjusting for confounding variables, the results were unchanged.

CONCLUSIONS: In this study comparing outcomes after fresh donor egg IVF transfer to recipients from a single multicenter fertility clinic, we found that uterine age did not affect pregnancy outcomes.

IMPACT STATEMENT: Recipient age does not significantly affect live birth rate in fresh donor egg IVF cycles.

Table 1: Blastocyst rate / number of eggs, number of MII, and Number of 2pn during 2019 Vs. 2020 and 2021.

<table>
<thead>
<tr>
<th>Year</th>
<th>Total Oocytes</th>
<th>MII</th>
<th>2PN</th>
<th>Blast</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>1224</td>
<td>1313</td>
<td>639</td>
<td>719</td>
</tr>
<tr>
<td>35-37</td>
<td>432</td>
<td>609</td>
<td>370</td>
<td>380</td>
</tr>
<tr>
<td>38-40</td>
<td>210</td>
<td>339</td>
<td>176</td>
<td>274</td>
</tr>
<tr>
<td>41-42</td>
<td>132</td>
<td>89</td>
<td>73</td>
<td>60</td>
</tr>
<tr>
<td>&gt;42</td>
<td>76</td>
<td>77</td>
<td>63</td>
<td>86</td>
</tr>
<tr>
<td>Total</td>
<td>2124</td>
<td>2394</td>
<td>1321</td>
<td>1469</td>
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</table>

REFERENCES:


P-368 6:45 AM Tuesday, October 25, 2022

A STUDY TO DETERMINE THE IMPACT OF DIMINISHED OOCYTE RESERVE (DOR) ON PREGNANCY OUTCOME IN WOMEN OF ADVANCED REPRODUCTIVE AGE. Jerome H. Check, M.D., Ph.D.,1 Jung Kyo Choe, M.D.,2 Kathleen Hollahan, R.N.,3 Michael Sobel, D.O.,4 Carrie K. Wilson, B.A.5 Cooper Medical School of Rowan University, Camden, NJ;2 Cooper Institute For Reproductive Hormonal Disorder, Mount Laurel, NJ;2 Waterford Works, NJ;4 Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ.

OBJECTIVE: Previous studies have determined that women < age 39 with DOR are only half as likely to have a successful live delivery compared to similarly aged women with normal oocyte reserve (NOR). The objective of the present study was to determine the impact of DOR in women aged 40-42 compared to age peers with NOR.

MATERIALS AND METHODS: Women aged 40-42 having in vitro fertilization-embryo transfer (IVF-ET) were divided into 2 groups based on their serum anti-mullerian hormone (AMH) levels: < 1 ng/mL, DOR; ≥ 1 ng/mL (NOR). They agreed to have a day 3 ET and were allowed to

Table 1: Blastocyst rate / number of eggs, number of MII, and Number of 2pn during 2019 Vs. 2020 and 2021.

<table>
<thead>
<tr>
<th>Total Oocytes</th>
<th>MII</th>
<th>2PN</th>
<th>Blast</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>1224</td>
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</tr>
<tr>
<td>41-42</td>
<td>132</td>
<td>89</td>
<td>73</td>
</tr>
<tr>
<td>&gt;42</td>
<td>76</td>
<td>77</td>
<td>63</td>
</tr>
<tr>
<td>Total</td>
<td>2124</td>
<td>2394</td>
<td>1321</td>
</tr>
</tbody>
</table>

Rate / egg: 73.7288 369.93998 61.36174
Rate / MII: 69.92337 73.27782 75.62968
Rate / 2pn: 44.65753 65.90909 59.58596
transfer 3 embryos but 2 were encouraged. Women with DOR were stimulated with an FSH receptor uptake technique that varied according to the degree of DOR and in general did not use more than 150 IU follicular stimulating hormone (FSH) unless cetrotrexil or ganirelix was given when an extra 75 IU could be added. Gonadotropin injections were not given if serum FSH was >13 mIU/mL in which the patients were monitored until endogenous FSH dropped to 12 mIU/mL or less by using endogenous estradiol (E2). If endogenous E2 was not rising or there is a history of a short follicular phase 20 mcg of ethinyl estradiol was given. Women in apparent ovarian menopause were included as long as they attained one mature follicle. A chemical pregnancy was considered if there was a rise in the serum beta human chorionic gonadotropin (hCG) levels x 2 and the beta hCG exceeded 100 mIU/mL.

RESULTS: There were 111 ETs in women with DOR vs. 101 with NOR. A positive pregnancy test was found in 32.4% in women with DOR vs. 30.7% with NOR. A gestational sac at 4 weeks from oocyte retrieval was seen in 27.9% with DOR vs. 23.8% with NOR. The live delivered pregnancy rate per transfer was 12.6% vs. 12.9%. The average number of embryos transferred was 1.7 vs. 2.4. Interestingly the implantation rate was 18.3% vs. 11.3%.

CONCLUSIONS: Interestingly, DOR does not seem to diminish the chance of a live pregnancy compared to age peers with NOR at least when the FSH receptor uptake technique is used for ovarian stimulation.

IMPACT STATEMENT: Some IVF centers may be willing to perform the procedure in women 40-42 as long as their serum AMH is normal. When the serum AMH is low they may be only willing to talk about the donor egg program. For some IVF centers, this may encourage them to consider including women age 40-42 even with DOR. However, for some IVF centers they may look at these results and conclude that if having a normal AMH does not improve live delivered pregnancy rates above those with DOR, they may decide to encourage donor egg programs even with normal AMH for this age group.

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DOES AGE MATTER WITH NATURAL CYCLE FROZEN-TA WED EMBRYO TRANSFER (FET) AFTER PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A)? Katie White, MD,1 Prachi N. Godiwala, MD,2 Reeva B. Makhijani, MD,3 Alison Bartolucci, PhD,4 John Nulsen, MD,5 Claudio A. Benadiva, MD, HCLD,6 Lawrence Engmann, MD,6 Daniel R. Grow, MD, MHCM7 1St. Francis Hospital, Hartford, CT; 2Center for Advanced Reproductive Services, Farmington, CT; 3University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT; 4University of Connecticut Health Center, Center for Assisted Reproductive Services, Farmington, CT; 5University of Connecticut (REI Division); 6Center for Assisted Reproductive Services, University of Connecticut School of Medicine, Farmington, CT; 7University of Connecticut Health Center, Farmington, CT.

OBJECTIVE: Optimal endometrial preparation is desired for the transfer of a euploid embryo. Recent works have shown advantages of natural cycle (NC) frozen-thawed embryo transfer (FET) for simplicity, implantation rate, and ANEUPLOIDY (PGT-A).

MATERIALS AND METHODS: 841 FET cycles with transfer of euploid embryos were performed between 2015-2020 utilizing a JC with GnRh-a, supplemental estradiol and intramuscular progesterone (n=414) or a NC with FET 6 days after a spontaneous LH surge (n=427) with supplemental progesterone. We compared clinical pregnancy rate (CPR), ongoing pregnancy rate (OPR), and clinical loss rate (CLR) among the SART age groups according to FET protocol type using chi-square.

RESULTS: Overall, the CPR was higher for NC vs. PC (67% vs. 60.4%, P<0.05), and the CLR lower for NC vs. PC (3% vs. 11%, p< 0.001). The decrease in CLR during NC FET as compared to PC FET was significant for patients < 37 years (p< 0.001) and those > 37 years (p=0.05). Within age groupings, each of the older age groups showed a higher OPR with NC FET, though statistical significance for each group was not reached. In no age group was OPR less with NC FET. The CPR for age >42 was not statistically different than for age < 35.

CONCLUSIONS: In patients with AMA undergoing PGT-A there was no statistically significant difference between NC or PC FET cycles regarding CPR or OPR. CLR was lower during NC FET.

IMPACT STATEMENT: The results of this study have implications for management of FET cycles in patients with AMA allowing for confidence in the use of NC vs PC in ovulatory patients.

SUPPORT: None

P-370 6:45 AM Tuesday, October 25, 2022

GENERATION OF BIG DATA FOR FERTILITY TREATMENT AT THE NATIONAL LEVEL IN SOUTH KOREA. Taehoon Ko, Ph.D.,1 Hyejun Lee, M.D.,2 Jiye Jung, M.D.,3 Jong Hyuk Park, Ph.D.,4 Hyung Min Kim, M.S.,5 Sunghan Woo, B.S.,6 Jaseong Koo, M.D.,7 Sung-Hun Min, Ph.D.,8 Miran Kim, M.D., Ph.D.9 Hye Jin Chang, M.D., Ph.D.,10 Mi Kyung Chung, Ph.D.10 Moon Kyoung Cho, M.D., Ph.D.10 Jisun Lee, M.D., Ph.D.10 1The Catholic University of Korea, Department of Medical Informatics, Seoul, Korea- South; 2Kai Health, Chief Executive Officer, Seoul, Korea- South., Seoul, Korea, Republic of (South); 3Miraewaheemang hospital, IVF clinic, Seoul, Korea- South; 4Seoul, South Korea; 5Good Moonhwa Hospital, Busan, Korea, Republic of (South); 6Ajou University School of Medicine; 7Ajou University School of Medicine, Suwon, Korea, Republic of (South); 8Seoul Rachel Fertility Center, Seoul, Korea, Republic of (South); 9Chonnam National University Medical School; 10Kyungpook National University School of Medicine.

OBJECTIVE: AI research projects to automatically grade embryos and predict pregnancy has been a popular topic. However, it is challenging to collect standardized embryo images and clinical data from multiple medical institutions using different electronic health records (EHR). Also, clinics use slightly different criteria to evaluate embryos. In South Korea, the cost of infertility treatment is covered by the National Health Insurance and fertility data has been accumulating. We would like to introduce the government funded project to collect and label fertility data at the national level.

MATERIALS AND METHODS: A total of 20 hospitals are participating in this project to minimize the bias in data generated by different types of microscopes and incubators. We plan to collect data for clinical information of parents undergoing fertility treatments, fertility treatment cycles and embryos. Physicians, embryologists and biomedical informaticians collaborated to create the standardized data structure. Embryo images were collected from microscopes and time-lapse incubators, and matched with gestational sac (G-sac) data.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>NC</th>
<th>PC</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;35 N=</td>
<td>127</td>
<td>141</td>
<td></td>
</tr>
<tr>
<td>CPR %</td>
<td>70.1</td>
<td>70.9</td>
<td>0.88</td>
</tr>
<tr>
<td>OPR %</td>
<td>69.3</td>
<td>61.7</td>
<td>0.19</td>
</tr>
<tr>
<td>CLR %</td>
<td>1.1</td>
<td>13</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age 35-37.99 N=</td>
<td>118</td>
<td>106</td>
<td></td>
</tr>
<tr>
<td>CPR %</td>
<td>67</td>
<td>68.9</td>
<td>0.75</td>
</tr>
<tr>
<td>OPR %</td>
<td>64.4</td>
<td>61.3</td>
<td>0.68</td>
</tr>
<tr>
<td>CLR %</td>
<td>3.8</td>
<td>11</td>
<td>0.09</td>
</tr>
<tr>
<td>Age 38-39.99 N=</td>
<td>89</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>CPR %</td>
<td>67.4</td>
<td>62</td>
<td>0.47</td>
</tr>
<tr>
<td>OPR %</td>
<td>65.2</td>
<td>56.3</td>
<td>0.25</td>
</tr>
<tr>
<td>CLR %</td>
<td>3.3</td>
<td>9.1</td>
<td>0.21</td>
</tr>
<tr>
<td>Age 40-41.99 N=</td>
<td>65</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>CPR %</td>
<td>70.8</td>
<td>63.6</td>
<td>0.43</td>
</tr>
<tr>
<td>OPR %</td>
<td>66.2</td>
<td>54.6</td>
<td>0.22</td>
</tr>
<tr>
<td>CLR %</td>
<td>6.5</td>
<td>14.3</td>
<td>0.27</td>
</tr>
<tr>
<td>Age 42+ N=</td>
<td>28</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>CPR %</td>
<td>75</td>
<td>69.2</td>
<td>0.58</td>
</tr>
<tr>
<td>OPR %</td>
<td>75</td>
<td>65.4</td>
<td>0.37</td>
</tr>
<tr>
<td>CLR %</td>
<td>0</td>
<td>5.6</td>
<td>0.17</td>
</tr>
</tbody>
</table>
RESULTS: We developed a standardized protocol to collect fertility treatment data. Clinical information consists of three data tables. The first data table contains patient information at the embryo level including date of birth, maternal height, weight, obstetric and medical history of parents. The second data table contains information about embryos such as date of oocyte collection, date of embryo transfer, cryopreservation, preimplantation genetic test (PGT) and intracytoplasmic sperm injection (ICSI). The last data table contains fertility treatment cycle information such as number of oocytes and mature/fertilized eggs. Embryo images will be consensus-labeled by embryologists with more than 10 years of experience. In total, 13,000 day 3 and 7,000 day 5 microscopic images and 1,500 time-lapse videos will be collected. In addition, outcomes such as G-sac and fetus heartbeat (FHB) will be achieved. To check the completeness of the data collection protocol, a deep learning model was trained on a sample batch of the dataset and the area under the receiver operating characteristic curve (AUROC) was 0.86 for automatic embryo grading.

CONCLUSIONS: After multiple discussions with fertility experts, we developed a standardized protocol to build datasets for fertility treatment. The pilot AI model developed with the first batch of the sampling data showed similar outcomes as the previous literatures. Using our standardized protocol, we are currently collecting data from 20 fertility clinics in South Korea.

IMPACT STATEMENT: We developed a standardized data collection protocol to generate big data for fertility treatment across multiple fertility clinics. This large-scale dataset will be a foundation to discover clinical evidence and develop robust artificial intelligence models to support fertility treatment.

E-POSTER ABSTRACT SESSION: T16

P-371 6:45 AM Tuesday, October 25, 2022

SIX CONSECUTIVE TIME-LAPSE IMAGES OVER 2 HOURS ON DAY 3 CAN PREDICT BLASTULATION BETTER THAN A SINGLE IMAGE. Hyejun Lee, M.D.,1 Taehoon Ko, Ph.D.,2 Jye Jung, M.D.,3 Jong Hyuk Park, Ph.D.,4 Hyung Min Kim, M.S.,5 Sunghan Woo, B.S.,5 Sungwook CHOI, M.D.6 Seoul, South Korea;7 The Catholic University of Korea, Seoul, South Korea;8 Konkuk University, Seoul, South Korea;9 Miraeahang Hospital, Seoul, Korea, Republic of (South);10 The Catholic University of Korea, Seoul, South Korea;11 Kai Health, Seoul, Korea, Republic of (South);12 M Fertility Clinic, Seoul, Korea, Republic of (South).

OBJECTIVE: To evaluate the convolutional neural network (CNN) model to predict blastulation of day 3 embryos using time-lapse images.

MATERIALS AND METHODS: We retrospectively collected 10,223 time-lapse videos from 1,015 patients at two private fertility clinics and developed a blastulation prediction model using two datasets. The first dataset consisted of only a single frame image at 66 hour post-insemination on day 3, and the second one extracted six frame images from 66 to 68 hour on the same day. We used a pre-trained VGG-16 model and applied fine-tuning methods to train our datasets. Three performance metrics were compared: area under the receiver operating characteristic curves (AUROC), F1-score and accuracy. We also used gradient-weighted class activation mapping (Grad-CAM) to verify that the model concentrated on the relevant features of the embryos.

RESULTS: In predicting blastulation on day 5 from a single frame image on day 3, the VGG16 pre-trained model showed performance of AUROC 0.71 and accuracy 0.61. When six consecutive images of day 3 embryos were used, the model showed higher performance of AUROC 0.85 and accuracy 0.76. The cut-off value that maximized the F1-score was selected for the performance metrics.

<table>
<thead>
<tr>
<th>VGG16 model with 1 image</th>
<th>VGG16 model with 6-images</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUROC</td>
<td>0.71</td>
</tr>
<tr>
<td>F1-score</td>
<td>0.64</td>
</tr>
<tr>
<td>Accuracy</td>
<td>0.61</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Accurate prediction of blastulation potentially increases pregnancy rates as embryos unlikely to survive till day 5 can be successfully transferred or frozen at a cleavage stage. In this study, we confirmed that a single Time-lapse image of day 3 embryos is very useful in predicting blastulation at fair robustness of AUROC 0.71. Furthermore, we demonstrated that using 6 consecutive images improved prediction accuracy. The 6 images were closely examined by the experienced embryologists but the developmental stage did not advance notably over the 2 hours. It is well known that the CNN model extracts features from each frame, but does not reflect associations between successive frames. Therefore, we expect that our model can further improve its performance by combining CNN and recurrent neural network (RNN) that reflects successive features.

IMPACT STATEMENT: The blastulation prediction model using a single image on day 3 can empower embryologists to make better clinical decisions, potentially leading to less embryo waste and higher pregnancy rates. It is noteworthy that multiple images consecutively taken over a couple of hours can further improve the predictive power for blastulation.

SUPPORT: None

P-372 6:45 AM Tuesday, October 25, 2022

APPLYING TWO ARTIFICIAL INTELLIGENCE-BASED EMBRYO SELECTION MODELS ON 5,624 BLASTOCYSTS: PREDICTION OF IMPLANTATION POTENTIAL WITH MACHINE LEARNING AND DEEP LEARNING SYSTEMS. Lorena Bori Arnal, PhD, Student,1 Rebeca Esteve Moreno, MSc,2 Arancha Galán, PhD,3 Jose Remohi Gimenez, MD PhD,4 Alberto Tejera, PhD,5 Marcos Meseguer, Ph.D.6 IVIRMA Global, Valencia, Spain;7 IVIRMA Valencia - University of Valencia, Valencia, Spain.

OBJECTIVE: To evaluate the correlation between automatic embryo scoring and IVF treatment success for two artificial intelligence-based embryo selection models.

MATERIALS AND METHODS: This retrospective study includes 878 IVF treatments whose embryos were cultured in EmbryoScope Plus incubators until the blastocyst stage. All the embryos (n=5624) were scored by a deep learning-based model using only time-lapse image sequences (iDAScore v1.0). Embryos with enough morphokinetic annotations, were also scored by a machine learning-based model (KIDScore D5 v3). This model requires annotations of PNs, t2, t3, t5, IB, IC and TE. Scores for both models range from 1 to 10, from lower to higher implantation probability. We studied the relationship between both scores and the conventional morphological grade according to ASETEBIR criteria. For single embryo transfers (SETs) we also studied the relationship between the scores and the implantation potential. Finally, we performed a multivariable logistic regression analysis to predict the implantation outcome and the performance of both models was compared.

RESULTS: The iDAScore and the morphology category (A, B, C or D) assigned by embryologists showed a direct association*. The mean and standard deviation was 9.1±0.8 for A; 8.2±1.3 for B; 6.9±1.7 for C and 4.4±2.1 for D. The implantation rate increased as the embryo score improved*: 37.3% for score ≤8 (n=209), 54.3% for score 8.1-8.90 (n=210), 61.70% for score 8.91-9.30 (n=240) and 65.8% for score >9.30 (n=149). The KIDScore was also related to conventional morphology and implantation potential. The mean and standard deviation was 6.1±2.3 for morphological embryos and 6.2±2.5 for morpho-implanted embryos*. The logistic regression analysis of iDAScore and KIDScore took into account possible confounding factors: type of embryo transfer (fresh vs. frozen); oocyte age and patient body mass index. iDAScore was related to implantation in treatments included in the oocyte donation program, (*OR=1.35; 95% CI [1.08-1.68]; n=355), in conventional treatments with autologous oocytes (*OR=1.28; 95% CI [1.06-1.56]; n=1242) and in treatments involving PGT-A (*OR=1.22; 95% CI [1.07-1.44]; n=344), in conventional treatments with autologous oocytes (*OR=1.20; 95% CI [1.06-1.35]; n=227) and in treatments involving PGT-A (*OR=1.23; 95% CI [1.07-1.42]; n=202). The performance of the models was identical for the oocyte donation program (AUC=0.63) and similar for conventional treatments (AUCs=0.66 for iDAScore and 0.63 for KidScore) and for the PGT-A program (AUCs= 0.60 for iDAScore and 0.61 for KidScore, *p<0.05.

CONCLUSIONS: This external validation demonstrated that both machine learning and deep learning model were correlated to the morphological evaluation performed by embryologist and implantation outcome.

IMPACT STATEMENT: The generalization of the fully automated embryo selection models implies the absence of manual evaluations and eliminates biases due to inter- and intraobserver variation.

SUPPORT: Supported by Spanish Ministry of Science and competitiveness (Instituto de Salud Carlos III) project: PI21/00283.
A NEW APPROACH TO ESTIMATING CUMULATIVE LIVE BIRTH RATES USING PREDICTED OUTCOMES OF ALL EMBRYOS. Justina Hyunjii Cho, M.A., M.S., 1 Valerie L. Baker, MD, 2 Kevin E. Loewke, Ph.D. 3 1Alife Health, Inc; 210751 Falls Road, Lutherville, MD.

OBJECTIVE: Current success estimators for IVF do not take into account unused embryos and may under-predict cumulative live birth rate (CLBR) for some patients. We aimed to develop a new approach that considers predicted outcomes of all embryos.

MATERIALS AND METHODS: We analyzed data from 2014-2019 in the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System (SART CORS), filtering for first autologous IVF cycles and linked frozen transfers. For reference, we trained a logistic regression model on 250,206 cycles to predict CLBR (probability of at least one live birth) using age, BMI, and diagnosis. We then developed a new approach. First, a negative binomial regression model was trained on 121,509 retrievals to predict the number of total blastocysts (transferred plus cryopreserved) using age, AMH, BMI, and diagnosis. Then, a logistic regression model was trained on 66,393 non-PGT single-blastocyst transfers to predict per-transfer live birth rate using age, BMI, AMH, transfer number, and diagnosis. CLBR was then estimated as \(1 - \prod_{i=1}^{N} (1-p_i)\), where \(N\) is the number of blastocysts and \(p_i\) is the predicted probability of live birth for transfer \(i\). We compared this approach to a similar model for euploid blastocysts (using published euploidy rates by age [1]) and per-transfer success rates of PGT transfers.

RESULTS: Compared to the reference model, our model provides similar predictions for CLBR between 0% - 40%. In this range, the average number of unused embryos is 0.6 to 1.5 per cycle. Above 40%, the average number of unused embryos is 1.9 to 7.3, and our model predicts CLBR 9-19% higher than the reference model.

<table>
<thead>
<tr>
<th>CLBR range (%)</th>
<th>0 - 10</th>
<th>11 - 20</th>
<th>21 - 30</th>
<th>31 - 40</th>
<th>41 - 50</th>
<th>51 - 60</th>
<th>61 - 70</th>
<th>71 - 80</th>
<th>81 - 90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted CLBR for reference model (%)</td>
<td>7</td>
<td>16</td>
<td>25</td>
<td>36</td>
<td>46</td>
<td>55</td>
<td>66</td>
<td>73</td>
<td>81</td>
</tr>
<tr>
<td>Predicted CLBR for new model (total blastocysts) (%)</td>
<td>9</td>
<td>14</td>
<td>21</td>
<td>39</td>
<td>55</td>
<td>70</td>
<td>87</td>
<td>93</td>
<td>97</td>
</tr>
<tr>
<td>Predicted CLBR for new model (euploid blastocysts) (%)</td>
<td>9</td>
<td>18</td>
<td>29</td>
<td>43</td>
<td>55</td>
<td>68</td>
<td>82</td>
<td>87</td>
<td>91</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Our model provides CLBR predictions that are comparable to other estimators, but higher for better-prognosis patients. Future work will focus on understanding why certain embryos have remained unfertilized, further improving the model, and expanding it for other cycle types.

REFERENCES:
REFERENCES:

P-375 6:45 AM Tuesday, October 25, 2022
LIVE DELIVERED PREGNANCY RATES FOLLOWING THE TRANSFER OF FROZEN-THAWED EMBRYOS DERIVED FROM DONOR OOCYTES ACCORDING TO THE MID-LUTEAL PHASE ENDOMETRIAL ECHO PATTERNS.
Jerome H. Check, M.D., Ph.D., 1 Carrie K. Wilson, B.A., 2 Jung Kyo Choe, M.D., 3 Kathleen O’Neill, A.A.S., 4 Jill Giangreco, B.S., 4, 5 Cooper Medical School of Rowan University, Camden, NJ; 6 Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ; 7 Cooper Institute for Reproductive Hormonal Disorders PC, Mount Laurel, NJ; 8 Cooper Institute For Reproductive Hormonal Disorde, Mount Laurel, NJ.

OBJECTIVE: Previous studies have found that though a triple-line (TL) endometrial echo pattern is uncommon in women using a graduated estradiol (E2)/progesterone (P) regimen, it is a trend for reduced live delivered pregnancy rates (LDPR) with advancing age. The decrease in LDPR may possibly be due to embryos derived from somewhat less quality oocytes not being able to overcome a less than ideal endometrium for implantation as age advances, or possibly age causes an adverse effect on the endometrium, or both. The objective of the present study was to evaluate whether the TL mid-luteal pattern increases in frequency with advancing age. Furthermore, to test the endometrial factor and eliminate the egg quality factor, the study would evaluate the LDPR according to the three endometrial echo patterns using frozen-thawed embryos derived from donor eggs.

MATERIALS AND METHODS: Women having frozen ETs using fresh donor eggs were treated with P in oil 100 mg daily and luteal phase vaginal P once there was attained an appropriate endometrial thickness following a graduated oral and vaginal estradiol regimen. The mid-luteal endometrial echo pattern was recorded as TL, isoechogenic (IE), or homogeneous hyper-echogenic (HH). Data was evaluated according to two age groups of recipients: age ≤ 42 vs. ≥ 43.

RESULTS: There were 480 ETs in women age ≤ 42. The HH pattern was found in 345 (75%), IE in 85 (18.5%), and TL in 30 (6.5%). For women age ≥ 43 there were 511 ETs. The HH pattern was found in 413 (80.8%), IE in 77 (15.1%), and TL in 21 (4.1%). The LDPRs were 48.1% with HH, 44.7% for IE, and 40.0% for TL in women age ≤ 42 vs. 48.7%, 42.9%, and 33.3% for TL in women aged ≥ 43. The implantation rates for age ≤ 42 were 33.0%, 33.2%, and 33.2% vs. 35.0%, 32.4%, and 21.1% for TL.

CONCLUSIONS: The estradiol/P regimen does not result in a higher % of TL in women age ≤ 42. The HH pattern was found in 413 (80.8%), IE in 77 (15.1%), and TL in 21 (4.1%). The LDPRs were 48.1% with HH, 44.7% for IE, and 40.0% for TL in women age ≤ 42 vs. 48.7%, 42.9%, and 33.3% for TL in women aged ≥ 43. The implantation rates for age ≤ 42 were 33.0%, 33.2%, and 33.2% vs. 35.0%, 32.4%, and 21.1% for TL. The objective of the present study was to evaluate whether the TL mid-luteal pattern increases in frequency with advancing age. Furthermore, to test the endometrial factor and eliminate the egg quality factor, the study would evaluate the LDPR according to the three endometrial echo patterns using frozen-thawed embryos derived from donor eggs.
MATERIALS AND METHODS: We analyzed all IVF/ICSI/PGT-A stimulation cycles at our center between 2017 and 2021 with at least one mature oocyte (MII) retrieved, along with all resulting FET. We also included cycles that resulted in no FET to account for the effect of FR on the likelihood of having embryos to transfer. First, FR quartiles were determined (F1-F4). To negate the effect of the number of available embryos, we analyzed blastulation rates (of the resulting fertilized oocytes), sustained implantation rate (SIR, defined as FET resulting in patient pregnant discharge), and SPR of the first FET. Finally, we also calculated a novel metric: retrievals resulting in discharge (RRD), the proportion of retrievals resulting in at least one pregnant discharge, which encapsulates the overall success of that oocyte cohort. As RRD is affected by the number of available embryos to transfer, this was adjusted for quartiles of MII retrieved (O1-O4).

RESULTS: 11,210 stimulation cycles resulting in 12,968 FET met inclusion criteria. FR quartile thresholds were F1: 0.0-75.0% (n = 3,317 cycles), F2: 75.0-85.7% (n = 2,540), F3: 85.7-100.0% (n = 5,335). Since more than 25% of cycles resulted in 100.0% fertilization rate, the top 50% were included in group F3. Blastulation rates were lower in F1 than F2 (41.6% vs 53.0%; p < 0.0001), and clinically similar although statistically different in F2 and F3 (53.0% vs 50.2%; p < 0.001). SIR was not statistically significant between groups (62.1%, 63.8%, and 63.9%, respectively; p = 0.2). As was SPR of first FET (63.5%, 64.6%, and 64.8%, respectively; p = 0.6). RRD results are summarized in Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>No</th>
<th>Yes</th>
<th>RR</th>
<th>IC 95%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>62.86% (22)</td>
<td>81.48% (22)</td>
<td>0.73</td>
<td>0.51</td>
<td>1.06</td>
</tr>
<tr>
<td>2</td>
<td>70% (14)</td>
<td>80.49% (33)</td>
<td>0.84</td>
<td>0.62</td>
<td>1.13</td>
</tr>
<tr>
<td>3</td>
<td>56.25% (9)</td>
<td>78.72% (37)</td>
<td>0.66</td>
<td>0.42</td>
<td>1.03</td>
</tr>
<tr>
<td>4</td>
<td>46.15% (6)</td>
<td>52.63% (10)</td>
<td>0.81</td>
<td>0.41</td>
<td>1.62</td>
</tr>
</tbody>
</table>

* Statistically significant vs F2 and F3. † Statistically significant vs F3.

CONCLUSIONS: A FR above 75% is associated with higher blastulation rates and higher likelihood of being discharged pregnant. However, the lack of association with SIR, both cumulatively and of first FET only, suggests that this effect is most likely related to increased fertilization resulting in more blastocysts available for transfer and, thus, more opportunities, rather than FR being a marker for oocyte or embryo quality.

IMPACT STATEMENT: This study suggests that FR is not an indicator for reproductive outcomes beyond the availability of more embryos to transfer.

P-379 6:45 AM Tuesday, October 25, 2022

WOMEN WITH POOR OVARIAN RESPONSE DIAGNOSED BASED ON POSEIDON OR BOLOGNA CRITERIA: HOW LIKELY ARE THEY TO HAVE AT LEAST ONE EUPLOID BLASTOCYST FOR TRANSFER? Andres Reig, MD, Pavan Gill, MD, Nola Herlihy, MD, Amber M. Klimczak, MD, Cheri K. Margolis, MD, Leah M. Roberts, MD, Emre Sel i, MD IVIRMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: To compare the probability of obtaining at least one euploid blastocyst for transfer in women with poor ovarian response (POR) per POSEIDON versus Bologna criteria, compared to normal responders.

MATERIALS AND METHODS: All IVF/ICSI cycles with PGT-A from 2019 to 2021 were included. Cycles using donor oocytes, surgical sperm, and patients with a cancer diagnosis were excluded. Cycles were classified by both systems: 5 POSEIDON groups: I, II, III, IV, and non-POSEIDON (NP) and 2 Bologna groups: Bologna (B) and non-Bologna (NB). First, correlation between POSEIDON and Bologna diagnoses were compared and contrasted. Next, cycle outcomes for each group were compared: number of mature oocytes (M2), fertilized oocytes (2PN), blastocysts, and euploid rate. Finally, the likelihood of obtaining at least one euploid blastocyst for transfer was compared between groups. T-tests were used to compare continuous variables and chi-square for categorical variables.

RESULTS: 6,948 cycles analyzed, of which 58% were categorized as POR by POSEIDON criteria (I: 1%; II: 3%; III: 13%; IV: 41%) and 27% by Bologna criteria. As expected, all cycles deemed POR by Bologna criteria also met POSEIDON criteria, but POSEIDON identified an additional 2,196 cycles as POR. Cycle outcomes are summarized in Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>No</th>
<th>Yes</th>
<th>RR</th>
<th>IC 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>62.86% (22)</td>
<td>81.48% (22)</td>
<td>0.73</td>
<td>0.51</td>
</tr>
<tr>
<td>2</td>
<td>70% (14)</td>
<td>80.49% (33)</td>
<td>0.84</td>
<td>0.62</td>
</tr>
<tr>
<td>3</td>
<td>56.25% (9)</td>
<td>78.72% (37)</td>
<td>0.66</td>
<td>0.42</td>
</tr>
<tr>
<td>4</td>
<td>46.15% (6)</td>
<td>52.63% (10)</td>
<td>0.81</td>
<td>0.41</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Embryos that were biopsied had better outcomes compared to their morphological equivalent non-biopsied embryos. However, in group 4, the difference between biopsied and non-biopsied embryos was smaller. Based on these findings, it is to question if biopsy on poor-quality embryos has the worst impact when compared to higher grade embryos. We understand this is a small sample study and that the statistical analysis performed did not evidence statistical difference, but it is to question if this trend could be observed in a large sample.

IMPACT STATEMENT: We should consider the impact of biopsy on poor-quality embryos based on morphological grading.
CONCLUSIONS: Use of POSEIDON criteria results in more cycles being diagnosed as POR than Bologna. While younger POSEIDON groups (I and III) have higher euploidy rates than older groups (II and IV), each incrementally higher POSEIDON group poses a higher risk of having no euploid blastocysts; with POSEIDON I being no different than non-POSEIDON, and Bologna having the worst prognosis.

IMPACT STATEMENT: This study is the first to show that POSEIDON groups linearly correlate with the likelihood of having at least one euploid embryo for transfer and compare it to the Bologna classification.

P-380 6:45 AM Tuesday, October 25, 2022
PREVIOUS INFECTION WITH SARS-COV-2 IMPACTS EMBRYO MORPHOKINETICS IN INTRACYTOPLASMIC SPERM INJECTION CYCLES. Edson Borges, Jr., PhD,1 Daniela Braga, PhD,1 Amanda Souza Setti, MSc,1 Edson Borges, Jr., MD2 1Fertility Medical Group / Sapientia Institute, Sao Paulo, Brazil; 2Fertility Medical Group, Sao Paulo, Brazil.

OBJECTIVE: Coronavirus disease 2019 (COVID-19) is caused by a novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which may infect any cell type expressing ACE2 and TMPRSS2 receptors. A sample of at least 111 embryos had 95% power to detect a 20% effect of maternal COVID-19 infection on embryo development remain inconsistent. Time-lapse imaging (TLI) systems allow for the mapping of morphological changes or possible effects on embryo development. Information concerning the susceptibility of the female reproductive systems to SARS-CoV-2 infection, and potential targets of SARS-CoV-2. A sample of at least 111 embryos had 95% power to detect a 20% effect of maternal COVID-19 infection on embryo development. Use of POSEIDON criteria results in more cycles being diagnosed as POR than Bologna. While younger POSEIDON groups (I and III) have higher euploidy rates than older groups (II and IV), each incrementally higher POSEIDON group poses a higher risk of having no euploid blastocysts; with POSEIDON I being no different than non-POSEIDON, and Bologna having the worst prognosis.

CONCLUSIONS: Previous SARS-CoV-2 maternal infection had significant impacts on embryo morphokinetic events and KIDScore rank.

IMPACT STATEMENT: This first study evaluating the impact of SARS-CoV-2 infection on embryo development post-ICSI suggests that women who have recovered from COVID-19 infection should be aware of a possible detrimental effect of the infection on embryo development. Its impact on implantation potential in vivo is particularly important and should be investigated.

SUPPORT: This study was funded by Ferring COVID-19 Investigational Grants.

P-381 6:45 AM Tuesday, October 25, 2022
IS THERE AN ADDED BENEFIT WITH EXTENDED EMBRYO CULTURE IN WOMEN OF ADVANCED MATERNAL AGE UNDERGOING IVF-ET? Peter Kovacs, MD, PhD,1 Samantha Sun, medical student,2 Yao Lu, MD,1 Diran Chamoun, M.D.,1 Steven R. Lindheim, M.D.,2 Dunamenti REK Reproduktios Kozpont, Budapest, Hungary;2 University of Central Florida College of Medicine, Center for Reproductive Medicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China;3 University of Central Florida College of Medicine, FL.

OBJECTIVE: Extended blastocyst culture and embryo transfer (ET) has proven to result in higher pregnancy (PR) and live birth (LBR) rate compared to cleavage stage transfer. While this is thought to be due to greater oocyte yield, optimal embryo selection and improved embryo-endometrium synchrony, limited data exists on the benefits of blastocyst culture in advanced maternal age (AMA) (>40 years) women whose embryos may be less likely to resist prolonged in vitro conditions. We compared pregnancy outcomes of those undergoing d-3 vs d-5 ET in AMA women and secondarily analyzed those who had a d-3 ET, but otherwise met criteria for extended culture (3 or more good morphology embryos on day 3) to those undergoing d-5 ET.

MATERIALS AND METHODS: All fresh IVF-ICSI cycles performed from Jan 2020 to Dec 2021 in AMA women that progressed to ET were considered for analysis. Baseline demographic, cycle stimulation characteristics, embryoology and pregnancy outcomes were collected and analyzed using t-test, chi square test and ANOVA analysis as appropriate.

RESULTS: In the study period, 824 cycles were initiated; 168 cycles were excluded for cancellation during stimulation, retrieval, fertilization failure, embryonic arrest or elective cryopreservation. Compared to d-5 (n=184), those patients undergoing d-3 ET (n=472), were older (41.9 ± 1.4 (SD) vs 41.4 ± 1.3 yrs, p<0.01), had lower ovarian reserve (AMH: 1.4 ± 2.6 vs 2.0 ± 1.6 mg/mL, p=0.01), had fewer oocytes retrieved (4.4 ± 2.9 vs 8.8 ± 4.2, p<0.001) and had lower number of ET (1.6 ± 0.5 vs 1.8 ± 0.5, p=0.001).

Table 1. Average M2, 2PN, blastocysts, and euploidy rate (with 95% CI) per stimulation cycle, and percentage of cycles in which at least one euploid blastocyst was obtained (with 95% CI). All p-values < 0.0001 versus all other groups unless otherwise noted.

<table>
<thead>
<tr>
<th>Group</th>
<th>M2</th>
<th>2PN</th>
<th>Blastocyst</th>
<th>Euploidy Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>NP</td>
<td>14.1</td>
<td>11.8</td>
<td>5.9</td>
<td>71.2% (70.5% - 71.9%) NS vs NB, 91.0% (89.9% - 92.0%) p &lt; 0.05 vs IV</td>
</tr>
<tr>
<td>I</td>
<td>NS vs II, NB</td>
<td>8.9</td>
<td>4.5</td>
<td>80.3% (76.3% - 83.8%) NS vs III, 96.9% (91.3% - 99.2%) p &lt; 0.05 vs NP</td>
</tr>
<tr>
<td>II</td>
<td>9.8</td>
<td>NS vs I, NB</td>
<td>3.4</td>
<td>54.6% (51.0% - 58.1%) NS vs IV, 77.4% (71.4% - 82.5%)</td>
</tr>
<tr>
<td>III</td>
<td>5.0</td>
<td>NS vs IV</td>
<td>4.0</td>
<td>78.7% (76.7% - 80.6%) NS vs I, 63.6% (60.4% - 66.6%)</td>
</tr>
<tr>
<td>IV</td>
<td>4.8</td>
<td>NS vs III</td>
<td>3.9</td>
<td>50.3% (48.7% - 51.9%) p &lt; 0.05 vs II</td>
</tr>
<tr>
<td>NB</td>
<td>10.9</td>
<td>NS vs I, II</td>
<td>4.3</td>
<td>70.4% (69.8% - 71.0%) NS vs NP, 80.1% (79.0% - 81.2%)</td>
</tr>
<tr>
<td>B</td>
<td>4.1</td>
<td>3.4</td>
<td>1.0</td>
<td>40.1% (37.9% - 42.3%) NS vs NB, 27.7% (25.7% - 29.8%)</td>
</tr>
</tbody>
</table>
p < 0.001). Significantly lower PR (15.8% [74] vs 31.5% [58], p < 0.001) and ongoing (OG)-PR (10.5% [50] vs 24.4% [45], p < 0.001) were in d-3 compared to d-5 ET group. In those undergoing d-3 ET, but who met criteria for extended culture (n=135), age (41.8 ± 4.1 vs 41.3 ± 3.3 yrs); AMH (2.0 ± 1.4 vs 2.9 ± 1.6 ng/mL); number of retrieved oocytes (8.8 ± 4.2 vs 8.8 ± 4.2); and PR (25.1% [74] vs 31.5% [58]) were comparable to the d-5 group. However, OG-PR was significantly lower (13.3% [18] vs 24.4% [45], p = 0.01) and miscarriage rates higher (47% [16] vs 22.4% [13], p = 0.01). CONCLUSIONS: Blastocyst culture provides a significant benefit to AMA patients who meet criteria for extended culture, resulting in higher OG-PR and lower pregnancy loss compared to cleavage stage ET. While concerns regarding extended culture may result in higher cycle cancellation, the psychological burden of pregnancy loss and delays in treatment can be avoided.

IMPACT STATEMENT: In advanced maternal age women, those meeting criteria for blastocyst embryo culture have higher ongoing pregnancy rates and reduced pregnancy loss.

SUPPORT: None.

REFERENCES:
Pantos K et al., Influence of advanced age on the blastocyst development rate and pregnancy rate in assisted reproductive technology. FS 1999;71:1144-6

Milki AA et al. Comparison of blastocyst transfer to day 3 transfer with assisted hatching in the older patient. FS 2002;78:1244-7.


P-382 6:45 AM Tuesday, October 25, 2022

EFFECT OF REDUCED OXYGEN TENSION ON OUTCOMES OF SINGLE, EUPLOID FROZEN BLASTOCYST TRANSFER. Natasha Raj-Derouin, MD, MS, Laura C. Gemmell, MD, MSc, Robert W. Prosser, MSc, Sasha Sadowy, M.Sc., Eric J. Forman, M.D. 1LA Canada Flintridge, CA; 2New York, NY; 3Columbia University Fertility Center; 4Columbia University Irving Medical Center, New York, NY.

OBJECTIVE: To evaluate the relationship between reduced oxygen tension (5%) vs. atmospheric oxygen tension (20%) in embryo culture environment and outcomes after single, euploid frozen-thawed blastocyst transfer following in vitro fertilization (IVF).

MATERIALS AND METHODS: Retrospective, single-institution cohort study evaluating 1,033 single, euploid frozen embryo transfers (FETs) that occurred between December 1, 2015 and February 1, 2021 at a single academic medical center. Only FETs in which a single embryo was transferred and was confirmed to be euploid via PGT-A were included. FETs involving more than one embryo, did not undergo PGT-A, tested to be mosaic, involved donor egg or donor embryo, and any embryos frozen in 20% but thawed in 5% oxygen tension were excluded from the study. The data were collected and analyzed using STATA/BE 17.0 to perform chi-square tests, two-tailed t-tests, and logistic regression models. Results are given as medians.

RESULTS: Embryos cultured in 5% oxygen had a higher live birth rate (50.4% vs. 35.3%, p < 0.001, OR 1.86, 95% CI 1.32-2.61) and clinical pregnancy rate (59.6 vs. 42.4%, p < 0.001) compared to those cultured in 20% oxygen. There was no statistically significant difference in biochemical pregnancies or clinical pregnancy loss between the two groups as well as no statistically significant difference in gestational age at delivery or birthweight.

CONCLUSIONS: Embryos cultured in 5% oxygen tension to better reflect the in vivo environment of the female reproductive tract can improve IVF outcomes such as live birth rate per FET, even after controlling for euploid status with PGT-A.

IMPACT STATEMENT: While there have been other studies demonstrating the beneficial impact of reduced oxygen tension in embryo culture systems, they have not controlled for ploidy status and assessed outcomes from euploid blastocystcs that were screened with PGT-A. Our results demonstrate that even with controlling for euploid embryos, there is an increase in live birth rate per single, euploid FET. In doing so, we have accounted for this important confounding factor and further isolated reduced oxygen tension as an important parameter of the embryo culture environment.

P-383 6:45 AM Tuesday, October 25, 2022


OBJECTIVE: At many fertility centers across the United States patients undergoing in vitro fertilization (IVF) with pre-implantation genetic testing for aneuploidy (PGT-A) are given the option of indicating their preference for embryo transfer based on best quality or sex of embryo. The purpose of the current study was to evaluate trends in patient preferences for selecting an embryo for transfer based on sex vs. best quality over the past decade and to determine whether these choices have clinical implications.

MATERIALS AND METHODS: This was a retrospective cohort study including all patients between January 2012 and December 2021 undergoing their first embryo transfer after IVF with PGT-A testing at a university-affiliated infertility clinic in the United States. Only cycles with at least one embryo of each sex available at time of transfer were included for analysis. The primary outcomes were evaluating patient preferences for selecting an embryo for transfer based on sex (best quality vs sex selection) as well as preferences for male or female embryo. Trends in preference over a ten-year time period were evaluated. IVF pregnancy outcomes were compared between groups. Mean and standard deviation were used to describe descriptive data. Chi-square test was used for comparison of categorical variables and t-test was used for comparison of continuous variables. Significance was accepted at p < .05.

RESULTS: 5145 embryo transfer cycles were included for analysis. 2804 (54.5%) patients selected the best quality embryo for transfer and 2341 (45.5%) selected their embryo for transfer based on preference for a certain sex; 1324 (56.5%) selected a male embryo and 1017 (43.5%) selected a female embryo. A greater proportion of patients consistently selected the best quality embryo for transfer, with no difference over the decade (p=0.30). In those who transferred based on sex selection, a male embryo for transfer was consistently preferred over the ten years (p=0.04). In those who transferred based on sex selection, a male embryo for transfer was consistently preferred over the ten years (p=0.04). Embryo grade was significantly higher in the best quality embryo group (p<0.001). While the clinical pregnancy rate (CPR) was significantly higher in the best quality group (74.4% vs. 71.9%, p = 0.04), the sustained implantation rate (SIR) was similar in both groups (64.9% vs. 63.4%, p = 0.25). Pregnancy outcomes were not significantly different among those who selected a male as the outcome of each sex available at time of transfer were included for analysis. The primary outcomes were evaluating patient preferences for selecting an embryo for transfer based on sex (best quality vs sex selection) as well as preferences for male or female embryo. Trends in preference over a ten-year time period were evaluated. IVF pregnancy outcomes were compared between groups. Mean and standard deviation were used to describe descriptive data. Chi-square test was used for comparison of categorical variables and t-test was used for comparison of continuous variables. Significance was accepted at p < .05.

CONCLUSIONS: Sex selection at time of first embryo transfer remains an important priority for patients with nearly half of patients selecting their embryo based on sex. Trends in preference over a ten-year period. There is a higher preference for a male embryo among those who transfer an embryo based on sex selection. While CPR rates were lower in the sex selection group, SIR rates were equivalent across both groups.

TABLE 2. Single euploid FETs, frozen and thawed in 20% oxygen versus frozen and thawed in 5% oxygen. * denotes statistical significance, P < 0.05

<table>
<thead>
<tr>
<th>20% Oxygen</th>
<th>5% Oxygen</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=170)</td>
<td>(n=863)</td>
</tr>
<tr>
<td>Positive pregnancy test rate, n (%)</td>
<td>85 (51.2)</td>
</tr>
<tr>
<td>Biochemical pregnancy loss rate, n (%)</td>
<td>15/87 (17.2)</td>
</tr>
<tr>
<td>Clinical pregnancy rate, n (%)</td>
<td>72 (42.4)</td>
</tr>
<tr>
<td>Clinical Pregnancy Loss rate, n (%)</td>
<td>12/72 (16.7)</td>
</tr>
<tr>
<td>Live birth rate n, (%)</td>
<td>60 (35.3)</td>
</tr>
<tr>
<td>Adjusting for age Odds Ratio = 1.86 95% CI [1.32-2.61]</td>
<td>P &lt;0.001*</td>
</tr>
</tbody>
</table>
DO IMPLANTATION AND LIVE BIRTH RATES WITH TRANSFER OF SINGLE EUPLOID BLASTOCYSTS CORRELATE TO THEIR MITOSCORE? Vaani Nanavaty, MS; Christine E. Hur, M.D.; Meng Yao, MS; Nina Desai, Ph.D., HCLD; Cleveland Clinic, Beachwood, OH; Cleveland Clinic Foundation, Cleveland, OH; Cleveland Clinic, Cleveland, OH.

OBJECTIVE: To examine data from single embryo transfer (SET) cycles with preimplantation genetic screening and Mitoscore assessment to better understand the value of Mitoscore in ranking euploid blastocysts for transfer.

MATERIALS AND METHODS: Patients undergoing in vitro fertilization (IVF) with preimplantation genetic testing (PGT) for aneuploidy had their zygotes cultured in the Embryoscope time lapse incubator. Morphokinetic (MK) data on embryos development was collected. Blastocysts were biopsied and subsequently frozen, awaiting PGT testing. This study is a retrospective review of prospectively collected data of patients that continued on to a frozen embryo transfer cycle. The euploid embryo for transfer was selected strictly on basis of development morphology and patient gender preference. For each transferred embryo, timing in hours post insemination for cleavage events, start of compaction (tSC), morula (tM), start of blastulation, blastocyst (tB), expanded blastocyst (tEB), and hatched blastocyst (tHB) were analyzed along with Mitoscore. Statistical analyses were performed using Chi square and Pearson correlation tests. A p-value of <0.05 was considered statistically significant.

RESULTS: A total of 49 vitrified-thawed blastocysts diagnosed as euploid were singly transferred. Mitoscore was significantly associated with kinetic parameters in developing embryos. A positive correlation was found between Mitoscores and t4 (0.35 [0.05, 0.56]; p = 0.022), and the second synchronous division t4-t3 (0.51 [0.27, 0.69]; p < 0.001). A positive correlation was also found for tSC (0.32 [0.04, 0.55]; p = 0.024), tM (0.44 [0.18, 0.64]; p = 0.001), tSB (0.40 [0.13, 0.61]; p = 0.004), tB (0.42 [0.16, 0.63]; p = 0.002), tEB (0.50 [0.24, 0.69]; p < 0.001), and tHB (0.44 [0.10, 0.68]; p = 0.012). Blastocysts sufficiently expanded to biopsy on day 5 had significantly lower Mitoscores than D6 biopsied blastocysts (p < 0.001).

CONCLUSIONS: Mitoscore was clearly reflective of embryo growth kinetics and timing of blastulation. Mitoscores did not differ between pregnant and non-pregnant patients. Whereas a trend towards lower implantation was observed with higher Mitoscores, this did not reach significance.

IMPACT STATEMENT: More data is needed from different centers to determine the value of Mitoscore for ranking of euploid blastocyst for transfer.

### Table: Mitoscore and Implantation Rate

<table>
<thead>
<tr>
<th>Factor</th>
<th>SET Cycles</th>
<th>Mitoscore (Mean ± SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day of Biopsy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>33</td>
<td>23.0 ± 5.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6</td>
<td>16</td>
<td>30.8 ± 5.3</td>
<td></td>
</tr>
<tr>
<td>Implantation (sac)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>31</td>
<td>25.0 ± 6.9</td>
<td>NS</td>
</tr>
<tr>
<td>No</td>
<td>16</td>
<td>27.1 ± 6.4</td>
<td></td>
</tr>
<tr>
<td>Implantation (fetal heart)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>28</td>
<td>25.9 ± 6.6</td>
<td>NS</td>
</tr>
<tr>
<td>No</td>
<td>19</td>
<td>25.4 ± 7.1</td>
<td></td>
</tr>
<tr>
<td>Live Birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27</td>
<td>25.7 ± 6.7</td>
<td>NS</td>
</tr>
<tr>
<td>No</td>
<td>20</td>
<td>25.7 ± 7.0</td>
<td></td>
</tr>
<tr>
<td>Mitoscore Rank</td>
<td>N</td>
<td>Implantation Rate</td>
<td>p-value</td>
</tr>
<tr>
<td>&lt;21</td>
<td>15</td>
<td>80% (12/15)</td>
<td></td>
</tr>
<tr>
<td>21-26</td>
<td>12</td>
<td>67% (8/12)</td>
<td></td>
</tr>
<tr>
<td>&gt;26</td>
<td>20</td>
<td>55% (11/20)</td>
<td></td>
</tr>
</tbody>
</table>

FERTILITY & STERILITY®

P-384 6:45 AM Tuesday, October 25, 2022

NON-MEDICAL EMBRYO SEX SELECTION RESULTS IN REDUCED IMPLANTATION COMPARED TO THE TRANSFER OF THE HIGHEST MORPHOLOGICAL GRADE BLASTOCYST: Alison Arnold, MS; Lauren Henry, BS; Rachel Lee, B.S.; Susanna McReynolds, PH.D.; William B. Schoolcraft, MD; Mandy Katz-Jaffe, PhD; CCRM Genetics, Lone Tree, CO; Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Non-medical embryo sex selection has become more accessible to infertile couples undergoing preimplantation genetic testing for aneuploidy (PGT-A). Couples report a combination of motivations for pursuing non-medical embryo sex selection, including a desire to limit family size, family balancing and financial concerns about multiple subsequent pregnancies. The aim of this study was to evaluate the clinical impact of performing euploid embryo selection based on sex chromosomes in preference to the highest morphological grade blastocyst.

MATERIALS AND METHODS: Infertile patients (n = 132; mean maternal age = 35.4 ± 3.3 years) who chose non-medical embryo sex selection following PGT-A were compared to a maternal age-matched control group of frozen embryo transfers (n = 904; mean maternal age = 35.5 ± 0.5 years) where a single euploid blastocyst of the best morphological grade, independent of sex chromosomes, was selected. Primary outcomes included clinical pregnancy with fetal heart tone (FHT), implantation with FHT, miscarriage and live birth rates. A two-sided Fisher’s exact test with odds ratio calculated significance at p < 0.05.

RESULTS: There was no significant gender preference observed in this cohort of non-medical embryo sex selection IVF cycles, however there was a potential trend towards a skewed gender ratio (male sex chromosomes = 42.4%, female sex chromosomes = 49.2% and double embryo transfer of both genders = 8.5%). Upon comparison to the control group FETs with euploid embryo selection based on the best morphological grade blastocyst, implantation with FHT after non-medical embryo sex selection was significantly reduced (63.3% vs. 72.1% control; p < 0.05, OR 0.67). Other clinical outcomes including pregnancy with FHT (65.2% vs. 70.8% control) and live birth rates (60.6% vs. 65.4% control) also displayed a trend downwards following FET based on non-medical embryo sex selection but were not statistically significant. In contrast, miscarriage rates were comparable between the two euploid embryo selection groups (7.0% non-medical embryo sex selection vs. 7.5% control).

CONCLUSIONS: The debate over the accessibility of non-medical embryo sex selection in IVF is dynamic and complex. Some of the arguments against the practice include the likely disruption in the gender ratio and the inequality of access. Our data echoed a potential trend towards a skewed gender ratio but more importantly revealed a significant trend towards reduced implantation rate when choosing euploid embryos based on a priority for sex chromosomes over the highest morphological grade.

IMPACT STATEMENT: The best morphological-grade euploid blastocyst, independent of sex chromosomes, will always result in the most successful clinical outcomes for infertile patients.

SUPPORT: None

REFERENCES:


FERTILITY & STERILITY®

P-385 6:45 AM Tuesday, October 25, 2022

DOES INDIVIDUALIZED PRE- AND POST-EMBRYO TRANSFER ACUPUNCTURE AFFECT LIVE BIRTH RATES? Kate Philippi, D.A.O.M., M.S.C.; Lamya A. Kamel, L.Ac., Dipl. OM, D.A.O.M.; Lee E. Hullender Rubin, D.A.O.M., M.S.C.; Roohi Jeelani, M.D.; Tyler Soy, MA; Vios Fertility Institute, Chicago, IL; Aligned Modern Health, Chicago, IL; Portland, OR; Vios fertility Institute, Chicago, IL.

OBJECTIVE: To assess the effect of individualized, day of embryo transfer acupuncture on Frozen Embryo Transfer (FET) live birth rates compared with no acupuncture.

SUPPORT: None

REFERENCES:

MATERIALS AND METHODS: In this retrospective cohort study, 2,330 patients completed an FET at Vios Fertility Institute, Chicago, IL, from May 2018 – May 2021. Individualized acupuncture therapy was provided on-site, for 30 minutes before and immediately after embryo transfer (ET) by licensed acupuncturists (ACU group) in 579 records, and 1,751 elected FET alone (FET group). Our main outcome measure was live birth rates. Groups were compared by age, diagnosis, number of cycles, ET day, and number of autologous embryos transferred. Means were compared using analysis of variance and proportions with Chi-square and logistic regression.

RESULTS: Demographics differed between groups on several variables. See Table 1. Individualized acupuncture pre- and post-ET was associated with more live births [Odds Ratio (OR)=1.55, 95% Confidence Interval (CI) 1.29-1.88, p<0.0001] and fewer biochemical pregnancies (OR=0.58, 95% CI 0.41-0.83, p=0.002). There was no difference between groups on the outcomes of miscarriage and ectopic pregnancy.

CONCLUSIONS: Individualized acupuncture on the day of embryo transfer was associated with 55% increase in FET live births and 42% reduction in biochemical pregnancies compared with FET alone.

IMPACT STATEMENT: Individualized day of embryo transfer acupuncture was associated with significant benefit to patients undergoing FET.

P-387 6:45 AM Tuesday, October 25, 2022

A COMPREHENSIVE MODEL FOR PREDICTING THE PROBABILITY OF LIVE BIRTH PRIOR TO THE START OF PROGESTERONE DURING ARTIFICIAL FROZEN EMBRYO TRANSFER CYCLES.

Fernanda Murillo Armijo, B.S, M.S.,1 Alan B. Copperman, MD,2 Kevin E. Loewke, Ph.D.,1 Alife Health, Inc;1Icahn School of Medicine at Mount Sinai/Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: To develop a comprehensive model for predicting the probability of live birth prior to the start of progesterone during artificial frozen embryo transfer (FET) cycles that can identify at-risk cycles and set expectations.

MATERIALS AND METHODS: Historical, de-identified EMR data was collected from a single IVF clinic in the United States. Records were filtered for autologous cryo-synthetic frozen embryo transfers (FETs) resulting in 5,813 cycles from 4,133 patients between 2014-2021. For endometrial response we extracted measurements from the end of the proliferative phase, a common decision point. Parameters with high variance inflation factor were dropped for accurate interpretation of regression results. We developed a mixed effects logistic regression model using parameters from the embryo, patient, and endometrial response for the primary outcome of live birth.

RESULTS: 13 parameters were found to be significant (P<0.01) with respect to live birth outcomes. The most important parameters positively associated with live birth were higher endometrial thickness (OR 0.51) and number of previous failed FETs (OR 0.29). Calibration curves showed predicted probabilities closely matched observed live birth rates, with an expected calibration error of 0.028 on a 25% hold-out test set.

CONCLUSIONS: We developed a comprehensive and well-calibrated model to predict live birth probabilities prior to the start of progesterone during artificial FET cycles. Future work will expand the dataset and develop additional tools for clinical decision support.

IMPACT STATEMENT: Successful outcomes in artificial FET cycles are dependent upon parameters related to the patient, embryo, and endometrial response, and modeling all parameters together enables accurate predictions of live birth rate for identifying at-risk cycles and setting expectations.
HOW MANY EUPLOID BLASTOCYSTS NEED TO BE TRANSFERRED IN OBESE PATIENTS TO ACHIEVE A LIVE BIRTH? AN ENDLESS PATIENT-DOCTOR NEGOTIATION STORY. Ahmed El-Damen, M.Sc.,1 Ibrahim Elkhatib, M.Sc.,2 Asina Bayram, M.Sc.,2 Andrea Abdala, M.Sc.,2 Daniela Nogueira, PhD, Raquel Del Gallego, PhD,1 Laura Melado, M.D, PhD,1 Lawrenz Barbara, M.D., PhD,1 Human M. M. Fatemi, M.D., PhD Prof.2 1ART Fertility Clinics, Abu Dhabi, Abu Dhabi, United Arab Emirates; 2ART Fertility Clinics, Abu Dhabi, United Arab Emirates; 2Abu Dhabi, Abu Dhabi, United Arab Emirates; 3Abu Dhabi, Abu Dhabi, United Arab Emirates; 4St Jean, France.

OBJECTIVE: To evaluate live birth rates of single and double euploid blastocyst transfer in relation to patients’ Body Mass Index (BMI).

MATERIALS AND METHODS: A single center retrospective observational study was performed between March 2017 and March 2021, including 1179 single and 842 double euploid frozen embryo transfer (FET) cycles respectively. Blastocysts transferred were biopsied on day (D) 5, D6 or D7 for preimplantation genetic testing for aneuploidy (PGT-A). The endometrium was prepared for FET either as a natural cycle (NC) or hormone replacement therapy (HRT). According to their BMI, patients were defined as normal weight, overweight or obese if their BMI fell in the range of 18.5-24.9, 25-29.9 or ≥ 30 kg/m2, respectively. One-way ANOVA test, Spearman’s correlation coefficient and a multivariate logistic regression analysis were performed. The strong positive correlation between BMI and miscarriage (r coefficient = 0.510, p< 0.00001) and a strong negative correlation between BMI and live birth (r coefficient = -0.186, p< 0.001). In SET cycles, obese patients had a significantly higher miscarriage rate (33.7% vs 18.6%, p= 0.011) and a significantly lower live birth rate (49.6% vs 45.1%, p= 0.015) and presented a significantly higher miscarriage rate (33.7% vs 18.6%, p= 0.014), they had a significantly higher miscarriage rate (33.7% vs 18.6%, p= 0.014).

CONCLUSIONS: Although obese patients might be encouraged to transfer two euploid blastocysts in an FET cycle in sake of slightly higher chances of a live birth, this recommendation should be delivered with caution due to the significantly higher risk of miscarriage and pregnancy complications. A proper patient counselling and risk assessment plan should be applied.

IMPACT STATEMENT: Besides its association with multiple diseases that threaten human lives leading to high mortality and morbidity rates, obesity significantly increases miscarriage rate especially in patients transferring two euploid vitrified warmed blastocysts.

SUPPORT: No financial support was received.

P-389 6:45 AM Tuesday, October 25, 2022

CLINICAL OUTCOME OF PERSONALIZED EMBRYO TRANSFER IN CONSIDERATION WITH EMBRYONIC DEVELOPMENTAL SPEED IN RECURRENT IMPLANTATION FAILURE PATIENTS. Yasuhiro Ohara, MD,1,2 Masakazu Doshida, MD, PhD,1 Takumi Takeuchi, M.D., Ph.D.,1 Hidehiko Matsumabashi, MD, PhD,2 Tomomoto Ishikawa, M.D., Ph.D.1 1Reproduction Clinic Tokyo, Tokyo, Japan; 2Reproduction Clinic Osaka, Osaka, Japan.

OBJECTIVE: Although aneuploid embryos and the asynchronization between an embryo and the window of implantation (WOI) can account for the major cause of implantation failure, several studies have investigated that even euploid blastocysts fail to implant in about 40% of personalized embryo transfers (pET) according to the widely used endometrial receptivity test. Failure of an euploid embryo to implant on the day recommended by the test may suggest the importance of more precisely synchronizing implantation timing of the blastocyst with the WOI. In this study, we investigate whether personalized embryo transfer in consideration with embryonic developmental speed improves the clinical outcome in recurrent implantation failure (RIF) patients.

MATERIALS AND METHODS: A retrospective review was performed for 999 RIF patients who had 3 or more failed embryo transfers and underwent a new endometrial receptivity test, ERPeakSM, in a private fertility clinic between April 2019 and March 2022. We evaluated clinical outcome of 289 receptive (R) patients who underwent pET in a subsequent HRT cycle after ERPeakSM testing with morphologically good quality embryos. Among R cases, we performed pET on the day where the ERPeakSM test indicated optimal receptivity (standard pET), or we also considered embryonic developmental speed for the first pET after ERPeakSM testing. We estimated the thawed blastocyst grade based on the past embryonic developmental pattern of each patient and set the day of transfer as follows: estimated blastocyst grades 3, 4, 5, and 6 were transferred on days P + 5, P + 5.5, P + 6.0, and P + 6.5, respectively. We defined this method as Tailor-made ET (TmET). In propensity score matching analysis, the clinical pregnancy rate (CPR) was compared for TmET group versus standard pET group. After adjusting 7 covariates, including age at ovum retrieval, AMH, gravidity, parity, infertility periods, the number of previous failed ET, and the number of transferred embryos, adjusted odds ratios (aOR) and 95% CI were calculated.

RESULTS: Of 999 RIF patients, ERPeakSM testing showed a shifted WOI in 548 patients (54.9%) and a R result in 451 patients (45.1%). Among R patients, 63 patients received TmET and 226 patients underwent standard pET. The CPR of the former group was significantly higher (54.0% vs. 35.0%, aOR: 2.73; 95% CI, 1.42-5.26, p < 0.01) compared to the latter.

CONCLUSIONS: pET for R patients in consideration with embryonic developmental speed may improve pregnancy outcome.

IMPACT STATEMENT: In this study, embryos were selected for transfer by morphology alone, rather than chromosomal screening, which may have affected the clinical outcome. pET in consideration with embryonic developmental speed could be more effective when euploid embryos, usually progressing to a better expansion grade after thawing, are transferred.

P-390 6:45 AM Tuesday, October 25, 2022

THE DILEMMA FOR PATIENTS WITH A THIN ENDOMETRIAL LINING: NATURAL CYCLES OR PROGRAMMED FROZEN EMBRYO TRANSFER CYCLES? Shunping Wang, PhD,1 Shih-Wern Tsaih, ScD,2 Nina Snowden, MD,2 Stephanie Gunderson, M.D.,1,3 Robert Rydze, MD,2 Kate D. Schoyer, MD2 1Medical College of Wisconsin, Milwaukee, WI; 2Medical College of Wisconsin, Milwaukee, WI; 3Menomonee Falls, WI.

OBJECTIVE: Although obesity is a progressive chronic disease that threatens human lives leading to high mortality and morbidity rates, obesity significantly increases miscarriage rate especially in patients transferring two euploid vitrified warmed blastocysts.

SUPPORT: No financial support was received.

P-389 6:45 AM Tuesday, October 25, 2022

CLINICAL OUTCOME OF PERSONALIZED EMBRYO TRANSFER IN CONSIDERATION WITH EMBRYONIC DEVELOPMENTAL SPEED IN RECURRENT IMPLANTATION FAILURE PATIENTS. Yasuhiro Ohara, MD,1,2 Masakazu Doshida, MD, PhD,1 Takumi Takeuchi, M.D., Ph.D.,1 Hidehiko Matsumabashi, MD, PhD,2 Tomomoto Ishikawa, M.D., Ph.D.1 1Reproduction Clinic Tokyo, Tokyo, Japan; 2Reproduction Clinic Osaka, Osaka, Japan.

OBJECTIVE: Although aneuploid embryos and the asynchronization between an embryo and the window of implantation (WOI) can account for the major cause of implantation failure, several studies have investigated that even euploid blastocysts fail to implant in about 40% of personalized embryo transfers (pET) according to the widely used endometrial receptivity test. Failure of an euploid embryo to implant on the day recommended by the test may suggest the importance of more precisely synchronizing implantation timing of the blastocyst with the WOI. In this study, we investigate whether personalized embryo transfer in consideration with embryonic developmental speed improves the clinical outcome in recurrent implantation failure (RIF) patients.

MATERIALS AND METHODS: A retrospective review was performed for 999 RIF patients who had 3 or more failed embryo transfers and underwent anew endometrial receptivity test, ERPeakSM, in a private fertility clinic between April 2019 and March 2022. We evaluated clinical outcome of 289 receptive (R) patients who underwent pET in a subsequent HRT cycle after ERPeakSM testing with morphologically good quality embryos. Among R cases, we performed pET on the day where the ERPeakSM test indicated optimal receptivity (standard pET), or we also considered embryonic developmental speed for the first pET after ERPeakSM testing. We estimated the thawed blastocyst grade based on the past embryonic developmental pattern of each patient and set the day of transfer as follows: estimated blastocyst grades 3, 4, 5, and 6 were transferred on days P + 5, P + 5.5, P + 6.0, and P + 6.5, respectively. We defined this method as Tailor-made ET (TmET). In propensity score matching analysis, the clinical pregnancy rate (CPR) was compared for TmET group versus standard pET group. After adjusting 7 covariates, including age at ovum retrieval, AMH, gravidity, parity, infertility periods, the number of previous failed ET, and the number of transferred embryos, adjusted odds ratios (aOR) and 95% CI were calculated.

RESULTS: Of 999 RIF patients, ERPeakSM testing showed a shifted WOI in 548 patients (54.9%) and a R result in 451 patients (45.1%). Among R patients, 63 patients received TmET and 226 patients underwent standard pET. The CPR of the former group was significantly higher (54.0% vs. 35.0%, aOR: 2.73; 95% CI, 1.42-5.26, p < 0.01) compared to the latter.

CONCLUSIONS: pET for R patients in consideration with embryonic developmental speed may improve pregnancy outcome.

IMPACT STATEMENT: In this study, embryos were selected for transfer by morphology alone, rather than chromosomal screening, which may have affected the clinical outcome. pET in consideration with embryonic developmental speed could be more effective when euploid embryos, usually progressing to a better expansion grade after thawing, are transferred.
OBJECTIVE: The management of patients with persistently thin endometrial linings presents a challenge to infertility providers. Prior studies have demonstrated lower clinical pregnancy and live birth rates when the endometrial thickness is ≤7mm. Emerging data has shown that clinical pregnancy rates are equivalent when comparing natural vs programmed cycles for frozen embryos transfers (FET). This current study set out to evaluate outcomes in patients with thin linings undergoing either a natural cycle or programmed cycle FET.

MATERIALS AND METHODS: This retrospective cohort study included all FET cycles at our institution from 2018-2021 when the endometrial lining was ≤7mm. We compared clinical pregnancy rates in natural cycles (timed FET 6 days after LH surge) vs. programmed cycles with estradiol and progesterone supplementation, with or without leuprolide acetate. One thousand one hundred and forty-seven single frozen embryo transfer cycles were performed during the specified time period of which 78 were included based on an endometrial lining of ≤7mm at time of mid-cycle ultrasound. Pearson’s Chi-squared test with Yates’ continuity correction was used for the categorical data with p<0.05 showing statistical significance.

RESULTS: Using a cut-off for endometrial thickness of 7 mm, there was a trend towards lower clinical pregnancy rates in natural cycle FETs (28%) when compared to programmed cycle FETs (45%). However, this was not statistically significant, likely due to low numbers in each category (25 natural FETs vs 53 programmed FETs). Of note, the clinical pregnancy rate of all programmed cycles (45%) was found to be equivalent to the clinical pregnancy rate of programmed cycles with endometrial linings ≤7mm (45%).

CONCLUSIONS: Deciding to cancel an FET based on endometrial thickness, in patients undergoing a programmed cycle FET is not supported by this current study. Given the trend, it may be appropriate to cancel a patient undergoing a natural cycle FET with a lining of 7mm or less in favor of a programmed cycle. However, further studies will be required to confirm these preliminary findings.

IMPACT STATEMENT: The current study will help in making evidenced-based decisions regarding management of resistant thin endometrial linings, specifically with regards to criteria for cancelling a frozen embryo transfer and choosing the optimal protocol.

E-PAPER ABSTRACT SESSION: T18

P-391 6:45 AM Tuesday, October 25, 2022

NOVEL TOOL FOR ENDOMETRIAL ASSESSMENT IN EMBRYO TRANSFER CYCLES: ENDOMETRIAL ELASTOGRAPHY. Volkan Emirdar, M.D.,1 Funda Gode, M.D.,2 Ibrahim Pala, Sr., B.Sc.3 Erkan Sahin, MD4 Izmir Economy University School of Medicine, Karsiyaka-Izmir, Turkey;2 Kent Hospital, Izmir, Turkey;3 Izmir Economy University Medical Park Hospital, izmir, Turkey.

OBJECTIVE: Currently evaluation of the endometrium by two dimensions(2D) ultrasonography with measuring 2D endometrial thickness, echogenicity, vascularity, any structures disturbing the normal anatomical planes of the endometrial lining is the only instrument for assessment of endometrium adequacy. But there are still limited findings for evaluation of the endometrium in ART. The shear-wave elastography (SWE) technology, as a newly developed elastic imaging technology, can directly reflect the stiffness of the tissue, by quantitatively analyzing the tissue hardness. The shear-wave elastography of the endometrium and myometrium may be a new informative tool for assessment of endometrial receptivity and ART outcome.

MATERIALS AND METHODS: 79 patients undergoing frozen-thawed embryo transfer between 2021-2022 at the Department of Obstetrics and Gynecology, IVF Unit, Izmir Economy University School of Medicine, Medicalpark Hospital, Izmir, Turkey were enrolled. Transabdominal ultrasound examinations of patients on the day of embryo transfer were performed. The shear wave elastography mode was initiated to obtain elastographic values. Corresponding highest endometrial thickness where we aim to transfer the embryo was adjusted, endometrial and myometrial elastography values of the patients. Conducting larger sample size studies will contribute the evidence on SWE technology use in ART.

RESULTS: Using a cut-off for endometrial thickness of 7 mm, there was a trend towards lower clinical pregnancy rates in natural cycle FETs (28%) when compared to programmed cycle FETs (45%). However, this was not statistically significant, likely due to low numbers in each category (25 natural FETs vs 53 programmed FETs). Of note, the clinical pregnancy rate of all programmed cycles (45%) was found to be equivalent to the clinical pregnancy rate of programmed cycles with endometrial linings ≤7mm (45%).

CONCLUSIONS: Deciding to cancel an FET based on endometrial thickness, in patients undergoing a programmed cycle FET is not supported by this current study. Given the trend, it may be appropriate to cancel a patient undergoing a natural cycle FET with a lining of 7mm or less in favor of a programmed cycle. However, further studies will be required to confirm these preliminary findings.

IMPACT STATEMENT: The current study will help in making evidenced-based decisions regarding management of resistant thin endometrial linings, specifically with regards to criteria for cancelling a frozen embryo transfer and choosing the optimal protocol.

P-392 6:45 AM Tuesday, October 25, 2022

SERUM P LEVELS MEASURED ON THE DAY OF EMBRYO TRANSFER IN FRESH IVF CYCLES WITH OWN OOCYTES ARE NOT RELATED TO PREGNANCY OUTCOME. Elena Labarta, MD, PhD,1 Cristina Rodriguez-Varela, M.Sc, Carmen Vidal, MD, PhD,1 Pilar Alama, MD, PhD,1 Jose Beller, MD, PhD,1 Juan Giles, MD, PhD,1 Jakob Pasquale Doblinger, MD,1 Fabio Cruz, MD,1 Alicia Marzal, MD, PhD,1 Inés Olmo, MD, PhD,1 Josep Lluís Romero, MD, Medicine, Stefania Puolli, MD, PhD,1 Jessica Subirá, MD,1 Ernesto Bosch, MD, PhD1 IVIRMA Valencia, Valencia, Spain;2 Biomedical Research Institute La Fe, Valencia, Spain.

OBJECTIVE: To evaluate if there is any correlation between serum progesterone (P4) levels measured on the embryo transfer (ET) day and reproductive outcome in fresh IVF cycles with own oocytes when using vaginal P4 for luteal phase support (LPS).

MATERIALS AND METHODS: Prospective cohort uncenteric study including infertile patients undergoing a fresh ET in day 5 or 6 of development (two blastocysts as maximum), from own oocytes. ETs were performed in the context of a stimulated cycle (ovarian stimulation protocol followed by a single injection of rec-hCG alone). Oocyte pick-up (OPU) took place 36 hours post-triggering, and ET 5/6 days after OPU. Micronized vaginal progesterone (MVP) was used for luteal phase support (200mg/12h), starting in the morning of the day after OPU. In this analysis we have correlated clinical pregnancy rate (CPR) with serum P levels on the ET day, measured within two hours before/ after transfer and after approximately 6 hours from the last insertion of MVP. Results: A total of 223 patients were analyzed. Mean age was 34.6±3.3 years, with a mean BMI of 23.9±4.4 kg/m2 and AMH of 1.96±1.66 ng/mL. On the triggering day the mean follicular count was 11.1±2.7, with a mean leading follicle size of 20.16±4.7 mm. The endometrium displayed a trilaminar pattern, with a mean thickness of 10.09±2.0 mm, and mean P and estradiol (E2) levels were 0.58±0.35 ng/ml and 1720.53±820.49 pg/ml, respectively. A mean of 1.1 blastocysts were transferred (90.7% were single ETs). On the day of ET, the mean serum P and E2 levels were 92.13±47.42 ng/ml and 1146.02±865.84 pg/ml, respectively. A lineal regression model showed that ovarian response was significantly and positively related to serum P4 levels on the ET day (aOR=4.1, 95% CI: 2.8-5.4, p<0.001). The overall CPR was 50.2% (112). CPR according to quartiles of serum P (ng/mL) was 44.4% (Q1, P<0.561), 48.2% (Q2, P=0.56-81.5), 57.1% (Q3, P=0.81-121.8), 51.8% (Q4, P>121.8), p=0.59. Multivariate logistic regression showed that serum P was not related with CPR after adjusting for age, BMI, E2, ovarian response and endometrial quality (aOR=1.0, 95% CI:0.99-1.01, p=0.69).

CONCLUSIONS: Serum P measured on the day of ET is not related with clinical pregnancy outcome when doing a stimulated cycle with vaginal P for luteal phase support. This implies no need to measure P levels in this scenario. E-PAPER ABSTRACT SESSION: When giving LPS with vaginal P in stimulated cycles, the majority of patients achieve adequate levels of serum P. Thus, do not have a significative impact on pregnancy outcome. Ongoing pregnancy and live birth rates should be evaluated in order to assess this impact more accurately. According to our data, there is no need to measure serum P levels on the luteal phase of this type of cycles.
OUTCOMES.

DICTOR OF EUPLOID FROZEN EMBRYO TRANSFER

THE EMBRYO FLASH IS NOT A MEANINGFUL PRE-TRIGGER ON FROZEN EMBRYO TRANSFER OUTCOMES. Ali Borazjani, MD PhD,1 Samad Jahandideh, PhD,2 Shan Dawood, BS,2 Kathleen Devine, MD,2 Michael J. Tucker, PhD3 Northwestern University, Chicago, IL; 1Shady Grove Fertility, Rockville, MD.

OBJECTIVE: Prior studies showed that elevated progesterone (EP) on day of ovulation trigger during controlled ovarian hyperstimulation is associated with decreased pregnancy rates in fresh but not frozen embryo transfers (FET). Although this effect of EP on day of trigger has been established, few studies have investigated the effect that duration of EP has on outcomes. In this study, we aimed to determine the effect of chronic EP (i.e. EP sustained for 1, 2, and 3 days prior to trigger) on clinical pregnancy (CPR) and livebirth rates (LBR) following FET.

MATERIALS AND METHODS: All programmed, autologous FET cycles performed across a multi-region IVF practice in 2019 were evaluated. These data were linked to serum progesterone (P4) levels from corresponding oocyte retrieval cycles. All patients who had P4 levels sampled for at least 2 consecutive days prior to ovulation trigger were included. FET following oocyte cryopreservation, retrievals at outside centers, or cycles with missing data were excluded. Primary and secondary analyses were conducted with thresholds for EP set at >1.5 ng/ml and >2.0 ng/ml, respectively. Univariate and multivariate analyses were performed as appropriate. P < 0.05 was considered statistically significant.

RESULTS: 5340 FET cycles were performed in 2019. Of these, 603 were excluded (criteria above). A total of 4022 FET cycles from 3279 patients had P4 levels sampled daily for ≥2 consecutive days prior to trigger and were included in analyses. The prevalence of EP for 1, 2, and ≥3 days prior to trigger was 38%, 21%, and 12%, respectively. There was no significant difference in CPR or LBR with increasing duration of EP (CPR: 62.3%, 62.9%, and 62.3%, p = 0.95; LBR: 49.9%, 50.1%, and 49.1%, p = 0.94; for 1, 2, and ≥3 days, respectively). Limiting analyses to only cycles where P4 levels were sampled daily for ≥3 days prior to trigger (n = 3170), there was no significant difference in CPR or LBR between those with EP sustained for 3 consecutive days prior to trigger vs those with no EP (CPR: 62.3% vs 58.4%, p = 0.165, LBR: 49.1% vs 47.4%, p = 0.5515; for EP vs no EP, respectively). Similar findings were noted when the threshold for EP was set to >2.0 ng/ml. These findings persisted after considering age, BMI, obstetric history and prenatal genetic testing.

CONCLUSIONS: EP sustained for ≥2 consecutive days prior to trigger affects over 1 in 5 retrieval cycles. However, we found no association between chronic EP and FET outcomes. These results further support the hypothesis that the poorer outcomes observed in fresh transfers following retrieval cycles affected by EP are driven by embryo-endometrium asynchrony rather than decreased embryo quality.

IMPACT STATEMENT: Chronic EP prior to ovulation trigger does not impact CPR or LBR in autologous programmed FET cycles.

SUPPORT: None

REFERENCES: None

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IMPACT OF CHRONIC PROGESTERONE ELEVATION (PRE-TRIGGER) ON FROZEN EMBRYO TRANSFER OUTCOMES. Devika Sachdev, M.D.,1 Leah M. Roberts, M.D.,1 Cheri K. Margolis, M.D.,1 Nola Herlihy, M.D.,1 Amber M. Klimczak, M.D.,2 Pavan Gill, M.D.,2 Enure Seli, M.D.,2 Paul A. Bergh, M.D.,2 Marie D. Werner, M.D.,2 Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ; 1IVIRMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: To evaluate if the presence of the embryo flash on ultrasound at the time of frozen euploid embryo transfer is associated with improved clinical pregnancy rates and subsequent outcomes.

MATERIALS AND METHODS: A retrospective cohort study of ultrasound-guided single euploid frozen embryo transfers at a large fertility center from October 2021 to December 2021 was performed. The embryo flash is a phenomenon whereby a column of air is visualized around the embryo at the time of injection from the catheter tip. The embryo flash was identified by visualizing this phenomenon on a video recording. The sensitivity, specificity, positive and negative likelihood ratios, and the accuracy of using the embryo flash as a test for pregnancy outcomes were analyzed.

RESULTS: In this study, 135 single euploid frozen embryo transfer cycles were analyzed for the presence or absence of a ultrasonographic flash at time of transfer. Primary outcome was defined as a positive pregnancy test (+HCG). Secondary outcomes included the detection of fetal heart tones (FHT) and discharge of a live pregnancy to obstetrical care at 8 weeks (DSCH). The sensitivity, specificity, positive and negative likelihood ratios are presented in the table below which demonstrate that detection of the flash was not a sensitive or specific predictor of outcomes. The likelihood ratios, in addition, suggest that the presence or absence of these outcomes are only minimally increased or decreased by the presence of an embryo flash, respectively.

<table>
<thead>
<tr>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive likelihood ratio</th>
<th>Negative likelihood ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCG 63.28%</td>
<td>44.12%</td>
<td>1.12</td>
<td>0.85</td>
</tr>
<tr>
<td>FHT 63.16%</td>
<td>42.37%</td>
<td>1.10</td>
<td>0.87</td>
</tr>
<tr>
<td>DSCH 66.00%</td>
<td>45.00%</td>
<td>1.19</td>
<td>0.77</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Ultrasound-guided embryo transfers are considered standard of care. However, not all embryo transfers result in a visualization of the embryo flash on ultrasound. The data suggests that the presence of an embryo flash on video is not a meaningful predictor of pregnancy outcomes. Further data and prospective studies are still needed to fully understand the phenomenon of an embryo flash.

IMPACT STATEMENT: Variations in embryo transfer technique have become integral in optimizing clinical pregnancy and live birth outcomes. When assessing for embryo flash at the time of frozen embryo transfers, this marker is neither sensitive nor specific in predicting pregnancies that result in positive beta-hCG, positive FHT, or pregnancy discharges. Given the increasing recognition of the embryo flash on ultrasound-guided embryo transfers and the conflicting results in the literature, this concept needs further exploration.

SUPPORT: None

REFERENCES: None

P-394 6:45 AM Tuesday, October 25, 2022

THE EMBRYO FLASH IS NOT A MEANINGFUL PREDICTOR OF EUPLOID FROZEN EMBRYO TRANSFER OUTCOMES. Ali Borazjani, MD PhD,1 Samad Jahandideh, PhD,2 Shan Dawood, BS,2 Kathleen Devine, MD,2 Michael J. Tucker, PhD3 Northwestern University, Chicago, IL; 1Shady Grove Fertility, Rockville, MD.

OBJECTIVE: To evaluate if the presence of the embryo flash on ultrasound at the time of frozen euploid embryo transfer is associated with improved clinical pregnancy rates and subsequent outcomes.

MATERIALS AND METHODS: A retrospective cohort study of ultrasound-guided single euploid frozen embryo transfers at a large fertility center from October 2021 to December 2021 was performed. The embryo flash is a phenomenon whereby a column of air is visualized around the embryo at the time of injection from the catheter tip. The embryo flash was identified by visualizing this phenomenon on a video recording. The sensitivity, specificity, positive and negative likelihood ratios, and the accuracy of using the embryo flash as a test for pregnancy outcomes were analyzed.

RESULTS: A total of 13,885 vitrified blastocyst transfer cycles were performed during the study period. Of those with a euploid FET, 3307 had an EMT ≥7mm (no prior thin endometrial lining) and 186 had an EMT <7mm. While the LBR after a euploid embryo transfer was significantly lower in those with an EMT <7mm compared to those with an EMT ≥7mm (P = 0.03), it remained high at 49.5% (Table 1). A sub-analysis was performed examining subsequent cycles of those patients who had a transfer cancelled due to a thin endometrial lining. There was no significant difference in LBR of euploid embryo transfers in cycles with a subsequent EMT ≥7mm compared to those that remained <7mm.

CONCLUSIONS: Ultrasound-guided embryo transfers are considered standard of care. However, not all embryo transfers result in a visualization of the embryo flash on ultrasound. The data suggests that the presence of an embryo flash on video is not a meaningful predictor of pregnancy outcomes. Further data and prospective studies are still needed to fully understand the phenomenon of an embryo flash.

IMPACT STATEMENT: Variations in embryo transfer technique have become integral in optimizing clinical pregnancy and live birth outcomes. When assessing for embryo flash at the time of frozen embryo transfers, this marker is neither sensitive nor specific in predicting pregnancies that result in positive beta-hCG, positive FHT, or pregnancy discharges. Given the increasing recognition of the embryo flash on ultrasound-guided embryo transfers and the conflicting results in the literature, this concept needs further exploration.

SUPPORT: None

REFERENCES: None
CONCLUSIONS: Achieving an EMT ≥7mm may not be feasible in all patients. In single euploid FETs, the LBR of 49.5% in patients with an EMT <7mm is reassuring and demonstrates that a transfer rather than cycle cancellation should be strongly considered given the potential impact of cycle cancellation. Achieving a subsequent EMT ≥7mm, in patients who previously had a thin lining did not appear to improve the LBR and was comparable to those who had a euploid embryo transfer with an EMT <7mm. This indicates that delaying a transfer to achieve a lining ≥7mm may not be necessary and may lead to delays without improving the chance of a live birth.

IMPACT STATEMENT: The LBR in patients with an EMT <7mm is reassuring and achieving a subsequent thicker lining did not increase LBR more than having a thin lining.

SUPPORT: None

Table 1: LBR in patients who underwent a euploid embryo transfer according to EMT

<table>
<thead>
<tr>
<th>EMT (mm)</th>
<th>Count</th>
<th>Live birth</th>
<th>LBR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (&lt;7)</td>
<td>186</td>
<td>92</td>
<td>49.5</td>
</tr>
<tr>
<td>3-4.9</td>
<td>7</td>
<td>4</td>
<td>57.1</td>
</tr>
<tr>
<td>5-5.9</td>
<td>27</td>
<td>14</td>
<td>51.9</td>
</tr>
<tr>
<td>6-6.9</td>
<td>152</td>
<td>74</td>
<td>48.7</td>
</tr>
<tr>
<td>Subsequent cycle ≥7</td>
<td>158</td>
<td>85</td>
<td>53.8</td>
</tr>
<tr>
<td>Subsequent cycle &lt;7</td>
<td>38</td>
<td>20</td>
<td>52.6</td>
</tr>
<tr>
<td>≥7 (no prior thin lining)</td>
<td>3307</td>
<td>1914</td>
<td>57.9</td>
</tr>
</tbody>
</table>

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TRANSDERMAL VERSUS ORAL ESTROGEN IN ENDOMETRIAL PREPARATION FOR FROZEN THAWED EMBRYO TRANSFER CYCLES. Cristiano Eduardo Busso, Sr., Phd.1 Mariana Cassara, MD,2 Claudia G. Glin, MD,1 Rodrigo Romano, M.D.,1 Leopoldo Tso, MD,1 Sidney Glin, M.D.,1 Newton Busso, M.D., Ph.D.1 Sonia Maria Maria Rolim Rosa Lima, M.D., Ph.D.1 1Projeto ALFA/BETA, São Paulo, Brazil; 2Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil; 3Projeto Alfa, São Paulo, Brazil.

OBJECTIVE: To compare the clinical outcome of two methods of endometrial preparation in frozen-thawed embryo transfer (FET) cycles: Estradiol hemihydrate transdermal gel and oral estradiol. MATERIALS AND METHODS: A total of 88 patients undergoing frozen-thawed blastocyst transfer (1 or 2 embryos) were randomized; 82 patients completed the study protocol. 44 received oral estrogen tablets (oral group) and 38 received transdermal gel (gel group). The primary end-points were pregnancy rates (biochemical) and ongoing pregnancy rates, endometrial thickness, plasma levels of estradiol, duration of estradiol administration and cycle cancellation rates between groups. Side effects were significantly lower (10.5% vs 34.1%, p: 0.017), in the gel group compared to the oral group. CONCLUSIONS: No significant differences were found in clinical outcomes between estradiol hemihydrate transdermal gel and oral estradiol in patients undergoing FET cycles. IMPACT STATEMENT: Transdermal estradiol is as efficacious as oral estradiol in FET cycles having an extra benefit of less side effects. SUPPORT: None

Table: Outcomes of FET cycles

<table>
<thead>
<tr>
<th>Transdermal Group</th>
<th>Oral Group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD / n (%)</td>
<td>Mean ± SD / n (%)</td>
<td></td>
</tr>
<tr>
<td>Duration of E2 administration (days)</td>
<td>14.86±2.37</td>
<td>14.43±1.56</td>
</tr>
<tr>
<td>Kg of embryos transferred</td>
<td>1.71±0.46</td>
<td>1.74±0.45</td>
</tr>
<tr>
<td>E2 value on the 7th and 10th day of the cycle</td>
<td>275.79 ± 193.40</td>
<td>224.57 ± 83.24</td>
</tr>
<tr>
<td>At least one embryo top-quality transferred</td>
<td>6/35 (17.1%)</td>
<td>6/42 (14.3%)</td>
</tr>
<tr>
<td>Cycle cancellation per started cycle</td>
<td>3/38 (7.9%)</td>
<td>2/44 (4.5%)</td>
</tr>
<tr>
<td>Clinical pregnancy per started cycle</td>
<td>18/38 (47.4%)</td>
<td>28/44 (63.6%)</td>
</tr>
<tr>
<td>Clinical pregnancy per started cycle</td>
<td>16/38 (42.1%)</td>
<td>21/44 (47.7%)</td>
</tr>
<tr>
<td>Clinical abortion / per clinical pregnancy</td>
<td>5/16 (31.3%)</td>
<td>5/21 (23.8%)</td>
</tr>
<tr>
<td>Side Effects</td>
<td>4/38 (10.5%)</td>
<td>15/44 (34.1%)</td>
</tr>
<tr>
<td>Headache</td>
<td>1/38 (2.6%)</td>
<td>8/44 (18.2%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>0</td>
<td>5/44 (11.4%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>1/38 (2.6%)</td>
<td>1/44 (2.3%)</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>1/38 (2.6%)</td>
<td>1/44 (2.3%)</td>
</tr>
<tr>
<td>Others</td>
<td>1/38 (2.6%)</td>
<td>3/44 (6.8%)</td>
</tr>
</tbody>
</table>

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THE TIMING OF PROGESTERONE CORRECTED AFTER ENDOMETRIAL TRANSCRIPTOMIC ANALYSIS DOES NOT IMPROVE REPRODUCTIVE OUTCOME IN WOMEN WITH ADENOMYOSIS AND NON-RECEPTIVE ENDOMETRIUM. Mauro Cozzolino, MD,1 Elena Juárez-Barber, MS,2 Ana Corachán, PhD,3 Diana Alecsandru, MD, Ph.D., Antonio Pelllicer, M.D.3 Hertensia Ferrero, PhD1 IVIIRMA-Rome, Rome, Italy; 2IIS La Fe - IVI Foundation, Spain; 3IVI Foundation - University of Valencia, Valencia, Spain; 4IVI Madrid-IVI Foundation, Health Research Institute La Fe, Valencia, Spain; 5Instituto Valenciano Infertilidad (IVI), Rome, Italy; 6Fundación Investigación Hosp. La Fe/ Fundación IVI, Valencia, Valencia, Spain.

OBJECTIVE: To analyze if endometrial mid-secretory phase transcriptome is altered in women with adenomyosis, as well as to evaluate if the timing of progesterone administration after transcriptomic analysis improves clinical IVF outcomes in these women. MATERIALS AND METHODS: A retrospective study was conducted on adenomyosis (n=81) and non-disease (n=231) patients (Age ≤45, BMI<28) who underwent transcriptomic analysis. Adenomyosis was diagnosed using magnetic resonance image or ultrasound. The impact of transcriptomic analysis on IVF outcomes in women with adenomyosis was studied comparing adenomyosis patients who underwent this test (n=59) versus those without test (n=66) after one previous failed embryo transfer (ET). Implantation rate per ET, biochemical and clinical miscarriage and live-birth rates per implanted embryo were considered primary outcomes.

RESULTS: A significantly altered endometrial mid-secretory phase transcriptome (non-receptive) was observed in adenomyosis [56.1% (43/81)] compared to non-disease patients [37.2% (86/231)] (p=0.0179). Adenomyosis patients had a relative risk of non-receptive endometrium 42.6% higher compared to non-disease (95%CI 41.5-44.5). However, no statistically significant differences were found in adenomyosis patients underwent transcriptomic analysis compared to patients without this analysis in terms of implantation rate [62.7% (17/41) vs 78.8% (52/66); p=0.0514], biochemical [13.5% (5/37) vs 3.9% (2/52); p=0.1223] and clinical miscarriage [10.8% (4/37) vs 15.4% (8/52); p=0.7543] and live-birth rates [75.7% (28/37) vs 80.8% (42/52); p=0.6066].

VALUES OF P<0.05 ARE CONSIDERED STATISTICALLY SIGNIFICANT. THE TIMING OF PROGESTERONE CORRECTED AFTER ENDOMETRIAL TRANSCRIPTOMIC ANALYSIS DOES NOT IMPROVE REPRODUCTIVE OUTCOME IN WOMEN WITH ADENOMYOSIS AND NON-RECEPTIVE ENDOMETRIUM.
CONCLUSIONS: Women with adenomyosis showed an altered expression of genes involved in endometrial decidualization, with a higher rate of non-receptive endometrium than control. Progesterone timing based on the transcriptomic analysis does not improve IVF outcomes in women with adenomyosis. Although progesterone is the essential hormone for implantation and pregnancy, its timing administration by endometrial transcriptomic signature does not improve IVF outcomes in patients with adenomyosis. Therefore, other molecular mechanisms may be involved in implantation failure in women with adenomyosis.

IMPACT STATEMENT: The time of progesterone administration based on endometrial transcriptomic analysis does not improve IVF outcomes in women with adenomyosis. Our findings open insights into the importance of studying other molecular mechanisms that could be affecting endometrial decidualization in adenomyosis.

MC & EJ-B contributed equally.


Table 1. Primary Parameters of the In Vitro Fertilization Patients Before and After COVID-19

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>N</th>
<th>Std. Dev.</th>
<th>Std. Err. Mean</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>T.OOCYTE QTY.</td>
<td>10.5556</td>
<td>9</td>
<td>5.59265</td>
<td>1.86422</td>
<td>0.250a</td>
</tr>
<tr>
<td>T.OOCYTE QTY.</td>
<td>8.6667</td>
<td>9</td>
<td>5.59017</td>
<td>1.86339</td>
<td></td>
</tr>
<tr>
<td>M2 OOCYTE QTY.</td>
<td>6.0000</td>
<td>9</td>
<td>4.00000</td>
<td>1.33333</td>
<td>0.738a</td>
</tr>
<tr>
<td>M2 OOCYTE QTY.</td>
<td>5.4444</td>
<td>9</td>
<td>4.53076</td>
<td>1.51025</td>
<td></td>
</tr>
<tr>
<td>Deg. OOCYTE QTY.</td>
<td>1.0000</td>
<td>9</td>
<td>2.64575</td>
<td>.88192</td>
<td>0.705b</td>
</tr>
<tr>
<td>Deg. OOCYTE QTY.</td>
<td>.3333</td>
<td>9</td>
<td>.50000</td>
<td>.16667</td>
<td></td>
</tr>
<tr>
<td>GV QTY.</td>
<td>1.4444</td>
<td>9</td>
<td>1.58990</td>
<td>.52997</td>
<td>1.000b</td>
</tr>
<tr>
<td>GV QTY.</td>
<td>1.4444</td>
<td>9</td>
<td>1.74005</td>
<td>.58002</td>
<td></td>
</tr>
<tr>
<td>DEG. / TOTAL</td>
<td>.0489</td>
<td>9</td>
<td>.11963</td>
<td>.03988</td>
<td>1.000b</td>
</tr>
<tr>
<td>DEG. / TOTAL</td>
<td>.0700</td>
<td>9</td>
<td>.16371</td>
<td>.05457</td>
<td></td>
</tr>
<tr>
<td>M2/TOTAL</td>
<td>.6033</td>
<td>9</td>
<td>.26249</td>
<td>.08750</td>
<td>0.198a</td>
</tr>
<tr>
<td>M2/TOTAL</td>
<td>.7600</td>
<td>9</td>
<td>.20821</td>
<td>.06940</td>
<td></td>
</tr>
</tbody>
</table>

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IMPACT OF MATERNAL RACE AND ETHNICITY ON PREGNANCY OUTCOMES IN INFERTILE WOMEN WITH AND WITHOUT POLYCYSTIC OVARY SYNDROME (PCOS) UNDERGOING IN VITRO FERTILIZATION (IVF) IN THE UNITED STATES (US).

OBJECTIVE: The primary objective was to compare IVF live birth rates in White (W), Asian (A), Hispanic (H) and African American (AA) women with and without PCOS in the US.

MATERIALS AND METHODS: This is a retrospective study using a large de-identified cohort from the SART-CORS database. It includes 256,018 patient records from 2014-2017, and 128,703 met our study inclusion criteria, which were women 21-40 years of age, who were undergoing their first non-donor fresh IVF cycle. PCOS was defined as oligo-anovulation (<6 cycles/year) and polycystic appearing ovaries. Controls were non-PCOS patients with other causes of infertility. Race and ethnicity were self-reported by patients. Logistic regression models were used to calculate the primary outcome, live birth rate, and other secondary outcomes. These models examined race per PCOS patient, adjusting for patient’s age, BMI, smoking status, and number of embryos transferred. Two-way ANOVA was used to compare continuous variables and Chi-square for categorical variables. A p-value <0.05 was considered statistically significant.

RESULTS: There were 21,866 women in the PCOS group and 106,837 without PCOS. The live birth rate in the PCOS group was highest in W women (49.5%) compared to H (42.7%), A (41.6%), and AA (36%) women (p<0.001 testing equality of all groups). The live birth rate in the non-PCOS group was highest in W (45.1%), compared to H (40.5%), A (35.4%), and AA (34.3%) women (p<0.001). The pregnancy loss rate in PCOS was highest in AA (19.5%), followed by H (15.3%), A (8.8%) and W (8.2%) women (p<0.001). Similarly, in non-PCOS the
pregnancy loss rate was highest in AA (13.4%), compared to A (10.1%), H (9.4%) and W (9.3%) women (p<0.001). The neonatal death rate in the PCOS group was highest in H (3.9%), followed by AA (3.6%), A (1.5%) and W (1.1%) women (p< 0.001). In the non-PCOS group, the neonatal death rate was highest in AA (2.3%), compared to H (1.5%), W (0.8%), and A (0.6%) women (p<0.001). There were no significant differences for congenital defects between races and ethnicity in the PCOS (W 0.6%, H 0.6%, A 0.1%, AA 0.0%; p=0.192) and non-PCOS (W 0.5%, H 0.6%, A 0.5%, AA 0.7%; p=0.646) groups.

CONCLUSIONS: Live birth rate was significantly decreased in AA, H and A women with and without PCOS, when compared to W women. In addition, the pregnancy loss rate was significantly increased in AA women with and without PCOS compared to W, A and H women. The neonatal death rate was significantly increased in AA and H women with and without PCOS compared to W and A women.

IMPACT STATEMENT: This is the largest IVF study to date assessing the impact of maternal race and ethnicity on pregnancy and neonatal outcomes in infertile women with and without PCOS in the US. Our data suggest that there are significant racial and ethnic outcome disparities in infertile women undergoing IVF in the US. Further large prospective studies are urgently needed to confirm our study findings.

SUPPORT: None

**Predictive variables of Live Birth**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.95 (0.93-0.98)</td>
<td>0.94 (0.92-0.97)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.99 (0.98-1.01)</td>
<td>0.98 (0.97-1.01)</td>
</tr>
<tr>
<td>PGT</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>1.41 (1.17-1.70)</td>
<td>1.52 (1.23-1.87)</td>
</tr>
<tr>
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<td>1</td>
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<tr>
<td>LH on day of surge (IU/L)</td>
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</tr>
<tr>
<td>&lt;15</td>
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<td>1</td>
</tr>
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<td>15.1-19.9</td>
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<td>1.77 (0.50-6.21)</td>
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<td>≥30</td>
<td>1.10 (0.38-3.19)</td>
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<td>1</td>
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<td>1</td>
</tr>
<tr>
<td>0.1-10%</td>
<td>1.01 (0.71-1.43)</td>
<td>1.08 (0.74-1.58)</td>
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<td>10.1-19.9%</td>
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<td>0.92 (0.64-1.33)</td>
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<tr>
<td>≥20%</td>
<td>1.00 (0.82-1.21)</td>
<td>1.08 (0.86-1.36)</td>
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<td>&lt;1.0</td>
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<td>1-1.4</td>
<td>0.96 (0.79-1.16)</td>
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<td>1.5-1.9</td>
<td>1.07 (0.74-1.53)</td>
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<td>≥2</td>
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<td>1.16 (0.53-2.55)</td>
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<td>P4 rise</td>
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<td>1</td>
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<tr>
<td>No</td>
<td>0.87 (0.58-1.35)</td>
<td>0.119 (0.59-1.44)</td>
</tr>
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</table>

**DAY OF SURGE HORMONAL PARAMETERS AS PREDICTORS OF OUTCOME IN NATURAL FROZEN-THAWED EMBRYO TRANSFER (FET) CYCLES – THE WINDOW OF IMPLANTATION IS WIDE.** Katherine Koniares, MD,1 Daniel R. Grow, MD, MHCM,2 John Nulsen, MD,3 Claudio A. Benadiva, MD, HCLD,4 Lawrence Engmann, MD5 University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT; 5Center for Advanced Reproductive Services, University of Connecticut School of Medicine, Farmington, CT.

OBJECTIVE: The criteria for determining the timing of frozen-thawed embryo transfer (FET) in natural cycles is conflicting. The objective of this study was to determine which criteria used to determine the day of lutetizing hormone (LH) surge is predictive of live birth in natural cycle FET.

MATERIALS AND METHODS: This retrospective study included 2,236 natural cycle blastocyst FETs (including 718 PGT cycles) in women aged 18 - 42 years performed from 1/2007 - 2/2022. The day of surge was considered the day with the highest serum LH level regardless of estradiol (E2) decline or progesterone (P) rise. Alternatively, the day of surge was identified as the day before E2 decline and/or P rise regardless of LH level. Vaginal P was started 2 days after the day of surge and blastocyst transfer was performed 6 days after the day of surge. We evaluated the predictive probability of live birth based on the day of surge serum LH, percent change in E2 (% E2 decline), P on day of surge and P rise as categorized in the Table. LH and P on the day of surge were categorized into 4 groups (see Table). The % E2 decline from 1 day prior to the day of surge was categorized into 4 groups (see Table). The presence of a P rise on the day of surge was categorized binomially. A binary logistic regression was used to assess the predictive probability of day of surge parameters for live birth whilst controlling for potential covariates.

RESULTS: There were no differences in mean age and BMI between the 4 LH categories. The lowest day of surge LH that resulted in a live birth was 10.5 IU/L. None of the day of surge hormonal parameters were predictive of live birth in the overall group or when the data was limited to only PGT cycles.

CONCLUSIONS: This is the largest study, to date, to evaluate predictive value of live birth based on criteria for determining day of surge in natural cycle FET. We demonstrated that none of the hormonal parameters on the day of surge were predictive of live birth.

IMPACT STATEMENT: The criteria for determining day of surge and timing of embryo transfer is flexible.

REFERENCES:
P-401 6:45 AM Tuesday, October 25, 2022
PREGNANCY COMPLICATIONS AND PLACENTAL HISTOLOGY IN IN-VITRO FERTILIZATION PREGNANCIES WITH INITIAL LOW SERUM B-HCG LEVELS. Hadas Ganer Herman, MD, Alexander Volodarsky-Perel, M.D., Tuyet Nhung Ton Nu, MD, Alexandre Machado-Gedeon, MD, Yiming Cui, MD, Jonathan Shaul, MD, Michael H. Dahan, M.D. McGill University Health Centre, Montreal, Canada.

OBJECTIVE: To assess perinatal outcomes and placental findings following in vitro fertilization (IVF) with an initial low serum β-human chorionic gonadotropin (HCG).

MATERIALS AND METHODS: This was a historic cohort of live singleton deliveries after IVF at a single university medical center between 2009 and 2017. Included were pregnancies following IVF, while oocyte recipients were excluded. Perinatal outcomes and placental findings were compared between patients for whom day 16 embryo age β-HCG following transfer was low, defined as the lower 10th percentile for the cohort (low β-HCG group), and patients with an initial β-HCG above the lower 10th percentile (control group). Placental examination was performed for all deliveries irrelevant of complication status. Placental pathologic findings were categorized according to the Amsterdam Placental Workshop Group Consensus. Outcomes were placental findings, including anatomic, inflammatory, vascular malperfusion and villous maturation lesions and obstetric and perinatal complications. Continuous and categorical variables were compared as appropriate, and multivariate regression analysis employed to control for confounders. Data is presented as mean±SD or n (%) as appropriate.

RESULTS: The lower 10th percentile of β-HCG results corresponded to 149 mIU/mL. There were 103 cases in the low β-HCG group, and 928 in the control group. Maternal demographics were similar between the groups, while blastocyte transfer was more common in the control group. Deliveries in the low β-HCG group were associated with an increased rate of preterm births, 15.5% vs. 8.1%, p=0.01, which maintained significance after adjustment for blastocyte transfer. Placentas in the low β-HCG group were notable for a higher rate of velamentous cord insertion, 19.4% vs. 7.7%, p<0.001, and single umbilical artery 3.8% vs. 0.6%, p=0.01.

CONCLUSIONS: Live births following IVF with an initial low b-HCG level are associated with a two-fold increase in preterm births, and placentar gross and histological changes.

IMPACT STATEMENT: The correlation between initial low b-HCG and pregnancy viability is much established, yet less so regarding outcomes in viable pregnancies. Our findings point to a significantly higher risk of preterm birth and placental pathology in IVF pregnancies with an initial low β-HCG. It may thus be considered to follow such cases in a high-risk pregnancy setting.

P-402 6:45 AM Tuesday, October 25, 2022
THE EFFECT OF HIGHER ESTRADIOL LEVELS DURING STIMULATION ON PREGNANCY COMPLICATIONS AND PLACENTAL HISTOLOGY. Hadas Ganer Herman, MD, Alexander Volodarsky-Perel, M.D., Tuyet Nhung Ton Nu, MD, Alexandre Machado-Gedeon, MD, Yiming Cui, MD, Jonathan Shaul, MD, Michael H. Dahan, M.D. McGill University Health Centre, Montreal, Canada.

OBJECTIVE: We aimed to assess obstetric outcomes and placental histology in stimulated in vitro fertilization (IVF) cycles with a higher serum estradiol level.

MATERIALS AND METHODS: This was a retrospective cohort of live singleton deliveries after IVF at a single university medical center between 2009 and 2017. Included were pregnancies following controlled ovarian stimulation with fresh embryo transfer. Excluded were IVF cycles with oocyte recipients and with a diagnosis of diminished ovarian reserve. High estradiol was defined as peak value above the upper quartile for the cohort, corresponding to 8700 pg/mL. We compared perinatal outcomes and placental histology in pregnancies following stimulation with higher estradiol and controls (lower estradiol). Placental examination was performed for all deliveries irrelevant of complication status. Placental pathologic findings were categorized according to the Amsterdam Placental Workshop Group Consensus. Outcomes were placental findings, including anatomic, inflammatory, vascular malperfusion and villous maturation lesions and obstetric and perinatal outcomes. Continuous and categorical variables were compared as appropriate, and multivariate regression analysis employed to control for confounders. Data is presented as mean±5D or n (%) as appropriate.

RESULTS: Overall, 147 deliveries in the higher estradiol group were compared to 427 deliveries in the control group. No differences were demonstrated in patient demographics and infertility workup, except for a significantly higher antral follicle count in the high estradiol group, 21.5±13.1 vs. 17.3±10.7 follicles, p<0.001 and lower rate of single embryo transfer, 51.7% vs. 73.5%, p<0.001. No differences were demonstrated between the groups in pregnancy and obstetric outcomes investigated, including gestational age, preterm delivery, preeclampsia, cesarean delivery, birth weight and low birth weight. Placental histological examination was notable for a higher rate of velamentous cord insertion in the higher estradiol group, 12.2% vs. 6.7%, p=0.03, more so in a sub analysis of cases of very high estradiol 15.7% vs. 7.3%, p=0.02.

CONCLUSIONS: Placental histology following IVF with high estradiol level was notable for a higher rate of velamentous cord insertion.

IMPACT STATEMENT: High estradiol levels are associated with an increased rate of velamentous cord insertion, which has been correlated to adverse neonatal outcomes in published studies. Otherwise, serum estradiol levels do not seem to alter placental pathology in additional significant ways. Freezing all embryos and subsequently transferring a frozen thawed embryo could maximize maternal fetal safety, but needs confirmatory data.

P-403 6:45 AM Tuesday, October 25, 2022
THROMBIN PRODUCTION VARIES ACROSS AN IVF CYCLE AND A SIGNIFICANT DIFFERENCE IS NOTED WITH WOMEN WHO CONCEIVE VERSUS THOSE WHO DO NOT. Carleigh B. Nesbit, DO,1 Tia Y. Brodeur, MD, PhD,1 Thomas Orfeo, PhD,2 Elizabeth A. McGee, MD MBA,1 Ira Bernstein, MD,1 Maria Cristina Bravo, PhD 1University of Vermont Medical Center, Burlington, VT; 2University of Vermont, Burlington, VT.

OBJECTIVE: To measure thrombin generation across time points of in vitro fertilization (IVF) and to investigate differences between women who do and do not conceive.

MATERIALS AND METHODS: A subgroup analysis from a prospective IRB-approved study of hemostatic balance was performed. Samples were collected at four timepoints: during the follicular phase prior to IVF; prior to starting gonadotropins, 30-90 minutes prior to oocyte retrieval, and 14 days after oocyte retrieval. Using a standardized protocol to measure prothrombotic potential, coagulation was initiated using exogenous tissue factor (TF) and peak thrombin generation was determined. Additional measures were performed in the presence of 10nM soluble thrombomodulin (TM) to initiate the inhibitory protein C pathway (TF + TM). A ratio ([TF+TM]/ TF) was calculated to estimate the relative potency of this inhibitory pathway. Statistical analyses were performed using two-sample t-tests and repeated measures analyses to assess the main effects of group and time and their interaction effect adjusting for age and BMI. Significant interactions were followed with an examination of the simple effects of group and time. Data were presented as mean± standard deviation with a significance threshold of p<0.05.

RESULTS: In the baseline at early follicular phase, the mean estradiol (E2) level was 79±67 pg/mL (n=16). Levels were suppressed (17±6 pg/mL) prior to initiation of gonadotropins and then rose (1340±385 pg/mL) at the time of oocyte retrieval. For women who conceived (n=10), E2 levels remained elevated 14 days after oocyte retrieval (1497±329 pg/mL) but began to decline in those who did not (1077±344 pg/mL). In all women, peak thrombin generation increased between the baseline follicular phase and initiation of gonadotropins by 20-40% (p<0.05 for all measures). Further rise was seen at the time of oocyte retrieval by 10-25% (p<0.05 for all measures). Fourteen days status post oocyte retrieval, thrombin generation in women who did not conceive had returned to baseline but remained elevated above baseline in those who conceived. Overall, there was a significant interaction (p<0.05) of conception outcome and time for the two experimental conditions. Women who conceived via IVF during the study had a lower TF peak at baseline than those who did not (209±46 nM vs 301±70 nM, p<0.05) but there were no other statistically significant differences in any of the experimental conditions between groups at any other time point.
CONCLUSIONS: In a small cohort of women undergoing IVF, estradiol generation increased during the IVF cycle in association with rising E2 levels and remained elevated above baseline in those who conceived. Those who conceived had lower baseline estradiol generation compared with those who did not.

IMPACT STATEMENT: This study provides information regarding estradiol generation throughout the IVF cycle and in early pregnancy including novel information on estradiol generation in the setting of preparations utilizing thrombomodulin. Data collection remains ongoing which will allow for future reports in larger samples of women undergoing IVF.

SUPPORT: Support for this work was provided by National Institute of Health (NHLBI) R33HL141797-04 and the Mead Foundation.

P-404 6:45 AM Tuesday, October 25, 2022
HIGH FOLLICLE STIMULATING HORMONE (FSH) LEVEL ON THE DAY OF TRIGGER IMPACTS NEGATIVELY THE EUPLOIDY RATE OF BLASTOCYSTS. Raquel Del Gallego, PhD,1 Lawrence Barbara, M.D., PhD,2 Rachana Patel, PhD,2 Laura Melado, M.D., PhD,1 Ibrahim El-Habib, M.Sc.,1 Asina Bayram, M.Sc.,1 Andrea Abdal, M.Sc.,1 Ahmed El-Damen, M.Sc.,1 Human M. M. Fatemi, M.D., PhD Prof.1 1ART Fertility Clinics, Abu Dhabi, United Arab Emirates; 2ART Fertility Clinics, Gurgaon, India; 3ART Fertility Clinics, Abu Dhabi, Abu Dhabi, United Arab Emirates.

OBJECTIVE: To evaluate, in ovarian stimulation cycles for IVF/ICSI, the impact of the systemic FSH level on the Day of Trigger (DoT) on the ploidy rate of the blastocyst cohort.

MATERIALS AND METHODS: Single center retrospective study performed between March 2017 and December 2020. All patients underwent ovarian stimulation in a gonadotropin releasing hormone (GnRH) antagonist protocol with recombinant FSH due to primary or secondary infertility. Cycles were monitored, according to clinical routine, by ultrasound and repeated measurement of FSH, luteinizing hormone (LH), estradiol and progesterone. All blastocysts underwent preimplantation genetic testing for aneuploidies (PGT-A) by next generation sequencing (NGS) with trophectoderm biopsy. Patients with polycystic ovary syndrome (PCOS), surgical sperm extraction and warmed oocytes cycles were excluded. Univariate and multivariate-adjusted logistical regression analysis were performed to determine the association between euploid rate and the parameters: age, body mass index (BMI), anti-Müllerian hormone (AMH), antil follicle count (AFC), baseline and DoT reproductive hormones, stimulation duration, starting and total gonadotropin dose and type of ovulation induction.

RESULTS: A total of 2,724 biopsied blastocysts from 427 patients were included into this analysis. Systemic FSH levels at DoT revealed a wide range of values, from 5.39 to 47.11 IU/L. Patients had an average age (<b>15.70</b> ± 2.78 years, BMI of 22.42 ± 5.12 kg/m², AMH of 3.12 ± 1.58 ng/ml and AFC of 15.92 ± 6.10. Mean number of collected oocytes per cycle were 15.70 ± 6.83. The univariate analysis showed a significant positive correlation of the euploid rate with AFC (β = 0.137, p < 0.01) and a significant negative correlation with age (β = -0.200, p < 0.001), FSH at DoT (β = -0.157, p < 0.005), gonadotropin starting and total dose (β = -0.128, p < 0.05 and β = -0.117, p < 0.05) and FSH at baseline (β = -0.122, p < 0.05). When the multivariate analysis was performed, FSH at DoT and age were the only covariates maintaining a significant negative correlation with ploidy (β = -0.139, p < 0.05 and β = -0.186, p < 0.01).

CONCLUSIONS: Additionally, systemic high FSH levels at DoT were significantly correlated to lower euploid rates in IVF/ICSI cycles. This accen- tuates the importance of individualizing ovarian stimulation treatment based on patient characteristics by selecting adequate starting doses and continuous monitoring of the stimulation for dose adjustments.

IMPACT STATEMENT: The findings emphasize the need of treatment individualization by analyzing systemic FSH levels during ovarian stimulation, as a predictor of euploidy at the blastocyst stage, to achieve precision medicine practice.

P-406 6:45 AM Tuesday, October 25, 2022
DON’T BE TRIGGER SHY: A LOW SERUM LUTEINIZING HORMONE (LH) RESPONSE TO GONADOTROPIN-RELEASELING HORMONE AGONIST (GNRHa) HITS THE MARK IN PRE-IMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A). Julia Buldo-Licciardi, M.D.,1 Ashley M. Willshire, M.D.,2 Jessica N. Tozour, MD,3 Dina Hamer, BA,4 David H. Mc Culloh, PhD,3 James A. Grifo, MD, PhD,6 Jennifer K. Blakemore, MD, MSc7 1New York University Grossman School of Medicine, New York, NY; 2New York University, New York, NY; 3NYU Langone - Long Island Hospital, Mineola, NY; 4NYU Grossman School of Medicine, Manhattan, NY; 5NYU Langone Health, New York, NY; 6NYU Langone Fertility Center, New York, NY; 7NYU Langone Fertility Center, New York, NY.

OBJECTIVE: The use of GnRH-a trigger in antagonist controlled ovarian hyperstimulation (COH) cycles has increased due to its enhanced safety profile. However, response, as measured by the serum LH level post trigger, vary considerably.1-6 We investigated the impact of serum LH response to GnRH-a trigger in antagonist COH cycles on oocyte yield, oocyte maturity, blasto- cyst formation, PGT-A and pregnancy outcomes.

MATERIALS AND METHODS: This is a retrospective cohort study in a single university-based fertility center of all GnRH-antagonist COH cycles utilizing GnRH-a alone or in combination with 1000u of human choric gonadotropin (hCG) for trigger from 2017 to 2020. An optimal response to GnRH-a trigger was defined as LH ≥ 40 mIU/mL and suboptimal response

P-405 6:45 AM Tuesday, October 25, 2022
GONADOTROPIN BOOST ADMINISTRATION WITH OVULATORY TRIGGER IMPROVES IN VITRO FERTILIZATION CYCLE OUTCOMES IN THE SETTING OF ESTRADIOL PLATEAU. Charlene G. Echague, D.O.,1 Samad Jahandideh, PhD,2 Kathleen Devine, MD,2 Phillip A. Romanski, MD, MSc1 1Gaithersburg, MD; 2Shady Grove Fertility, Washington D.C., DC; 3Shady Grove Fertility, New York, NY.

OBJECTIVE: To evaluate whether the addition of a gonadotropin boost to the ovulatory trigger improves oocyte maturity and embryo development outcomes among patients with an estradiol plateau or decrease on the hCG ovulatory trigger day.

MATERIALS AND METHODS: All patients undergoing IVF/ICSI who experienced either a plateau or decline in estradiol levels on the ovulatory trigger day, defined as a less than 20% increase from the prior day, between 2010 and 2020 at a multicenter infertility practice were included. Cycle protocol and dose of gonadotropin boost were at the discretion of the physician. Patients that received a Lupon trigger and cycles that were cancelled prior to oocyte retrieval were excluded. Patient demographics, baseline characteristics, and cycle characteristics were recorded. The primary outcome of fertilization rate and secondary outcomes of oocyte maturity rate and usable embryo rate were compared between patients receiving a gonadotropin boost and those who did not. Generalized estimating equations were used to calculate rate ratio (RR) and 95% confidence intervals (CI), adjusting for priori for age (all outcomes) and use of ICSI (post-insemination outcomes).

RESULTS: A total of 10275 cycles were included of which 3849 received a gonadotropin boost on day of hCG trigger. Oocyte maturity rate was compar- ison between those who received a gonadotropin boost and those who did not (RR 0.99, CI 0.97 – 1.00). However, fertilization rate was improved after receiving a gonadotropin boost (68.26% vs 66.19%, RR 1.03, CI 1.01 – 1.05). Additionally, the usable embryo rate was also improved in patients who received a gonadotropin boost on the day of hCG trigger (49.15% vs 46.73%, RR 1.05, CI 1.02 – 1.08).

CONCLUSIONS: In addition to a surge in luteinizing hormone, natural ovulation involves an increase in follicle stimulating hormone (FSH). The role of the FSH surge has been presumed to promote an optimal environment for nuclear and cytoplasmatic maturation of the oocyte. An estradiol plateau or decline during ovarian stimulation suggests insufficient gonadotropin levels to stimulate the developing follicules and thus this patient cohort may be the most vulnerable to insufficient FSH levels at the time of hCG-only ovulatory trigger. Based on our findings, while the oocyte maturity rate was comparable between those who received a gonadotropin boost on the day of hCG trigger and those who did not, a significantly improved pregnancy rate was seen in both fertilization and usable embryo rates after adjusting for age and utilization of ICSI.

IMPACT STATEMENT: Cycles with a plateau or decrease in estradiol levels on the day of hCG ovulatory trigger may benefit from administration of a gonadotropin boost, specifically to improve fertilization and usable embryo rates. However, the results of this study suggest that improvement is minimal best and must be balanced with the cost to the patient of recommending an additional gonadotropin dose.

SUPPORT: None.
RESULTS: This study included 3,833 retrieval cycles with 1,435 single thawed euploid embryo transfers (STEET) among 2,618 patients. Ten percent (351/3,446) of retrieval cycles had suboptimally and 90% (3,446/3,833) had optimal response to GnRH-a trigger. There was no difference in median oocyte yield (16 vs 17 oocytes per cycle, p = 0.92), or oocyte maturity (77% vs 76%, p = 0.43), fertilization (76% vs 77%, p = 0.48) and blastocyst formation (51% vs 52%, p = 0.88) rates by response. There were no significant differences in the rate of euploidy (35% vs 39%, p = 0.55), aneuploidy (51% vs 47%, p = 0.56) and simple mosaic (11% vs 11%, p = 1) between groups. Seven percent (102/1435) of STEETs utilized embryos from a cycle with suboptimal response and 93% (1333/1435) from optimal response to GnRH trigger. There were no significant differences in BPR [11/144 (8%) vs 152/1907 (8%), p = 1] and OP/LBR [152/144 (59%) vs 1271/1907 (59%), p = 1]. No differences in pregnancy outcomes were found in the subanalyses of LH ≥40 mIU/mL on the morning after trigger. Subanalyses of LH ≥ 15 mIU/mL and LH < 15 mIU/mL were also performed. Primary outcomes included oocyte yield, oocyte maturity rate, blastocyst formation rate, euploidy rate, aneuploidy rate and simple mosaic rate. Secondary outcomes included biochemical pregnancy rate (BPR), spontaneous abortion rate (SABR) and ongoing/pregnancy live birth rate (OP/LBR). Primary and secondary outcomes were also stratified by age, race and BMI. Descriptive statistics (median +/- range for continuous variables), Mann Whitey U and Fisher’s Exact tests were performed accordingly with p<0.05 defined as significant.

RESULTS: Out of 586 non-duplicate studies, 138 were assessed for eligibility and 60 met the eligibility criteria (48 with IVF/ICSI, 5 with IUI, 7 without ART). Five studies analyzed the CLB rate according to AMH levels in infertile women having undergone in vitro fertilization (IVF) with or without intracytoplasmic sperm injection (ICSI) and failed to find any difference in these hormone values between patients having conceived or not, with a high heterogeneity [difference in mean (95% CI) 0.90 (-0.2, 2.01), p = 0.11, I² = 99%]. However, after excluding two studies with a high risk of bias, mean serum AMH levels were significantly higher in women with at least one live birth when compared to those without live birth, with no heterogeneity [ difference in mean (95% CI) 0.85 (0.53 – 1.16), p<0.0001, I²=0%]. Although the relationship between AMH levels and CLB rate may be considered as a polynomial fraction, no discriminating AMH threshold was found. There was not enough article/data to assess the ability of AMH to predict CLB rate after intrauterine insemination or in women without history of infertility trying to conceive without ART.

CONCLUSIONS: Serum AMH levels are linked to CLB rate after IVF/ICSI but no discriminating threshold can be established. Data are lacking concerning its predictive value after intrauterine insemination or in women trying to conceive without ART. IMPACT STATEMENT: Our findings may be only helpful to counsel candidate couples to IVF-ICSI.

P-408 6:45 AM Tuesday, October 25, 2022

FERTILIZATION BY INTRACYTOPLASMIC SPERM INJECTION (ICSI) IS ASSOCIATED WITH LOWER RATES OF EUPLOIDY IN NON-MALE FACTOR INFERTILITY COMPARED TO CONVENTIONAL INSEMINATION (CI). Karishma Patel, M.D.,1 Denis A. Vaughan, M.D.,2 Angie Mac Rodday, PhD, M.S.,1 Denny Sakkas, PhD1 Tufts Medical Center, Boston, MA; 3Boston IVF - The Eugin Group, Waltham, MA.

OBJECTIVE: The use of ICSI in non-male factor infertility cases has dramatically increased worldwide and in many clinics is used for all cases, regardless of sperm characteristics. The objective of this study was to examine differences in euploidy rates between CI and ICSI in non-male factor infertility cases.

MATERIALS AND METHODS: A retrospective cohort data analysis was performed at a single, academically affiliated infertility center in the U.S. from January 2014 to December 2021. Fertilization was performed by CI or ICSI. All cycles that had pre-implantation testing for aneuploidy (PGT-A) performed by trophectoderm biopsy and had a post preparation sperm concentration >4 million total motile sperm per milliliter were included. The primary outcome was embryo euploidy rate per embryo biopsied in the CI versus ICSI group. We used multiple imputation to account for missing data. Generalized estimating equations with a Poisson distribution was used to estimate the euploidy rate (with total embryos biopsied as an offset), while accounting for multiple retrievals per patient. To adjust for confounding, a propensity score model was fit for ICSI using 14 baseline maternal and

Table 1: Cycle Characteristics following Propensity Score Weights, mean

<table>
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<th>CI, n=3043</th>
<th>ICSI, n=1873</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oocytes Retrieved</td>
<td>14.3</td>
<td>14.3</td>
<td>0.85</td>
</tr>
<tr>
<td>Fertilization Rate (per oocyte retrieved)</td>
<td>0.66</td>
<td>0.64</td>
<td>0.01</td>
</tr>
<tr>
<td>Embryos Biopsied</td>
<td>4.1</td>
<td>4.1</td>
<td>0.92</td>
</tr>
<tr>
<td>Euploid Embryos</td>
<td>2.0</td>
<td>1.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Euploid Rate (per embryo biopsied)</td>
<td>0.49</td>
<td>0.44</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

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paternal characteristics including age, hormonal profiles, and sperm characteristics. We applied the propensity score using stabilized inverse probability weights and adjusted our Poisson model for the variables included in the propensity score.

RESULTS: A total of 3554 patients underwent 4897 IVF cycles. Of these, 3039 cycles (62%) used CI and 1858 (38%) used ICSI. Propensity score weighting ensured similar baseline characteristics. Oocytes retrieved and number of embryos biopsied were similar in both groups, while fertilization rate per oocyte retrieved was significantly higher with CT (Table 1). The proportion of euploid embryos in the ICSI group was significantly lower when compared to CI (0.44 vs. 0.49, p < 0.01). Based on the multivariable adjusted, propensity score weighted model, the rate ratio for euploid rate in the ICSI group compared to CI was 0.90 (p < 0.001).

CONCLUSIONS: In the setting of non-male factor infertility, ICSI resulted in a lower fertilization rate and a 10% lower embryo euploid rate compared to CI. The use of propensity score weighting ensures similar characteristics in both groups.

IMPACT STATEMENT: Routine use of ICSI for non-male factor infertility should be reconsidered due to the decreased embryo euploidy rate.

SUPPORT: Turksoy Fund supported statistical analysis.

EVIDENCE TO SUPPORT THE OOPLASMIC ROLE IN MODULATING MALE GENOME INTEGRITY. Olena M. Kocur, B.A.,1 Philip Xie, B.S.,2 Carina Sung, B.S.,2 Sydney Souness, B.S.,1 Zev Rosenwaks, M.D.,1 Gianpietro D. Palermo, M.D., Ph.D.1 The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY, 1New York, NY.

OBJECTIVE: To examine whether oocyte repair mechanisms can improve the effect of sperm chromatin fragmentation (SCF) on ICSI clinical outcomes.

MATERIALS AND METHODS: From 2004 to 2022, 341 men with an elevated SCF underwent ICSI cycles resulting in a suboptimal clinical outcome despite a relatively young female partner. A TUNEL assay was used to measure SCF on ≥500 spermatozoa utilizing a 15% threshold. To control for an eventual confounding female factor, 67 additional couples who utilized donor oocytes were identified. Fertilization, implantation, clinical pregnancy, and delivery outcomes were compared between the above-mentioned groups.

To further examine the ability of a young, healthy oocyte to repair a fragmented male genome, we compared clinical outcome between cycles within the same couples who used their own oocytes and subsequently donor eggs.

A paired t test was used to compare ages and semen parameters, and χ² analysis to compare clinical outcomes.

RESULTS: We included a total of 408 men with the following semen parameters: average volume of 2.5 mL, concentration of 22.4x10⁶/mL, 30.9% motility, and normal morphology of 1.7. Of these men, 341 (42.2 ± 8.7 yrs) oocytes, resulting in a 67.1% fertilization, 14.4% embryo implantation, 28.0% clinical pregnancy, and a 23.7% ongoing/delivery. We then assessed 67 couples (44.2 ± 6.6 yrs) with a comparably high SCF who underwent 98 ICSI cycles utilizing donor oocytes (21-34 yrs), resulting in remarkably higher fertilization (78.1%; P < 0.00001) and embryo implantation rates (29.1%; P < 0.0001). This resulted in a clinical pregnancy and ongoing/delivery rate of 36.1% and 29.2%, respectively.

To further confirm the role of the ooplasmic repair mechanisms on the male genome, we identified a cohort of 52 couples who also had severely elevated SCF and underwent an ICSI cycle using their own as well as donor oocytes in a subsequent cycle. Female partner oocytes yielded a fertilization of 68.1%, an embryo implantation of 3.2%, and a clinical pregnancy of 7.1%, resulting in an ongoing/delivery of 1.2%. Cycles using donor oocytes yielded a 76.4% fertilization (P < 0.001), 32.5% implantation (P < 0.00001), and 40.4% clinical pregnancy (P < 0.0001), and 28.8% ongoing/delivery (P < 0.00001).

CONCLUSIONS: Despite the female factor component, it can be argued that a suboptimal male gamete genome can impair ICSI clinical outcome. Ooplasmic repair mechanisms of healthy, young oocytes appear to improve the deleterious impact of sperm DNA fragmentation on ICSI clinical outcome.

IMPACT STATEMENT: In couples with a compromised male genome, a healthy young ooplasm is better able to enhance the developmental competence of the male gamete than an aged oocyte.

MAXIMIZING NUMBER OF OOCYTES RETRIEVED INCREASES NUMBER OF 2PNs, BLASTOCYSTS, AND CUMULATIVE LIVE BIRTH RATES, WITHOUT IMPAIRING PRIMARY TRANSFER LIVE BIRTH RATES. Michael Fanton, Ph.D.,1 Valerie L. Baker, MD,2 Kevin E. Loewke, Ph.D.3 Alife Health, Inc., San Francisco, CA; 110751 Falls Road, Lutherville, MD, 2Alife Health, Inc.

OBJECTIVE: To investigate the association between the number of oocytes retrieved during ovarian stimulation and 2PNs, blastocysts, cumulative live birth rate (CLBR), and primary transfer live birth rate (PT-LBR).

MATERIALS AND METHODS: We analyzed 365,473 autologous, non-cancelled retrieval cycles from 2014-2019 in the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System (SART CORS). The relationships between the number of oocytes retrieved and the number of 2PNs and total blastocysts (number of blastocysts frozen plus transferred) were assessed using Pearson correlation. The CLBR was calculated per retrieval cycle, defined as at least one live birth from all linked embryo transfers. The PT-LBR was calculated per embryo transfer, defined as a live birth from the first embryo transfer associated with each retrieval cycle. The PT-LBR was stratified by fresh transfers (n = 230,708), frozen transfers without PGT (n = 42,209), and frozen transfers with PGT (n = 74,622). All results were calculated for 10 different quantiles of oocytes retrieved.

RESULTS: Across all retrieval cycles, there was a positive linear correlation between oocytes and 2PNs (r = 0.86, p < 0.01) and between oocytes and blastocysts (r = 0.85, p < 0.01). The CLBR per retrieval cycle increased with oocyte yield. Sub-analyses of CLBR by different AMH and age groupings revealed similar increasing trends. The PT-LBR per attempted embryo transfer increased with the number of oocytes until approximately 15 oocytes, at which point it began to plateau.

<table>
<thead>
<tr>
<th>Oocytes</th>
<th>&lt;= 4</th>
<th>5 - 6</th>
<th>7 - 8</th>
<th>9 - 10</th>
<th>11 - 12</th>
<th>13 - 14</th>
<th>15 - 16</th>
<th>17 - 20</th>
<th>21 - 25</th>
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<tr>
<td>2PNs</td>
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<td>3.3</td>
<td>4.5</td>
<td>5.7</td>
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<td>8.0</td>
<td>9.2</td>
<td>10.9</td>
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<tr>
<td>Blastocysts</td>
<td>1.5</td>
<td>2.1</td>
<td>2.6</td>
<td>3.1</td>
<td>3.6</td>
<td>4.1</td>
<td>4.5</td>
<td>5.3</td>
<td>6.3</td>
<td>8.4</td>
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</tbody>
</table>

Cumulative live birth rate (%) - per retrieval

All transfers 15.3 25.6 31.9 38.0 43.6 47.8 51.5 55.0 59.6 64.9
Primary transfer live birth rate (%) - per attempted transfer

All transfers 23.2 33.3 38.1 41.5 44.8 46.7 48.4 49.6 52.0 53.4
Fresh 19.5 28.7 33.5 37.2 40.5 42.2 43.7 44.4 46.0 45.4
Frozen - no PGT 24.6 33.5 36.9 40.5 44.6 46.4 47.3 49.0 53.4 54.8
Frozen - PGT 51.2 53.6 53.3 53.5 54.3 55.2 56.9 57.2 57.8 58.8
CONCLUSIONS: Previous studies have suggested that retrieval cycles with high yields above 10-15 oocytes may be detrimental to live birth outcomes. Using the SART CORS dataset, we found that maximizing the number of oocytes is associated with higher CLBR, even in high-yield patients, and does not appear to impair oocyte quality or reduce PT-LBR. We note that our estimates of CLBR are conservative because we assumed that unused frozen embryos had zero probability of live birth.

IMPART STATEMENT: For patients undergoing ovarian stimulation, maximizing the number of oocytes retrieved is associated with increased 2PNs, blastocysts, and CLBR.

E-POSTER ABSTRACT SESSION: T20

P-411 6:45 AM Tuesday, October 25, 2022

OOCYTE COHORT MATURITY IS POSITIVELY CORRELATED TO BLASTOCYST DEVELOPMENT AND EUPLOID RATES. Ilan Tur-Kaspa, M.D.,† David P. Cohen, B.S., M.D., , Seth Lev rant, M.D., Jaclyn Janbe Steimmler, B.S.C., M.S.C., Ph.D., Corr ina Delorenzo, M.Sc., . John X. Zhang, PhD, Institute for Human Reproduction (IHR), Pin nacle Fertility, Chicago, IL; Institute for Human Reproduction (IHR), Chicago, IL.

OBJECTIVE: To study relationship between the percent of mature oocytes and percent of euploid blastocysts originated from the same cohort.

MATERIALS AND METHODS: This retrospective study included 891 consecutive ICSI-PGT cycles (from 583 patients with an average age at cycle start of 38.1, ranging from 25 to 45) performed between January, 2020 and December, 2021, in a private, academically-affiliated ART center. Cycles using donor oocytes were excluded. Possible association of rates of MII-stage oocytes (maturity) with euploid blastocysts was examined using Pearson correlation analyses. To control for maternal age, the 891 cycles were allocated to three groups according to maternal age at cycle start: Groups A, B and C each includes maternal age <35, between 35 and 38 and older >38 years old, respectively. Chi-squared comparison analyses were employed to compare blastocyst rates and euploid rates between cycles with oocyte maturity in the top 25 percentile and those in the bottom 25 percentile within each age group.

RESULTS: Oocyte maturity was positively correlated with blastocyst rates (r=0.12, p<0.05) and with euploid rates (r=0.11, p<0.05) (Pearson correlation analyses). Oocyte maturity was not correlated with maternal age, the number of days of ovarian stimulation, fertilization rates, or average Mito sure score. In Group A, cycles with oocyte maturity in the top 25 percentile (>86%, 39 cycles, average age=32.0) had usable blastocyst rates of 61% and euploid rates of 71%, in comparison with respective rates of 50% (p<0.05) and 59% (p<0.05) in cycles with oocyte maturity in the bottom 25% (<66%, 41cycles, average age=31.3). In Group B, cycles with oocyte maturity in the top 25 percentile (>86%, 113 cycles, average age=36.6) had usable blastocyst rates of 56% and euploid rates of 51%, compared with respective rates of 50% (p<0.05) and 44% (p<0.01) in cycles with oocyte maturity in the bottom 25% (<64%, 110 cycles, average age 36.7). In Group C, cycles with oocyte maturity in the top 25 percentile (>87, 90 cycles, average age=42.1) had usable blastocyst rates of 43% and euploid rates of 30%, compared with respective rates of 36% (p=0.29) and 23% (p=0.22) in cycles with oocyte maturity in the bottom 25% (<58%, 89 cycles, average age=42.1).

CONCLUSIONS: This study confirmed previous reports that oocyte cohort maturity is positively correlated with blastocyst rates. Furthermore, we demonstrated that it is also positively correlated with embryo euploid rates. This relationship was found to be independent of maternal age.

IMPACT STATEMENT: Our findings explain why low cohort oocyte may lead to lower implantation and pregnancy rates. While oocyte cohort maturity may reflect the biology and quality of oocytes, it may be a result of suboptimal ovarian stimulation protocols used. Therefore, further investigations are needed to examine whether optimized ovarian stimulation protocols will improve oocyte cohort maturity and embryo euploid rates.

P-412 6:45 AM Tuesday, October 25, 2022

OUTCOMES OF AUTLOGOUS SINGLE THAWED EUPLOID EMBRYO TRANSFER IN WOMEN WITH HISTORY OF A PREVIOUS CESARIAN SECTION. Tamar Alkon-Meadows, MD, Carlos Hernandez-Nieto, MD, Jenna Friedenthal, MD, Joseph A. Lee, BA, Benjamin Sandler, MD, Martha Luna Rojas, MD, Alan B. Copperman, MD, Erkan Buyuk, MD Reproductive Medicine Associates of New York, New York, NY; Icahn School of Medicine at Mount Sinai, New York, NY; RMA of New York, International Mexico, SC, Ciudad De Mexico, Mexico; Tcahn School of Medicine at Mount Sinai/Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Patients with a previous cesarean delivery (CS) who underwent a single euploid embryo transfer (SEET) have been shown to have a marked reduction in implantation, ongoing pregnancy and live birth. However, whether the mode of conception for the first pregnancy (i.e. spontaneous pregnancy vs pregnancy via assisted reproductive technology (ART)) and subsequent CS has any effect on the outcome of a subsequent SEET is yet to be understood. The objective of this study is to compare clinical outcomes of secondary pregnancy attempt via SEET in patients with initial ART treatment and primary CS compared to patients with initial spontaneous pregnancy and primary CS.

MATERIALS AND METHODS: The study included all patients undergoing autologous SEET at an academic center with a prior CS from 2016 to January 2022. Cases included patients with 1 prior CS with history of ART treatment prior to their delivery. Controls included patients with 1 prior CS with history of a spontaneous pregnancy. Exclusion criteria included patients with >1 previous live birth, history of vaginal delivery and donor/recipient cycles. Only the first SEET cycle after the CS was analyzed. Our primary outcome was implantation rate (IR); secondary outcomes were ongoing pregnancy/live birth rate (OP/LBR), biochemical pregnancy rate (BPR), and clinical loss rate (CLR). Baseline demographics were obtained: age at (time of retrieval and transfer), body mass index (BMI), obstetric history, endometrial thickness at time of transfer (ETATT), and embryologic characteristics. Statistical analyses were performed using Student’s t-test, Wilcoxon rank, and chi-squared. Multivariable logistic regression models were used to calculate odds ratios and to adjust for confounders.

RESULTS: 308 SEETs met inclusion criteria and were included in analysis (cases n=213; controls n=95). Patients in the control group were older at time of retrieval and transfer (36.8 vs 34.4, p=0.001 and 38.4 vs 36.5, p=0.004) than those with history of prior infertility. Women in the case group had higher day 3 FSH levels (IU/mL) (6.2 vs 5.0, p=0.02) than their counterparts. Demographic data were otherwise similar. In univariate analysis, IR and OP/LBR were similar among groups. After adjusting for confounding factors, patients with a history of ART treatment and prior CS did not experience lower odds of implantation (aOR 1.24, 95% CI 1.05-1.45) nor higher odds of clinical pregnancy loss (aOR 0.70, p=0.02). The odds of live birth were 1.03 (95% CI 0.60-1.7) nor higher odds of clinical pregnancy loss (aOR 0.70, 95% CI 0.2-2.1).

CONCLUSIONS: Our study found no association with secondary IVF outcomes in patients with initial ART treatment and primary CS compared to patients with initial spontaneous pregnancy and primary CS.

IMPACT STATEMENT: This is the first study to demonstrate that the mode of conception for the first pregnancy does not impact secondary IVF outcomes in women with history of a prior CS. Patients with prior infertility and CS can be reassured that the odds of achieving a healthy pregnancy are similar to those that did not have prior ART treatment.

REFERENCES:

P-413 6:45 AM Tuesday, October 25, 2022

LIVE BIRTH FROM NATURAL CONCEPTION FOLLOWING ASSISTED REPRODUCTIVE TECHNOLOGY: ANALYSIS OF A LARGE POPULATION RETROSPECTIVE COHORT STUDY. Addison William Alley, MD, Joshua J. Horns, PhD, Joseph M. Letourneau, MD, James Hotuling, MD University of Arizona College of Medicine - Phoenix, Phoenix, AZ; University of Utah, Salt Lake City, UT; University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT.

OBJECTIVE: To determine the live birth rate from natural conception (NC) amongst couples within the Subfertility, Health, and Assisted Reproduction (SHARE) Study database who previously received infertility treatment with assisted reproductive technology (ART) and to identify any significant predictive factors.
P-415 6:45 AM Tuesday, October 25, 2022

ANTI-MULLERIAN HORMONE (AMH) AND EMBRYO EUPOLOYD IN SUBPOPULATIONS OF WOMEN PURSUING IN VITRO FERTILIZATION (IVF) WITH PREIMPLANTATION GENETIC TESTING.

Yael R. Stovezky, BA,1 Philip A. Romanski, MD, MSc,2 Pietro Bortoletto, MD, MSc,3 Steven D. Spandorfer, MD3 1Weill Medical College of Cornell University, New York, NY;2New York, NY;3The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: While the negative effect of aging on the quantity and quality of oocytes is well established, it is currently unknown whether these processes occur independently. To date, studies which investigated the quantity-quality relationship using embryo aneuploidy as a qualitative marker have primarily focused on the infertile population and produced inconclusive findings (1-2). This study seeks to determine whether AMH, a quantitative biomarker for ovarian reserve, is associated with euploidy rates in two patient populations: the general population of women pursuing IVF with preimplantation genetic testing for aneuploidy (PGT-A) (“infertile” group) and women pursuing IVF with preimplantation genetic testing for monogenic disorders (PGT-M) due to risk for hereditary monogenic diseases (“non-infertile” group). To our knowledge, the latter, with a reproductive potential presumed to be equivalent to the general population, is studied in this context for the first time.

MATERIALS AND METHODS: Women <40 years who underwent oocyte retrieval with trophectoderm biopsy for PGT in an academic hospital setting between 07/2010-06/2020 were placed into “infertile” or “non-infertile” groups and stratified based on AMH levels, with low AMH defined as <1.1 ng/ml in accordance with Bologna criteria (3). In a sensitivity analysis, we compared patients in <10th percentile with patients in the interquartile range (IQR) for AMH. Primary outcome was proportion of euploid embryos per ovarian stimulation cycle. Secondary outcomes were number of biopsied blastocysts and proportion of mosaic and aneuploid embryos. Poisson regression was used in the analyses and adjusted a priori for female age.

RESULTS: 1141 women were included (“infertile”: n=926; “non-infertile”: n=215). Age-adjusted regression models showed a positive relationship between AMH and number of biopsied blastocysts for the “infertile” (RR:1.86, 95% CI: 1.71-2.03) and “non-infertile” (RR:2.00, 95% CI: 1.65-2.41) groups. No significant association was identified for proportion of euploid, mosaic or aneuploid embryos in either group. Patients in <10th percentile compared with patients in the IQR had lower euploidy rates (“infertile”: <10th percentile 41.6±35.8, IQR 50.9±27.1; “non-infertile”: <10th percentile 46.1±33.2, IQR 53.3±26.8). However, no significant association between AMH and proportion of euploid, mosaic or aneuploid embryos was identified in either group. A sensitivity analysis of women younger than 35 years, and women 35-40 did not identify additional relationships between AMH and euploidy outcomes.

CONCLUSIONS: We observed no relationship between AMH and euploidy rates in “fertile” and “non-fertile” women undergoing IVF with PGT-A. This finding persisted even after comparing the <10th percentile with patients in the IQR and after conducting age-appropriate sensitivity analyses.
OBJECTIVE: The glycosylation profile of recombinant human FSH (r-hFSH) is an important attribute of this molecule, defining its net biological effect, safety and efficacy. The most recently developed r-hFSH (r-hFSH-delta) is produced in a human cell line and has a distinct pharmacokinetic/pharmacodynamic (PK/PD) profile versus r-hFSH-alfa, which is produced in a hamster cell line: r-hFSH-delta had a higher elimination half-life and produced a higher ovarian response and higher cumulative live birth rates (cLBRs). Thus, we analyzed this correlation in our ART program focusing on the high AMH patients first.

MATERIALS AND METHODS: Total 2994 cycles between Jan 01, 2014 and Dec 31, 2020 were retrospectively reviewed. We included the condition of GnRH antagonist protocol cycle with ovulation induction for more than 5 days and the cumulative live birth rate were finished and followed up until Sep 30, 2021. The high AMH group was identified as Group 1 with AMH 4 ~ 6 ng/ml (n=210 cycles) and Group 2 with AMH over 6 ng/ml (n=250 cycles). The DOI was classified as 7~8 days (group A), 9~10 days (group B), 11~12 days (group C) and over 13 days (group D). The statistics were carried out by SPSS-PC ver. 22.0 with p<0.05 as statistical significance.

RESULTS: The cLBRs were 60.0%, 80.0%, 76.5% and 64.3% in group 1A, 1B, 1C and 1D respectively. The cLBRs were 82.4%, 78.2%, 89.9% and 88.9% in group 2A, 2B, 2C and 2D respectively. There were no statistically significant differences between these groups in group 1 or group 2. However, the results revealed that the highest cLBRs came from DOI of 9~10 days in Group 1 and 11~12 days in Group 2. Group 1A has significantly less follicles over 18mm in diameter on triggering day as compared to group 1B and 1C (3.2 vs 5.0 vs 5.0) and less estimated follicular maturation rates (53.6% vs 64.5% vs 66.6%). Group 2A and 2D had significantly higher unexpected suboptimal oocytes retrieval (Psoeidon group 2) (11.1% vs 9.1% vs 0.7%). Group 1A and 2A had significantly lower serum P4 level and highest est ET rates as compared to their longer DOI counterparts.

CONCLUSIONS: Our study revealed the optimal DOI for high AMH patients for better cLBRs was 9~12 days for those with AMH 4~6 ng/ml and longer than 11 days for those with AMH above 6 ng/ml. Waiting for higher number of dominant follicles (up to 5) by increasing DOI before triggering may finally result in better cLBRs. However, shorter DOI has the advantage of lower risk of premature P4 rise and better chance of fresh embryo transfer with slightly reduced but still satisfactorily high cLBRs.

IMPACT STATEMENT: Our study will lead to a better understanding of the correlation between the DOI and the cLBRs. This will allow us to optimize the medication used during ovulation induction.

OBJECTIVE: Duration of ovulation induction (DOI) is considered to influence the maturation of the oocytes and the resultant embryos. However, there is few studies focused on the DOI and the cumulative live birth rates (cLBRs). Thus, we analyzed this correlation in our ART program focusing on the high AMH patients first.

MATERIALS AND METHODS: Total 2994 cycles between Jan 01, 2014 and Dec 31, 2020 were retrospectively reviewed. We included the condition of GnRH antagonist protocol cycle with ovulation induction for more than 5 days and the cumulative live birth rate were finished and followed up until Sep 30, 2021. The high AMH group was identified as Group 1 with AMH 4 ~ 6 ng/ml (n=210 cycles) and Group 2 with AMH over 6 ng/ml (n=250 cycles). The DOI was classified as 7~8 days (group A), 9~10 days (group B), 11~12 days (group C) and over 13 days (group D). The statistics were carried out by SPSS-PC ver. 22.0 with p<0.05 as statistical significance.

RESULTS: The cLBRs were 60.0%, 80.0%, 76.5% and 64.3% in group 1A, 1B, 1C and 1D respectively. The cLBRs were 82.4%, 78.2%, 89.9% and 88.9% in group 2A, 2B, 2C and 2D respectively. There were no statistically significant differences between these groups in group 1 or group 2. However, the results revealed that the highest cLBRs came from DOI of 9~10 days in Group 1 and 11~12 days in Group 2. Group 1A has significantly less follicles over 18mm in diameter on triggering day as compared to group 1B and 1C (3.2 vs 5.0 vs 5.0) and less estimated follicular maturation rates (53.6% vs 64.5% vs 66.6%). Group 2A and 2D had significantly higher unexpected suboptimal oocytes retrieval (Psoeidon group 2) (11.1% vs 9.1% vs 0.7%). Group 1A and 2A had significantly lower serum P4 level and highest est ET rates as compared to their longer DOI counterparts.

CONCLUSIONS: Our study revealed the optimal DOI for high AMH patients for better cLBRs was 9~12 days for those with AMH 4~6 ng/ml and longer than 11 days for those with AMH above 6 ng/ml. Waiting for higher number of dominant follicles (up to 5) by increasing DOI before triggering may finally result in better cLBRs. However, shorter DOI has the advantage of lower risk of premature P4 rise and better chance of fresh embryo transfer with slightly reduced but still satisfactorily high cLBRs.

IMPACT STATEMENT: Our study will lead to a better understanding of the correlation between the DOI and the cLBRs. This will allow us to optimize the medication used during ovulation induction.
RESULTS: A total of 308 patients were included in the study (n=196, dual trigger group; n=112, HCG only group). Both groups had similar age and weight, but a higher proportion of patients in the HCG only trigger group had diminished ovarian reserve (p<0.001) demonstrated by lower baseline androgen and antral follicle count (both p<0.001). Number of follicles ≥15mm at time of trigger and number of oocytes retrieved were lower in the HCG only group (both p<0.001). The maturity rate, fertilization rate, blastocyst conversion rate, percentage of good and fair quality blastocysts, and euploid rate were comparable between groups along with all pregnancy outcomes after a first single embryo transfer. Among patients with a fresh embryo transfer, the embryo quality transferred on day 5 was better in the dual trigger group versus HCG only group (p=0.013).

CONCLUSIONS: Despite increased oocyte yield and higher embryo quality for fresh embryo transfer, both dual trigger and HCG alone yielded similar pregnancy outcomes and percent of euploid embryos. Therefore, clinicians should select the most cost-effective trigger to reduce ovarian hyperstimulation syndrome as clinical outcomes are similar.

IMPACT STATEMENT: Despite the higher numbers of available follicles and eggs retrieved, the blastocyst conversion rate and the percentage of good quality and euploid embryos were similar between patients who underwent a dual trigger versus HCG trigger alone for final oocyte maturation in GnRH antagonist ICSI protocols.

P-419 6:45 AM Tuesday, October 25, 2022

PREGNANCY OUTCOMES OF SINGLE PGT-A (PRE-IMPLANTATION GENETIC TESTING FOR ANEUPLOIDY) TESTED FROZEN EMBRYO TRANSFER CYCLES IN WOMEN WITH PCOS – ANALYSIS OF 79,416 CYCLES FROM SART CORS DATABASE. Sara Kuokkanen, MD, PhD,1 Meredith Akerman, MS,2 Lubna Pal, MBBS3 1NYU Langone, Mineola, NY; 2NYU Langone - Long Island Hospital, Mineola, NY; 3Yale University, Orange.

OBJECTIVE: To determine pregnancy outcomes in women with PCOS compared to those with other infertility diagnoses following frozen-thawed embryo transfer (FET) of a single preimplantation genetically tested (PGT-A) blastocyst.

MATERIALS AND METHODS: Retrospective cohort analysis of the SART CORS database 2016-2018. Autologous single embryo transfer cycles of PGT-A tested blastocysts were included. Exclusion criteria were recurrent pregnancy loss, gestational carrier and cycles using donor oocytes or embryos. We examined pregnancy outcomes in women with PCOS compared to those without PCOS diagnosis for the SART specified outcomes: biochemical pregnancy (BP), pregnancy loss (PL, loss at 5<20 weeks), preterm birth (PTB), stillbirth (SB), ectopic pregnancy (EP) and live birth (LB). Term birth (TB) was defined as live birth at ≥37 weeks. Univariate and multivariable analysis were performed using STATA V13.0. Covariates adjusted for included age, BMI, race/ethnicity, smoking, endometrial thickness, uterine factor and AMH. The data are presented as odds ratios (OR) and 95% CI.

RESULTS: 79,416 FET cycles of single PGT-A tested embryos met eligibility criteria, of these 12,230 (15%) were in women with PCOS. Compared to the other infertility diagnoses, the diagnosis of PCOS was significantly associated with greater likelihood of BP, PL and PTL, and lower likelihood of LB (Table). The outcomes of SB and EP were unrelated to the PCOS diagnosis.

CONCLUSIONS: We found that compared to other infertility etiologies, the diagnosis of PCOS is associated with adverse outcomes in pregnancies following transfer of a single PGT-A tested blastocyst. Our results suggest that other factors than embryo aneuploidy are contributors to attenuated pregnancy success in women with PCOS.

IMPACT STATEMENT: In women with PCOS, pregnancy outcomes are compromised following transfer of a single genetically tested embryo. Intensified pregnancy surveillance may be warranted in women with PCOS. The future research needs to confirm the observed adverse pregnancy outcomes in women with PCOS and explore the underlying mechanisms.

SUPPORT: None.

P-420 6:45 AM Tuesday, October 25, 2022

FACTORS INFLUENCING THE PREVALENCE OF EMBRYO PLOIDY IN IVF CYCLES. Daniela Nogueira, PhD, Human M, M. Fatemi, M.D., PhD, Prof.; Lawrence Barbera, M.D., PhD; Rachana Patel, PhD,<Color>Andrea Abdala, M.Sc.,1 Ibrahim Elkhaitib, M.Sc.,1 Laura Marquetta, MD,3 Asina Bayram, M.Sc.,1 Laura Melado, M.D, PhD4 ART Fertility Clinics, Abu Dhabi, United Arab Emirates; 5 ART Fertility Clinics; 6 ART Fertility Clinics, United Arab Emirates; 7 ART Fertility Clinics, Abu Dhabi, Abu Dhabi, United Arab Emirates.

OBJECTIVE: To determine the relationship between female age and nature of human embryonic aneuploidy.

MATERIALS AND METHODS: Single center observational study including data from 10556 blastocysts after PGT-A. Embryos were obtained from 2564 IVF/ICSI cycles of infertile couples, from November 2016 to December 2020. Only blastocysts with ploidy information were included. Mosaic and non-informative embryos were excluded. Trophoectoderm biopsy was performed on day 5, 6 or 7 blastocysts using Next Generation Sequencing (NGS) platform for all embryos. Ethical approval was obtained from the Research Ethics Committee (REFA023b).

RESULTS: Mean age of the female partner was 34.7±6.1 (18-50) years. These female patients presented a BMI of 28.6±4.4 (14.3-45.0) and AMH of 2.5±2.7 (0.01-23.0) ng/mL. The laboratory outcomes from these couples showed that 10.1±6.5 (1-50) MII oocytes were inseminated with a 73.3±19.3% (5.3-100%) normal fertilization resulting in 7.3±5.1 (1-42) mean number of embryos. Following culture until day 5-7, the achieved blastulation rate (useful blastocysts/2PN) was 61.0±25.7% (4.3-100) with an euploid rate (euploid/total blastocysts) of 39.4±35.2% (0-100). The multivariate regression analysis showed, as expected, that maternal age had a significant impact on aneuploidy incidence (OR 1.12; p<0.0001). A low AMH value of <0.5ng/ml showed a significant impact on aneuploidy (OR 1.43; p=0.012) while higher values did not (0.5-1.3= OR 0.92; p=0.3 and >6.25= OR 0.87; p=0.1).

The no euploid embryo rate within a cycle increased 3% per each year of increasing age (β=3.09, p<0.001), and the probability of obtaining at least one euploid embryo for transfer decreased by 23% per each year of increased age (OR 0.77; p<0.001).

Concerning embryos abnormalities, in younger patients (<25-35-year-old), the prevalence of segmental aneuploidies, monosomies and trissomies ranged between 25%- 45% of embryos analysed. In older patients, however, the prevalence of monosomies and trissomies were significantly higher (36-40-year-old: 50%; 41-45-year-old: 65%), while segmental aneuploidies accounted only for <15% of embryo abnormalities.

CONCLUSIONS: The present data emphasizes the impact of low AMH and increasing age on euploidy rates and calls attention for the prevalence of types of chromosomal abnormalities encountered in each age group, including very young patients.

IMPACT STATEMENT: Awareness of the effect of the above factors and the incidence of embryo abnormality with each advancing year is essential to understand the impact of delaying IVF treatment on the health of developed embryos. Furthermore, this data is informative when counselling patients and may be transposed to the general population as guidance not to delay parenthood, once desired.

E-POSTER ABSTRACT SESSION: T21

P-421 6:45 AM Tuesday, October 25, 2022

SERUM ESTROGEN AND PROGESTERONE LEVELS AS PREDICTORS OF OUTCOME IN WOMEN UNDERGOING ARTIFICIALLY PREPARED FROZEN EMBRYO TRANSFER CYCLES. Ayseen Yuceturk, M.D.,1

Table 1: Pregnancy outcomes of PGT-A FET cycles in women with PCOS vs. those with other infertility diagnoses.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Unadjusted OR (CI)</th>
<th>Adjusted OR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biochemical pregnancy</td>
<td>1.10 (1.03-1.18)</td>
<td>1.14 (1.04-1.24)</td>
</tr>
<tr>
<td>Pregnancy loss</td>
<td>1.14 (0.90-1.20)</td>
<td>1.11 (1.03-1.19)</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>1.31 (1.20-1.44)</td>
<td>1.34 (1.17-1.53)</td>
</tr>
<tr>
<td>Term birth</td>
<td>0.86 (0.81-0.90)</td>
<td>0.93 (0.95-1.0)</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>1.62 (0.79-1.66)</td>
<td>1.12 (0.71-1.76)</td>
</tr>
<tr>
<td>Live birth</td>
<td>0.92 (0.89-0.96)</td>
<td>0.91 (0.87-0.96)</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>1.00 (0.75-1.32)</td>
<td>0.92 (0.63-1.33)</td>
</tr>
</tbody>
</table>

Covariates in adjusted models: age, BMI, race/ethnicity, smoking, endometrial thickness, uterine factor and AMH.
*statistically significant

Vol. 118, No. 4, Supplement, October 2022
OBJECTIVE: The aim of the current study was to evaluate the effects of serum estradiol (E2) and progesterone (P4) levels at different time points on pregnancy outcomes in frozen embryo transfer (FET) cycles.

MATERIALS AND METHODS: This was a prospective cohort study that was performed in patients undergoing frozen single blastocyst transfer. Patients under 40 years of age with at least one good quality blastocyst were included in the study. Preimplantation genetic testing for aneuploidy (PGT-A) was not performed. Patients with endometriosis, uterine pathologies (i.e., fibroid, polyp, Mullerian abnormalities), hydrosalphinx, history of poor ovarian response or primary ovarian insufficiency, recurrent implantation failure, recurrent pregnancy loss, and severe male factor were excluded from the study. For endometrial preparation, 14 days of oral estradiol use (2x2 mg for 5 days, 3x2 mg for 4 days, and 4x2 mg for 5 days) was followed by vaginal progesterone twice a day and 50 mg intramuscular progesterone twice a day. Embryo transfer was scheduled 116-120 hours after the initiation of progesterone. Serum E2 and P4 levels were examined at 4 time points: (1) At the start of the menstrual cycle prior to the initiation of hormone supplementation (T1); (2) on the day of progesterone start (T2); (3) on the day of embryo transfer (T3); (4) on the third day after embryo transfer (T4).

RESULTS: A total of 205 women were included in this study (mean age 32.4; 4.9 SD). Clinical pregnancy (defined as gestational sac >6 weeks of gestation) rate was 50.2%. Serum E2 levels on T1 and T2 were higher in patients who achieved pregnancy compared to those who did not (p<0.005 and p=0.017, respectively). P4 levels on T3 were also higher in patients with a clinical pregnancy (p=0.021). Serum E2 levels on T3 and T4, and serum P levels on T1, T2, and T4 were not statistically different between the patients with or without a pregnancy. E2 measurement on T1 best classified clinical pregnancy outcome with an AUC of 0.618 (95% CI [0.539-0.698]) and it had the optimal threshold value at 23.2 pg/mL with the maximum sensitivity of 45% and specificity of 83%. On T2, a serum E2 threshold of 204.0 pg/ml had a sensitivity of 84% and specificity 37% for the detection of clinical pregnancy with an AUC of 0.606 (95% CI [0.523-0.688]). The P4 measurement on T3 had an AUC of 0.610 (95% CI [0.527-0.693]). It had a sensitivity of 74% and specificity of 49% for prediction of clinical pregnancy at the threshold value of 14.97 ng/ml.

CONCLUSIONS: Our findings suggest that in women undergoing frozen embryo transfer with hormonal replacement, serum E2 levels >204.0 pg/ml on the day of the start of progesterone, and serum P4 levels >14.97 ng/ml on embryo transfer day are associated with clinical pregnancy.

IMPACT STATEMENT: In women undergoing frozen embryo transfer with hormone replacement protocols, serum estradiol and progesterone levels at critical timepoints are predictive of pregnancy outcomes.

Table 1: Patient and cycle characteristics by relapse within 3 months of ART

<table>
<thead>
<tr>
<th>No Relapse (N=105 cycles)</th>
<th>Relapse (N=5 cycles)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>36.6 (3.8)</td>
<td>34.2 (2.5)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>81 (77.1%)</td>
</tr>
<tr>
<td>Asian</td>
<td>8 (7.6%)</td>
</tr>
<tr>
<td>Black</td>
<td>11 (10.5%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3 (2.9%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td></td>
</tr>
<tr>
<td>18.5-24.9</td>
<td></td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>1 (1.0%)</td>
</tr>
<tr>
<td>25-29.9</td>
<td>57 (54.3%)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>20 (19.0%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>17 (16.2%)</td>
</tr>
<tr>
<td>Disease modifying therapy</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>61 (58.1%)</td>
</tr>
<tr>
<td>Yes</td>
<td>42 (40.0%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>COH + ET</td>
<td>59 (56.2%)</td>
</tr>
<tr>
<td>COH</td>
<td>16 (15.2%)</td>
</tr>
<tr>
<td>ET</td>
<td>30 (28.6%)</td>
</tr>
<tr>
<td>COH Protocol a</td>
<td></td>
</tr>
<tr>
<td>Antagonist</td>
<td>51 (68.0%)</td>
</tr>
<tr>
<td>Agonist</td>
<td>12 (16.0%)</td>
</tr>
<tr>
<td>Flare</td>
<td>4 (5.3%)</td>
</tr>
<tr>
<td>Mini-stim</td>
<td>3 (4.0%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>5 (6.7%)</td>
</tr>
<tr>
<td>Peak estradiol (pg/mL) b</td>
<td></td>
</tr>
<tr>
<td>2113.4 (1098.9)</td>
<td>2069.8 (771.5)</td>
</tr>
<tr>
<td>ET outcome d</td>
<td></td>
</tr>
<tr>
<td>Ongoing pregnancy or live birth</td>
<td>42 (47.7%)</td>
</tr>
<tr>
<td>Not pregnant, biochemical, or spontaneous abortion</td>
<td>45 (51.1%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (1.1%)</td>
</tr>
</tbody>
</table>

Values expressed as mean (SD) or N(%) as appropriate. aAmong COH cycles only, n=80. bMissing for n=18. cAmong ET cycles only, n=91.
VALIDATION OF SPERM CHROMATIN DISPERSION (SCD) TEST USING A MAIL-IN, AT-HOME SEMEN COLLECTION KIT. Felipe Navarrete, PH.D., Anthony R. Anderson, D.S.C., M.S.C., M.S., Kristina R. Burgess, M.D., Michael Reed, PH.D., Paul Simon, B.S.C., M.S.C., PH.D., Ramy Abou Ghayda, MD, MHA, MPH, Give Legacy Inc, Melrose, MA; 2Reproductive Medicine Associates of Texas, PA, Spring Branch, TX, 3GiveLegacy; 4The Fertility Center of New Mexico, LLC, 5University Hospitals, Cleveland, OH.

OBJECTIVE: The covid-19 pandemic has accelerated the use of direct-to-consumer offerings of at-home, mail-in kits for sperm DNA fragmentation. However, mail-in semen collection kits involve incubation in transport media and overnight shipping. DNA fragmentation can be confounded by multiple extrinsic factors such as storage temperatures, transportation media, handling conditions, time after ejaculation, and oxidative stress. The objective of this study was to validate the sperm chromatin dispersion test using at-home, mail-in sperm collection kits. To do so, we evaluated and assessed the effect of transportation media and shipping on sperm DNA integrity using a Halosperm® G2 kit in normozoospermic human sperm samples.

MATERIALS AND METHODS: We included a control group of ten healthy normozoospermic humans whose semen samples were analyzed for sperm DNA fragmentation using a Halosperm® G2 kit. Fifty healthy normozoospermic human semen samples were included in the study. The mean age of men in the entire cohort was 34.9 ± 8 years. These samples were divided into two equal groups. The first group was directly analyzed for sperm DNA fragmentation using a Halosperm® G2 kit in the lab. The second group was incubated for 24 hours in transportation media (TM), then these incubated semen samples were packaged. Shipping simulation was achieved by putting the semen samples in a cargo van for 5 hours, where temperatures, pressure, and handling fluctuated. The samples were then returned to the lab, where they were subsequently analyzed for sperm DNA fragmentation using a Halosperm® G2 kit.

To estimate the inter-observer variability in the scoring of sperm cells with fragmented DNA, 20 aliquots from 10 different frozen semen specimens of the control group were processed at our internal lab. The other 10 aliquots were shipped to an independent, third-party CLIA-certified laboratory and processed using the same Halosperm® G2 kit technique.

RESULTS: The Sperm DNA fragmentation index was not statistically significantly different between the non-incubated freshly analyzed sperm samples (20 %, SD +/-9%) and the 24-hour incubated samples with shipping conditions (24% SD +/- 13) (p-value: 0.0549).

During the external validation study, when the internal and external lab technicains scored the same samples, the sperm DNA fragmentation percentage (SDFs) were not statistically significantly different (p-value: 0.1213) correlated (r = 0.85, p = 0.0016).

CONCLUSIONS: This study revealed that the sperm DNA fragmentation index of normozoospermic human sperm sample is not statistically significantly improved by a 24-hour transport media incubation and subsequent exposure to shipping conditions.

IMPACT STATEMENT: Our study showed that the accuracy and validity of DNA fragmentation detection using the Halosperm® G2 kit of TM-incubated and shipped human sperm samples was comparable to those of fresh samples analyzed at the lab in normozoospermic human sperm samples. Therefore, at-home mail-in kits may provide a viable testing option for DNA fragmentation index, helping to mitigate the barriers to access of affordable fertility care.

SUPPORT: None.

IS THE USE OF DONATED Sperm ADVISABLE FOR PATIENTS WITH ADVANCED PATERNAL AGE? Marta Bellés, MSc,1 Mireia Florensa, MSc,2 Marga Esbert, PhD1 1IVI RMA Barcelona, Barcelona, Spain; 2IVI RMA Barcelona, Barcelona, Spain.

OBJECTIVE: Although it is well established that reproductive potential declines as women age, information regarding the effect of advanced paternal age (APA) is still conflicting. The use of sperm from healthy young donors has been proposed as a strategy to reduce harms associated with APA. The purpose of this study was to compare the IVF outcomes after the use of sperm samples from patients considered APA (defined as ≥ 45 years) with those found when donor sperm was used.

MATERIALS AND METHODS: Retrospective study including 2,584 couples who underwent an ICSI cycle between 2014 and 2020 at the same clinic. Inclusion criteria were the use of donor eggs to control for maternal factors and the performance of single blastocyst transfer. In 1,816 cycles ejaculated APA samples (49.2±4.1 yrs.) were used for microinjection, while 'and costs for a couple with a clinically significant varicocele.

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RESULTS: A total of 30,372 oocytes were donated to the couples. The number of mature donated gametes was similar between groups (113.4¿0 vs. 114.4¿0, p=0.88). Embryology outcomes were similar between the cycles using APA and donated sperm samples: Fertilization rate (76.0¿75.2%, p=0.33), blastulation rate (60.6¿61.6%, p=0.12) and usable blastocyst rate (39.9¿41.2%, p=0.07). Comparable clinical pregnancy rate (54.7¿58%, p=0.12), miscarriage rate (16.3¿16.0%, p=0.57) and live birth rate (42.4¿46.3%, p=0.08) was observed in both groups.
CONCLUSIONS: According to our study, samples from APA patients can achieve the same clinical results as the ones obtained with semen from a sperm bank. To our knowledge, this is one of the largest studies to evaluate the impact of advancing paternal age on IVF outcomes and our findings do not support the use of donated sperm in APA patients. In order to properly counsel our patients, more effort should be made to elucidate whether advanced paternal age is associated with disorders among offspring.

IMPACT STATEMENT: IVF outcomes of APA patients using their own sperm samples are comparable to the IVF results obtained with sperm donors.

P-427 6:45 AM Tuesday, October 25, 2022

DOES PATERNAL AGE AFFECT LIVE BIRTH RATE IN DONOR OOCYTE CYCLES? A SYSTEMATIC REVIEW AND META-ANALYSIS.

Emmanuelle Begon, MD, MSC, Tiphaine Lefebvre, MD, MSC, Elsaangela Arkow, MD, MSC, Boué Sarah, MD, MSC, Jaffre Frédérique, MD, MSC, Solene Languille, PhD, Dika Mellohu, MSc, Jean-Christophe Pont, PhD, PHARMAD, Noémie Rouset, PHARMAD, Thomas Freour, Ph.D., PHARMAD, CHU Bordeaux, Bordeaux, France; Centre Hospitalier Universitaire De Nantes, Nantes, France; Gedeon Richter France, Paris, France; CHU de Brest, Brest, France; Clinique Mutualiste La Sagesse, Rennes, France; Monitoring Force, Maisons Laffitte, France; Monitoring Force Group, Maisons Laffitte Cedex, France; Centre AMP NativFiv, Meaux, France; CHU de Nantes, Nantes, France.

OBJECTIVE: Negative impact of paternal age on in vitro fertilisation (IVF) outcomes is largely demonstrated, while the effect of paternal age remains unclear. This study aimed to systematically review the literature for qualitative and quantitative assessment of a relationship between paternal age and live birth rate (LB) in IVF.

MATERIALS AND METHODS: A systematic search of the literature was conducted on Pubmed, Embase, Cochrane Library from inception to June 30, 2021. Search terms related to paternal age, oocyte donation and LB were used. Were included all studies that involve subfertile couples undergoing IVF with oocyte donation and where LB is reported according to male age. Study selection, bias assessment and data extraction from published reports were performed by two independent reviewers according to Cochrane methods. Data sensitivity analyses were performed using R software.

RESULTS: Eleven studies involving 10,527 cycles were included in the systematic review and meta-analysis. 10 studies for the relationship and 8 studies for the threshold effect. Only 4 on 11 studies reported a threshold effect of paternal age varying between 37.0 years and 50.0 years). The meta-analysis showed a significant and linear decrease in the chance of LB with increasing paternal age (estimate -0.0055; 95%CI [-0.0093; -0.0016]; p = 0.006, n = 10 studies), with a low heterogeneity ($I^2 = 25\%$). Sensitivity analyses by excluding some studies (outliers, studies with at least one high-risk of bias or using a leave-one-out method) led to the same conclusions.

CONCLUSIONS: This meta-analysis demonstrates that increasing paternal age at which the first child is conceived. Studies considering donated oocytes consumed, respectively. After adjusting for donor and maternal age taking A as reference, these differences were still statistically significant with p <0.001 for all the cases.

CONCLUSIONS: CLBR per inseminated oocyte, embryo transferred and ET until LB were significantly different between the paternal age groups, so paternal age could be a relevant factor affecting the number of inseminated oocytes transferred and ET needed until 1st LB in donor IVF-ICSI and it should be considered for improving fertility care.

IMPACT STATEMENT: Despite its retrospective nature, this study includes a considerable sample size showing a possible influence of paternal age on reproductive outcomes, which must be taken into account due to current fatherhood delay. Moreover, it considers donated oocytes which confers the benefit of controlling for female factor focusing on male factor contribution.

SUPPORT: None.

P-429 6:45 AM Tuesday, October 25, 2022

SIGNIFICANT EFFECT OF PATERNAL AGE ON CUMULATIVE LIVE BIRTH RATES (CLBR) PER INSEMINATED OOCYTE, EMBRYO TRANSFER (ET) AND EMBRYO TRANSFERRED IN IVF-ICSI WITH AUTOLOGOUS OOCYTES.

Ana Navarro Gomez-Lechon, MSc, María Gil Juliá, MSc, MRes, Laura Mossetti, MSc, Rocío Rivera-Egea, PhD, Nicolás Garrido Puchalt, PhD, IVI Foundation - IIS La Fe Biomedical Research Institute, Valencia, Spain; IVIRMA Roma, Rome, Italy; IVIRMA Valencia, Valencia, Spain; IVI Foundation, Valencia, Spain.

OBJECTIVE: In recent years, there has been an increase of the average paternal age at which the first child is conceived. Studies addressing paternal age and reproductive outcomes frequently show controversial results, probably because of the wrong statistical approach. We aimed to assess paternal age influence on reproductive outcomes in terms of CLBR per inseminated oocyte, ET and embryo transferred in donor IVF-ICSI to better measure the involvement of paternal age by taking into account the contribution of all the embryo cohort.

MATERIALS AND METHODS: This retrospective observational multicentric cohort study has included data from IVF-ICSI performed to couples at Spain IVIRMA clinics between January 2008 and March 2020 using patients’ own sperm and autologous oocytes. We evaluated men with different age ranging from 18 to 71 years. The study population was categorized in 3
groups: 18-30 (A), 30-40 (B) and >40 (C). Reproductive success was measured in terms of reproductive outcomes per ET and CLBR per inseminated oocyte, embryo transferred and ET until the first LB. Kaplan-Meier was used for CLBR analysis. P<0.05 was considered statistically significant.

RESULTS: There were significant differences for biochemical pregnancy, clinical pregnancy and ongoing pregnancy rate per ET (n=59208) between the groups, being 62.0%, 53.5%, 46.7% for A; 55.2%, 46.5%, 38.2% for B; and 44.5%, 36.9%, 28.1% for C; respectively. LB rate per ET, 44.7% for A, 36.5% for B and 26.5% for C, was also significantly different between the groups. P<0.001 for all the cases.

In terms of CLBR per number of inseminated oocytes, the results were for 5, 10 and 15 oocytes 10.3%, 33.6%, 52.9% for A; 10.8%, 30.4%, 46.7% for B; and 6.6%, 19.7%, 33.4% for C; respectively. There were statistically significant differences in the CLBR per inseminated oocyte between the age groups (p<0.0001). The same occurred for CLBR calculated per number of embryos transferred until LB (p<0.0001): A (43.0%, 64.3% and 77.9%), B (35.3%, 52.2% and 64.3%) and C (29.9%, 41.4% and 51.4%), for 3, 5 and 7 embryos transferred, respectively. When computed per ET, CLBR was also significantly different between the study groups (p<0.0001), being 29.0%, 46.3%, 76.6% for A; 21.9%, 36.7%, 64.7% for B; and 17.9%, 29.5%, 53.7% for C, for the 1st, 2nd and 5th ET, respectively. After adjusting for maternal age taking A as reference, these differences were still statistically significant.

CONCLUSIONS: CLBR per inseminated oocyte, embryo transferred and ET until LB were significantly different between the paternal age groups, therefore paternal age could be an important factor to consider for improving fertility counselling as it could affect the number of inseminated oocytes, embryos transferred and ET needed until LB in autologous IVF-ICSI.

IMPACT STATEMENT: Despite its retrospective nature, this study in-"
Blastulation rates achieved in the m-TESE, TESA and ejaculated sperm cohorts were 30.11%, 43% and 34.83% respectively. A higher blastulation rate was achieved in the TESA cohort compared to the m-TESE cohort (p = 0.0109).

Implantation rates achieved in the m-TESE, TESA and ejaculated sperm cohorts were 63.16%, 42% and 32.56% respectively. IR in the m-TESE cohort was significantly higher compared to the ejaculated sperm cohort (p = 0.0256).

We achieved comparable clinical pregnancy rates in the m-TESE, TESA and ejaculated sperm cohorts (63.16%, 82% and 63.64% respectively).

COMES AFTER INTRATESTICULAR INJECTION OF PLATELET RICH PLASMA (PRP). CONCLUSIONS: Based on the findings of this study, the use of surgically retrieved sperm via TESA or m-TESE for ICSI may not improve reproductive outcomes compared to ejaculated sperm in cryptozoospermia. Surgical interventions are not without their risks and it is imperative that individuals suffering from Cryptozoospermia to be counselled appropriately, before they undergo infertility treatment.

IMPACT STATEMENT: The type of sperm used for intracytoplasmic injection (ICSI) in cryptozoospermic individuals makes no difference to their outcomes. We specifically to determine association between ADI and concentration and total progressive motile count (TPMC).

### Table 1: Semen parameters according to area deprivation index (ADI).

<table>
<thead>
<tr>
<th>Variable</th>
<th>ADI1</th>
<th>ADI2</th>
<th>ADI3</th>
<th>ADI4</th>
<th>ADI5</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total N (%)</td>
<td>3521 (16.7%)</td>
<td>5210 (24.7%)</td>
<td>4864 (23.1%)</td>
<td>4804 (19.2%)</td>
<td>3459 (16.4%)</td>
<td>21094 (100%)</td>
<td></td>
</tr>
<tr>
<td>Concentration</td>
<td>68 (31-124)</td>
<td>73 (33.2-128)</td>
<td>72 (32-128)</td>
<td>68 (31-121)</td>
<td>69.35 (30-123)</td>
<td>70 (32-125) missing=3862</td>
<td>P = 0.011</td>
</tr>
<tr>
<td>Volume</td>
<td>3 (2-4)</td>
<td>3 (2-4.3)</td>
<td>3 (2-4.2)</td>
<td>3 (2-4.2)</td>
<td>3 (2-4.2) missing=1552</td>
<td>3 (2-4.2)</td>
<td>P = 0.027</td>
</tr>
<tr>
<td>Total motility</td>
<td>60 (48-71)</td>
<td>60 (48-71)</td>
<td>60 (46-71)</td>
<td>60 (48-72)</td>
<td>60 (47-72)</td>
<td>60 (48-71) missing=3131</td>
<td>P = 0.741</td>
</tr>
<tr>
<td>Total motile count</td>
<td>124.6</td>
<td>136</td>
<td>133</td>
<td>129.5</td>
<td>124.74</td>
<td>130.2 (48.2-252.7)</td>
<td>P = 0.045</td>
</tr>
<tr>
<td>Sperm concentration</td>
<td>(48.2-242.4)</td>
<td>(52.7-257.9)</td>
<td>(48-256.2)</td>
<td>(47.2-249.8)</td>
<td>(43.4-254.1)</td>
<td>missing=6006</td>
<td>P = 0.288</td>
</tr>
<tr>
<td>Azooospermia</td>
<td>82 (2.3%)</td>
<td>114 (2.2%)</td>
<td>81 (1.7%)</td>
<td>90 (2.2%)</td>
<td>71 (2.1%)</td>
<td>438 (2.1%)</td>
<td></td>
</tr>
<tr>
<td>Severe oligospermia</td>
<td>130 (3.7%)</td>
<td>208 (4.0%)</td>
<td>214 (4.4%)</td>
<td>174 (4.3%)</td>
<td>151 (4.4%)</td>
<td>877 (4.2%)</td>
<td></td>
</tr>
<tr>
<td>Oligozoospermia</td>
<td>212 (6.1%)</td>
<td>300 (5.8%)</td>
<td>303 (6.2%)</td>
<td>213 (5.3%)</td>
<td>207 (6.0%)</td>
<td>1235 (5.9%)</td>
<td></td>
</tr>
</tbody>
</table>
RESULTS: We identified 21,094 men who underwent SA during the study period. ADI was fairly evenly distributed across the cohort with 3,521 (16.7%) and 3,459 (16.4%) men in the lowest and highest ADI categories, respectively. Median sperm concentration was similar in the lowest versus highest ADI categories (68, interquartile range [IQR] 31-124 vs 69, IQR 30-123). Median total motility was similar in the lowest versus highest ADI categories (60, IQR 48-71 vs 60, IQR 48-71), as was TMC (107, IQR 35-208 vs 106, IQR 32-216). There were no differences in the prevalence of azoospermia, severe oligospermia, or oligospermia between men in the lowest versus highest ADI categories (p=0.288).

CONCLUSIONS: In a large, population-based cohort, there were no differences in bulk semen parameters in men from high and low SES areas.

IMPACT STATEMENT: These data suggest that previously described differences in fertility outcomes among men with lower SES may be partly driven by access to and quality of care rather than inherent biological differences.

SUPPORT: None.

DECREASED TOTAL MOTILE SPERM COUNT IS NOT ASSOCIATED WITH INCREASED FREQUENCY OF SEGMENTAL ANEUPLOIDIES. Chelsea M. Cunen, MD,1 Lauren Walters-Sen, PhD, FACMG,2 Carlos Hernandez-Nieto, MD,1 Natan Bar-Chama, MD,3 Joseph A. Lee, BA,1 Alan B. Copperman, MD,1 Erkan Buyuk, MD,1 Icahn School of Medicine at Mount Sinai, New York, NY;2Invitae, San Francisco, CA;3Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) results can report segmental aneuploidies in the human embryo. It has been shown that segmental aneuploidies can be associated with parent-of-origin. Specifically, the paternal allele can be affected in up to 2/3 of complex segmental imbalances which are characterized by the presence of two or more aberrations on the same chromosome. There are currently no studies investigating the link between abnormal semen parameters such as total motile count (TMC) and segmental aneuploidies. This study aims to assess the association between concentration of TMC and the frequency in segmental aneuploidies.

MATERIALS AND METHODS: This study included in vitro fertilization (IVF) cycles with Intracytoplasmic sperm injection (ICSI) and PGTA at a single academic center from September 2016-March 2021. All PGT-A testing was analyzed by a modified FAST-SeqS NGS-based PGT method and bioinformatics pipeline after trophoderm biopsy. Cycles were grouped into percentiles based on total motile count (TMC) of the sperm specimen used for fertilization (Group 1: <25th percentile TMC (<17.82 million); Group 2: 25-75th percentile TMC (between 17.82 million-133.2 million); Group 3 >75th percentile TMC (>133.2 million)). Demographic and embryonic characteristics were collected. The primary outcome was the percentage of embryos with segmental aneuploidy. Comparative statistics were performed with ANOVA, Kruskal-Wallis, and chi-square. Data was also analyzed using a multivariate regression analysis fitted with a general estimate equation (GEE) model. A sample size of 1471 cycles per group was calculated to have 80% power to detect a 5% difference in percentage of segmental aneuploidies (α=0.05).

RESULTS: A total of 5,902 IVF cycles were identified. The percentage of segmental aneuploidies was similar across all groups (p=0.31). A sub-analysis was performed analyzing cycles using testicular sperm vs ejaculate sperm, with no difference in percentage of segmental aneuploidies. In a multivariate logistic regression analysis adjusted for oocyte age, paternal age, maternal BMI, anti mullerian hormone, number of embryos biopsied, use of fresh vs frozen sperm specimen, and use of TESE vs ejaculate sperm, there was no difference in the frequency of segmental aneuploidies between the groups with <25th percentile TMC and >75th percentile TMC (aOR 0.93, 95% CI 0.66, 1.29).

CONCLUSIONS: The paternal allele is often affected in complex segmental aneuploidies, suggesting that segmental aneuploidies could be associated with male factor and abnormal semen parameters. Our study shows that there are similar rates of segmental aneuploidies regardless of the TMC in couples who undergo IVF with PGT-A.

IMPACT STATEMENT: Couples can be reassured that the risk of segmental aneuploidy is not increased with sub-optimal TMC.

SUPPORT: None.

REFERENCES

EXPANDING THE GENETIC ETIOLOGY OF MULTIPLE MORPHOLOGICAL ABNORMALITIES OF THE SPERM FLAGELLA: A CASE REPORT OF TWO NOVEL DNAH1 VARIANTS. Emily Anderson, B.S.,1 Ellen Johnson, M.G.C.S.,2 Katie Hornberger, B.S., M.S.C.,1 Megan Bell, B.S.,2 Jason Flanagan, M.S.,3 Steffen P. Christensen, M.D.,4 & NxGen MDx, Grand Rapids, MI;5 Sanford Reproductive Medicine, Fargo, SD; Seattle Sperm Bank, Seattle, WA;6 Sanford Health, Sioux Falls, SD;7 Sanford Fertility and Reproductive Medicine, Sioux Falls;8 Sanford Reproductive Medicine, Fargo, ND.

OBJECTIVE: This research reports two novel variants in DNAH1 identified in a male with infertility associated with significant asthenoteratospermia (AT). The patient presented for an infertility evaluation following abnormal semen analysis which identified oligoasthenospermia. Repeat analysis confirmed complete asthenospermia and reported normal morphology, including shortened tails and tail-less heads. Following genetic counseling, a 46–Primary Ciliary Dyskinesia (PCD)/Infertility Cilia Syndrome panel utilizing next generation sequencing and deletion/duplication analysis was ordered. Genetic testing identified two novel heterozygous DNAH1 variants. The couple proceeded with in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) utilizing autologous sperm. A second IVF cycle utilized donor sperm and ICSI. RESULTS: A 46–PCD/Infertility Cilia Syndrome panel identified two novel heterozygous DNAH1 variants (c.6139–1G>A and c.11667_11668insC). DNAH1 variants have been associated with both PCD and multiple morphological abnormalities of the sperm flagella (MMAF), which is consistent with the patient’s history of asthenospermia and noted flagellar abnormalities. The autologous IVF cycle resulted in the retrieval of 18 mature oocytes, 13 of which fertilized. Ultimately, two embryos developed into blastocysts and were biopsied for elective preimplantation genetic testing for aneuploidy (PGT-A) resulting in both embryos classified as mosaic. The donor sperm cycle resulted in the retrieval of 16 mature oocytes, 12 of which fertilized. Five embryos developed into blastocysts and were biopsied for elective PGT-A, resulting in three embryos classified as euploid and two as aneuploid. Autologous IVF cycle fertilization rate was similar to the donor cycle (72% vs 75%, respectively), while overall blastocyst development was higher in the donor IVF cycle (15% vs 42%, respectively). CONCLUSIONS: This case adds to the growing body of evidence of cases of DNAH1 variants in relation to an MMAF–specific phenotype, further distinguishing it from previous PCD associations.

This case also provided the opportunity to compare outcomes from autologous sperm with MMAF and donor sperm IVF cycles utilizing otherwise identical protocols. The fertilization rate was similar between the two cycles, while there was a lower rate of blastocyst development in the autologous cycle. This is consistent with previous research that has hypothesized that MMAF may have a negative impact on blastocyst development.

IMPACT STATEMENT: The results of this case report add to the existing evidence of DNAH1 and its association with the etiology of MMAF. Identifying additional variants, understanding associated phenotypes, and comparing IVF cycle outcomes can inform management of future MMAF cases.

SUPPORT: None.

INCIDENCE OF Y CHROMOSOME MICRODELETIONS AND MICRODISSECTION TESTICULAR SPERM EXTRACTION (MICRO TESE) IN JAPANESE AZOOSPERMIC PATIENTS. Tomomoto Ishikawa, M.D., Ph.D.,1 Kohei Yamaguchi, M.D., Ph.D.,2 Yasuhiro Ohara, M.D.1 Masakazu Doshida, MD, PhD.,2 Hidehiko Matsubayashi, MD, PhD.,2 Takumi Takeuchi, M.D., Ph.D.3 Reproduction Clinic Osaka, Osaka, Japan; Reproduction Clinic Tokyo, Tokyo, Japan.

OBJECTIVE: After Klinefelter syndrome, Y chromosome microdeletions are the second most frequent genetic cause of male infertility, with a prevalence of 2%-10% in non-obstructive infertility and more frequent in patients with azoospermia. The classical correlation of histopathology phenotypes with these three microdeletions comprises of complete absence of germ cells (Sertoli cell only syndrome) in patients with AZFa microdeletions, maturation arrest of meiosis in patients with AZFb microdeletions, and hypospermatogenesis in patients with AZFc microdeletions, however, individual variation in the extent of deletions has led to various spermatogenic phenotypes.

MATERIALS AND METHODS: We investigated the frequency of AZF microdeletions and SRR by micro TESE in patients with these microdeletions and therefore aimed to evaluate the correlation between AZF microdeletions and micro TESE results. A total of 1373 azoospermic in our clinics between September 2013 and December 2021 were enrolled. After the diagnosis of azoospermia, karyotype analysis and detection of Y chromosome microdeletions were performed on peripheral blood lymphocytes of these patients. Y chromosome microdeletions in AZFa, AZFb, and AZFc were detected using Promega Y Chromosome AZF Analysis System version 2.0 (Promega Co.). Twenty sequence-tagged sites within the AZF region of Yq11 and the sex-determining region Y gene were targeted for polymerase chain reaction (PCR) amplification.

RESULTS: One hundred and fifty-two AZF microdeletions (11.1%) were detected in the azoospermic patients. The most common deleted region was AZFb (60 cases, 4.4%). Among the patients, 17 (1.2%), 1 (0.1%), 42 (3.1%), 13 (1.0%), and 6 (0.5%) had AZFa, AZFb, AZFb+c, AZFb, and AZFb+a+b+c microdeletions, respectively. When the cases were grouped according to causes of infertility that could be detected, no Y chromosome microdeletions were detected in some cases (cases with Klinefelter Syndrome, hypogonadotropic hypogonadism, congenital absence of vas deferens, and 47, XXY karyotype). Fifty-three azoospermic men with AZF microdeletions underwent micro TESE, and spermatzoa were detected in 88.7% (47/53) of these men. In contrast, we detected spermatzoa in only 20.4% (109/534) of the azoospermic men without AZF microdeletions. The SRR was much higher in patients with AZFc microdeletions than that of patients without AZF deletions. Although three azoospermic men with AZFb+c microdeletions had also undergone micro TESE following patient request, we did not retrieve spermatzoa.
CONCLUSIONS: NOA patients with AZFc microdeletions had a high percentage of successful sperm retrieval by micro TESE. Our study emphasizes that diagnosis of Y chromosome microdeletions is critical for preconception genetic counseling and provides clinically valuable prognostic information to couples considering surgical sperm retrieval.

IMPACT STATEMENT: This study shows a high impact for the non-obstructive azoospermic couples with AZF microdeletions.

SUPPORT: None declared.

P-439 6:45 AM Tuesday, October 25, 2022
CRITICAL FERTILITY ISSUES FOR MEN WITH AZOOSPERMIA FACTOR C (AZFc) MICRODELETIONS.
Jessica A. Marinaro, MD, Nahid Punjani, MD MPH, Caroline Kang, MD, PhD, Peter N. Schlegel, MD, Weill Cornell Medicine, New York, NY; NewYork-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY.

OBJECTIVE: To evaluate semen parameters, sperm retrieval rates (SRR) and fertility outcomes for men with AZFc microdeletions.

MATERIALS AND METHODS: We retrospectively identified 157 men with a complete AZFc deletion on Y-chromosome microdeletion (YCMD) testing performed at a single academic institution between 4/1996 and 3/2022. Of these, 136 men had at least 1 documented semen analysis (SA), and 74 planned to pursue in-vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI) using their own sperm. If a microdissection testicular sperm extraction (mTESE) was required, it was performed by a single high-volume surgeon. Of the 74 men pursuing IVF/ICSI, 16 had sperm in the ejaculate and never required mTESE. Nine men (9/74, 12.2%) had sperm in the ejaculate on the day of a planned mTESE despite at least 1 prior SA with azoospermia and/or prior testis biopsy negative for spermatogenesis. Of the 58 men who underwent mTESE, the overall SRR was 62.1% (38/62). When excluding patients with a history of a prior sperm retrieval procedure at an outside hospital, the SRR was 76.3% (29/38).

To evaluate IVF/ICSI outcomes, we reviewed 145 planned cycles: of these, 40 were canceled (n=21) or used donor sperm (n=19) due to failed mTESE. Of the remaining 105 cycles, fresh testicular sperm (n=59, 56.2%) and fresh ejaculated sperm (n=40, 38.1%) were primarily used, though 6 cycles used frozen testicular (n=5, 4.8%) or frozen ejaculated sperm (n=1, 1.0%). Of 105 cycles, there were 82 embryo transfers (ET): 48 using fresh testicular sperm, 30 using fresh ejaculated sperm, and 4 using frozen sperm. Live birth rates per ET were similar between cycles using fresh testicular sperm (37.5%, 18/48) and those using fresh ejaculated sperm (36.7%, 11/30).

CONCLUSIONS: This large series validates early work suggesting a high SRR among AZFc deletion patients, particularly those undergoing an initial sperm retrieval procedure. While most men with AZFc deletions are azoospermic (64.7%), over one-third can be found to have at least rare sperm in the ejaculate. These results may overestimate the frequency of azoospermia with AZFc deletions, as some men with sperm in the ejaculate may not have been tested for Y microdeletions. When used for IVF/ICSI, both fresh testicular and fresh ejaculated sperm have similar live birth rates.

IMPACT STATEMENT: Men with AZFc deletions should be encouraged to provide an ejaculated semen sample prior to undergoing mTESE, even if they have a history of azoospermia and/or prior testis biopsy negative for spermatogenesis. For the remaining men, sperm are commonly found with mTESE. When sperm from these men are used for IVF/ICSI, similar live birth rates are obtained with ejaculated and surgically retrieved sperm.

SUPPORT: Authors JM and CK are supported in part by The Frederick J. and Theresa Dow Wallace Fund of the New York Community Trust.

P-440 6:45 AM Tuesday, October 25, 2022
SEmen Microbiome Profiling in Men With Non-obstructive Azoospermia: A Next-Generation Sequencing Analysis.
Joseph M. Israeli, BA, Maria Camila Suarez Arbelaez, MD, Craig D. Tipton, BS, Joon Yau Leong, MD, Emad Ibrahim, M.D., H.C.L.D., Kajal Khodamoradi, PhD, Sabita Roy, PhD, Praveen K. Singh, PhD, Ranjith Ramasamy, M.D.1 University of Miami Miller School of Medicine, Miami, FL; 2RTR Genomics, MicrogenDX, Lubbock, TX; 3Thomas Jefferson University, Philadelphia, PA; 4University of Miami.

OBJECTIVE: Detection of a microbiome profile coupled with advanced genetic sequencing has opened a new research frontier. We hypothesized that the semen microbiome profile in men with non-obstructive azoospermia (NOA) would differ from that of fertile controls (FC).

MATERIALS AND METHODS: We did a prospective study of men with NOA including FC. NOA was diagnosed using semen analysis in combination with clinical characteristics (small testis size and FSH >10 IU/mL). FC were men who fathered children and later underwent vasectomy. We used Next Generation Sequencing (NGS) including quantitative PCR and 16s rRNA V1/V2 region comprehensive sequencing using Illumina MiSeq technology on semen samples. We analyzed alpha diversity through overall richness, Shannon diversity, and beta diversity via Bray-Curtis difference. Differential abundance was evaluated with ANCOMBC procedure. Variables were assessed for significant associations.

RESULTS: During the study period, 21 men with NOA and 36 FC were enrolled. BMI, age, antibiotic use, race, and ethnicity was similar between men with NOA and FC. Alpha diversity was not observed in overall richness testing. Shannon diversity, and hill1 diversity, suggesting that the groups were similar overall in species types and evenness. Beta diversity was insignificant based on Bray-Curtis, suggesting that the samples within each group were just as different from one another as they were to the other group’s samples. A total of 24 species varied significantly in abundance between men with NOA as compared to FC (q rounded to 0) - Table 1. Two genera varied significantly: Aerococcus was higher in NOA, and Burkholderia was higher in FC.

CONCLUSIONS: In terms of the types of species and overall intergroup comparisons there is no difference in seminal microbiome between NOA and FC. On the species and genus levels there is a significant difference in abundance – 24 species including known pathogen C. Trachomatis, and 2 genera varied between groups. This may be associated with the testicular microbiome or azoospermia etiology.

IMPACT STATEMENT: The pathogenicity/commensalism of differentially abundant bacteria warrants further study in the context of fertility and the genitourinary tract. These findings may direct further study on microbiome impacts on fertility by guiding the use of pre/pro/anti-biotics.

ACKNOWLEDGMENTS: Funding, sequencing, and statistical support from MicroGenDX. SUPPORT: MicrogenDX.

Most Differential Species Per Group

<table>
<thead>
<tr>
<th>NOA</th>
<th>FC</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. pilibacense</td>
<td>C. trachomatis</td>
</tr>
<tr>
<td>P. catoniae</td>
<td>P. melaninogenica</td>
</tr>
<tr>
<td>D. propionifaciens</td>
<td>B. cepacia</td>
</tr>
<tr>
<td>S. rhizogenes</td>
<td>T. aromaticivorans</td>
</tr>
</tbody>
</table>

E-POSTER ABSTRACT SESSION: W1

P-441 6:45 AM Wednesday, October 26, 2022
WHAT IS THE BEST TECHNIQUE TO RECOVER SPERMATOZOA FROM OBSTRUCTIVE Azoospermic Patients? Renato Fraietta, MD, PhD, Renata De Carvalho, PhD, Fernando Vasconcellos, MD Federal University of Sao Paulo, Sao Paulo, Brazil.

OBJECTIVE: Verify which sperm retrieval technique is more effective, by comparing reproductive outcomes, for men who have azoospermia due to obstructive causes.

MATERIALS AND METHODS: Review registry and Study selection The systematic review was built according to the PRISMA protocol, and it was registered on the PROSPERO platform.

Two independent authors carried out sensitive searches in the databases: MEDLINE, Cochrane Library, Lilacs, and Web of Science.
The PICO/PECO search strategy was used.

Data extraction

The main outcome considered was the retrieval rate of viable sperm. Secondary outcomes, such as cryopreservation possibility, fertilization, and pregnancy rates were also considered.

RESULTS: Literature Search

Using the inclusion/exclusion criteria previously established we had 70 studies to analyze. We used the Rayyan platform to perform the study selection, by two independent authors. At the end of this process, 11 articles were included in the systematic review.

Sperm Retrieval

Regarding the main focus of our study, 8 out of the 11 articles considered that PESA should be the first choice as a treatment. These articles advise that if the PESA approach fails, the next approach should be direct to the testes. However, when we analyze purely numerical data, in general, MESA retrieval rates are superior when compared to PESA. This can be seen on table 1.

Secondary Outcomes

Cryopreservation was the secondary outcome that most comparisons could be made, and again MESA proved to have higher rates of successful cryopreservation.

PESA's advantages, such as procedure cost, post-operative recovery, availability, and no need for hospitalization were considered in many studies.

CONCLUSIONS: The conclusion of our study points to MESA as being the best approach, considering men with obstructive azoospermia, due to its higher sperm retrieval rate and the possibility of cryopreservation.

IMPACT STATEMENT: This study has great importance because it shows evidence that PESA should be the first choice as a treatment. These articles advise that if the PESA approach fails, the next approach should be direct to the testes.

Table 1.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sperm retrieval (PESA/MESA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dohle</td>
<td>18/29 (62%); 4/4 (100%)</td>
</tr>
<tr>
<td>Tsirigitis</td>
<td>36/47 (76.6%); 6/6 (100%) + 2/11 (after PESA failed (18.2%))</td>
</tr>
<tr>
<td>Phillipson</td>
<td>6/6 (100%); 21/22 (95.4%)</td>
</tr>
<tr>
<td>Lin</td>
<td>66/109 (61%); 37/40 (93%) after PESA failed</td>
</tr>
<tr>
<td>Rosenlund</td>
<td>3/8 (37.5%); 3/5 (60%); TESA</td>
</tr>
<tr>
<td>Patrizio</td>
<td>46/46 (100%); NR</td>
</tr>
<tr>
<td>Glin</td>
<td>65/79 (82%); NR</td>
</tr>
<tr>
<td>Tsirigitis</td>
<td>59/69 (85.5%); NR</td>
</tr>
<tr>
<td>Levine</td>
<td>6/7 (85.7%); 1/1 (100%) after PESA failed</td>
</tr>
<tr>
<td>Schroeder</td>
<td>NR; 88/93 (94.6%)</td>
</tr>
<tr>
<td>Borges</td>
<td>27/40 (67.5%); NR; TESA</td>
</tr>
</tbody>
</table>

NR = not realized
TESA = testicular sperm aspiration

P-443 6:45 AM Wednesday, October 26, 2022

PROTOCOLS DESIGNED TO IMPROVE A MAN’S OVERALL HEALTH ARE LINKED TO INCREASED CAPACITATION ABILITY: A MULTICENTRIC, PROSPECTIVE, BLINDED ANALYSIS. Fady I. Sharaara, M.D.,1 Eric Seaman, M.D.,2 Anna Lysenko-Brockman, M.S.,1 Haneen Taha, M.S.,1 Cristina Cardona, Ph.D.,1 Garry Charles Ostermeier, Ph.D.,1 Alexander J. Travis, VMD, Ph.D.1 Virginia Center for Reproductive Medicine, Reston, VA;2 New Jersey Urology, MILLBURN, NJ;1 Androvia LifeSciences, Mountainside, NJ.

OBJECTIVE: Traditional semen analysis (SA) parameters are declining; hypotheses as to the cause focus on worsening men’s health due to environmental exposures and/or lifestyle. SA evaluates ejaculate volume, sperm motility, concentration, and morphology, but doesn’t assess sperm fertilizing ability, which causes half the cases of male infertility. It is therefore unknown whether reported declines in SA values have any impacts on actual male fertility. Prior to fertilization, sperm must capacitate. Cap-Score™ measures the capacitation ability of a man’s sperm and prospectively predicts his probability of generating a pregnancy (PGP). Here, we evaluate the effects of protocols designed to improve a man’s overall health on his SA and capacitation ability.

MATERIALS AND METHODS: 55 men questioning their fertility were evaluated for Cap-Score™ and SA at two independent clinics. Recommendations were made to improve overall health: Clinic 1) quit use of tobacco, marijuana, or alcohol; avoid laptops on laps or Jacuzzi/saunas; lose weight if obese; increase Vitamin D intake (≥ 2k IU/day); and start supplements (Androferti: n=30; vitamins C, E, B12, Folate, Zinc, selenium, L-carnitine, & coenzyme Q10), or Conception XR (n=8; vitamins C, E, D, Folate, Zinc, selenium, & Lycopene): Clinic 2) limit alcohol, tobacco, marijuana; exercise at least 3 times a week; avoid processed foods with pesticide residues; & start supplements N acetyl cysteine & Proexid Plus (n=17; Vitamins C, B12, Folic Acid, Zinc, Selenium, L-Carnitine, Acetyl-L-Carnitine, & coenzyme Q10). A second blinded analysis was done ~13 weeks later; paired t-tests were done to compare before and after lifestyle changes.
RESULTS: All supplements impacted measures similarly (p > 0.05; ANOVA). An increase in Cap-Score from 23.5 ± 0.9 to 27.6 ± 1.0 (p = 0.001; n = 55), corresponding to a 25% increase in a man’s PGF, was observed. Recommended lifestyle changes had no impact on semen volume (p = 0.479; n = 54), sperm concentration (p = 0.562; n = 54), or sperm motility (p = 0.112; n = 54). Strict normal morphology was available from Clinic 1 and improved (1.7 ± 0.2 to 3.3 ± 0.5; p = 0.001; n = 38). No relationship was detected between Cap-Score and strict normal morphology before (p = 0.566) or after (p = 0.156) lifestyle changes.

CONCLUSIONS: Similar lifestyle changes recommended by two independent clinics improved capacitation ability.

IMPACT STATEMENT: Promoting a man’s overall health through lifestyle change and nutritional supplementation increased capacitation ability and PGF.

SUPPORT: Androvia LifeSciences performed the Cap-Score as part of patient standard of care.Physicians received no compensation from Androvia.

P-444 6:45 AM Wednesday, October 26, 2022
SPERM GENOMIC AND EXTRAGENOMIC CARGO IN RECURRENT MISCARRIAGE AND IMPLANTATION FAILURE. Vidhu Dhawan, MD,1 Neena Malhotra, MD,1 DNB FRCOG,2 Neeta Singh, MD,1 Vaatsa Dadhwal, MD,2 Rima Dada, MD, PhD,2 1Room no. 1010, Dept. of Anatomy, First Floor, Teaching Block, All India Institute of Medical Sciences, New Delhi, India; 2All India Institute of Medical Sciences, Obstetrics & Gynaecology, New Delhi, India; 3Professor, New Delhi, India; 4All India Institute of Medical Sciences, Anatomy, New Delhi, India.

OBJECTIVE: The defects in the integrity of both nuclear and mitochondrial genome, oxidative stress, decreased telomeres and dysregulation in the expression of the genes critical for early embryonic development have been implicated as a cause of pregnancy loss. Assessing the expression of the genes critical for post fertilization events and reproductive outcomes may help us better understand the unknown molecular mechanism involved in the etiology of miscarriage and implantation failure. The objective of the present case control study was to analyze the contribution of sperm genomic and extragenomic cargo in pregnancy loss.

MATERIALS AND METHODS: The prospective case control study was conducted on the male partners of couples experiencing recurrent pregnancy loss (RPL) (n = 132), recurrent implantation failure (n = 79), and those with previous history of conception with congenital malformations (CMF) (n = 25), fertile controls (n = 102). Semen samples were obtained and analyzed by WHO 2010 criteria. The sperm gene expression was analyzed by 2-ΔΔCT method for the relative quantification of FOXG1, SOX3, STAT4, RPS6, RBM9, RPL10A, RPS17, RPL29, WNT5A, HSP90, TOMM7, EIF5A, OGG1 and PARP1 after normalization with internal controls GAPDH and β-actin. The levels of seminal ROS (RLU/s/10^6 sperm) and semen ROS and DFI were calculated by an elution method with an estimate DNA damage (%) and relative sperm telomere length (STL) were assessed by chemotherapy-induced apoptosis and sperm telomere length and telomere length assay (SCSA) and qPCR respectively. The data was analyzed by statistical software Statate 14.0. Kruskal Wallis H test followed by Bonferroni correction were used to compare outcome and markers among four group.

RESULTS: The expression of FOXG1, SOX3, RPS6, RBM9, RPS17, HSP90, TOMM7, EIF5A, and OGG1 showed significant difference between RPL patients and controls (p < 0.001***), while SOX3, RBM9, WNT5A, HSP90, TOMM7, and EIF5A showed significant difference in RIF group (p < 0.001****) and the expression of only HSP90, TOMM7, EIF5A varied significantly in CMF group (p < 0.001**). The relative STL was significantly lower in all patient groups (p < 0.001**), and ROS and DFI were significantly higher with respect to controls (p < 0.001***, p < 0.001*** respectively). The STL correlated negatively with ROS and DFI.

CONCLUSIONS: The current study supports the hypothesis that there may be differential expression pattern of genes pertinent for early embryogenesis between healthy fertile males and male partners of couples with pregnancy loss.

IMPACT STATEMENT: To the best of our knowledge the present study is one of the first studies to analyse the contribution of sperm molecular factors across three patient categories.

P-446 6:45 AM Wednesday, October 26, 2022
THE EFFECTS OF COLLECTION LUBRICANT REVISED: NEWER FORMULATIONS APPEAR TO HAVE LESS EFFECT ON POST-COLLECTION SEMEN QUALITY. Lindsay L. Penrose, PhD, Baylee Richardson, B.S., Alisa White, B.S., Samuel D. Prien, Ph.D. Texas Tech University Health Sciences Center, Lubbock, TX.

OBJECTIVE: It is common for patients seeking infertility treatments to use lubricant provided by the clinic to aid in sperm collection. Although lubricant effects on sperm motility have been studied, there is no universal consensus on a “safet” lubricant. Previous research has documented that lubricant contamination during collection can affect sperm motility, morphology, and swimming velocity, and it may adversely affect fertility treatment. The objective of the current study was to compare “newer” lubricants to those currently in use, including what has been described as an “organic, plant-based lubricant.”

MATERIALS AND METHODS: Semen samples were obtained from 12 individuals undergoing routine sperm analysis. Samples were obtained by masturbation at the clinic. The samples had to have a minimum of 40x10^6 motile cells to be included in the study. Samples underwent a routine semen prep for IUI but were diluted to a final volume of 9 mL to cross all treatments. A 24-well cell culture plate was prepared with an estimated 0, 10, 50, and 100 μL of four types of lubricants: Henry Schien Lubricating Gel (standard – A), Pre-Seed™ Fertility-Friendly Lubricant (fertility – B), Überlube (silicon – C), or Fav Lubricant (water – D). The final treatment was the control utilizing semen cultured alone without any treatment. Focusing on motility as the primary outcome, a standard lubricating gel was the control at moderate and high levels as early as 1 hr after exposure. Only the highest levels of contamination of the water-based lubricant had decreased motility over the 24 hrs compared to the control (P < 0.02), and the silicone lubricant (D) performed equally well to the control over the entire 24 hrs regardless of concentration (P = 0.643).

P-445 6:45 AM Wednesday, October 26, 2022
E-CIGARETTE AEROSOL EXPOSURE DECREASES SPERM CONCENTRATION IN MICE. Daniel Pelzman, MD,1 Patrick Walsh, BS,2 Miguel Brieno-Encinues, MD, PhD,2 Kathleen Hwang, MD1 UPMC, Pittsburgh, PA; 2University of Pittsburgh.

OBJECTIVE: E-cigarette usage, also known as vaping, has dramatically increased in popularity over the last decade, especially in young adults. The effects of e-cigarette aerosol exposure on spermatogenesis remains uncertain.

MATERIALS AND METHODS: We exposed mice to either commercially available, nicotine-containing e-cigarette fluid (exposure) or aerosolized glycine (control). Sixteen mice were placed in a 5-week protocol (8 control, 8 exposed), and sixteen mice were placed in a 10-week protocol. Durations were derived from normal time of spermatogenesis in mice (35 days). Exposure was performed using a commercially available whole-body aerosolization unit (La Jolla Alcohol Research, Inc). Glycerin was chosen as the control due to its safety. After exposure was completed, the mice were sacrificed and testes/epididymides were removed. Epididymal fluid sperm concentration was measured for each mouse using a hemocytometer.

RESULTS: There was no attrition during the experiment and all mice were included in the final analysis. In the 5-week cohort, exposed mice had a lower sperm concentration than control mice, although this result was not statistically significant (4.7±2.6 x 10^6 vs 7.4±4.1 x 10^6, p > 0.1). Interestingly, in the 10-week exposure group, sperm counts in both cohorts were higher, and there was no difference between groups (11.3±4.3 x 10^6 vs 10.0±4.3 x 10^6). Exposed animals demonstrated high levels of DNA fragmentation via COMET assay.

CONCLUSIONS: Five-week exposure to e-cigarette vapor reduced sperm concentrations in mice. A 10-week exposure did not appear to impact concentration. It is unclear why longer-term exposure was associated with higher sperm concentrations but may be related to compensatory mechanisms during spermatogenesis. Further research will be needed to understand other effects of e-cigarette usage on the male reproductive tract.

IMPACT STATEMENT: E-cigarettes may transiently decrease sperm concentration in mice, indicating a potentially harmful effect on spermatogenesis.
CONCLUSIONS: As in earlier studies, the data suggests that lubricant selection can adversely affect semen quality at the time of analysis and infertility treatment. However, new lubricant formulations appear to lessen these effects. Further study is needed to confirm these observations and their impact on cycle outcomes.

IMPACT STATEMENT: Lubricant selection at the time of collection may significantly impact fertility treatment.

SUPPORT: None.

P-447 6:45 AM Wednesday, October 26, 2022
DECLINE IN THE QUALITY OF SEMEN FROM SPERM DONORS ACROSS TWO DIFFERENT CLIMATES OVER THE COURSE OF A DECADE. David Miller, MD,1 Alexander Weber, BS,1 Rohit Reddy, B.S.,1 Ranjith Ramasamy, M.D.1,1 UPMC, Pittsburgh, PA;2 University of Miami, Miami, FL;1 University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: The effects of the environment on male fertility are incompletely understood and further research is needed to understand this complex interaction. We hypothesized that men from a warm climate would have poorer quality semen parameters than men from a cool climate. To better understand the impact of climate on male fertility, we assessed sperm in a population of sperm donors from two different climates.

MATERIALS AND METHODS: Sperm parameters from sperm donors at a sperm bank were obtained from 2008 and 2020. To delineate differences over time, semen parameters were assessed from two 3-year periods 2009-2011 and then from 2018-2020. Sperm donations occurred in two different locations with two different climates: Seattle, WA (cool climate) and Tempe, AZ (warm climate). Donors live in the surrounding area of these locations as they are required to donate a few times per month. The mean annual temperature for the counties where Seattle (King County) and Tempe (Maricopa County) was obtained from PRISM Climate Group.

RESULTS: There were a total of 46,995 total sperm donor records included in our study. The mean annual temperature for King County, WA was 50.2°F degrees Fahrenheit from 2009-2011 and 51.7°F from 2018-2020. The mean annual temperature for Maricopa County, AZ was 72.5°F from 2009-2011 and 72.9°F from 2018-2020. The mean sperm concentration for donors from the cool climate was 77.2 million/ml and 61.1 million/ml from 2008-2011 and 2018-2020 respectively. For donors from the warm climate mean sperm concentration was 74.7 million/ml and 57.7 million/ml from 2009-2011 and 2018-2020 respectively. Total sperm count was variable between climates for the time periods assessed but notably decreased across both climates from a mean total count of 390.2 million in the warm climate from 2009-2011 to 188.8 million from 2018-2020 and from a mean of 280.9 million in the cool climate from 2009-2011 down to 208 million from 2018-2020. Progressive motility also decreased from an average of 80% for both climate groups in 2009-2011 down to an average of 60% from 2018-2020 for both groups. 

CONCLUSIONS: There was an overall decrease in the quality of semen parameters over time for donors from both climates. There was a slight decrease in sperm concentration in donors from the warm climate as compared to the cool climate. However, these differences between climates did not extend to total sperm count or total motile sperm count.

IMPACT STATEMENT: Our results further expand on the growing body of literature showing continued declines in sperm concentration over time. Additionally, there was a decrease in sperm concentration in donors from a warm climate compared with peers from a cool climate.

P-448 6:45 AM Wednesday, October 26, 2022
LONG-TERM EVALUATION OF SPERM PARAMETERS FOLLOWING COVID-19 mRNA VACCINATION. Paris Díaz, BS,1 Alexandra Dullea, MS,1 Mehul S. Patel, MD,1 Ruben Blachman-Braun, MD, M.Sc.,2 Rohit Reddy, B.S.,1 Kajal Khodamoradi, PhD,1 Emad Ibrahim, M.D., H.C.L.D.1 Joginder Bidhan, MSc,1 Akhil Muthig, MD,1 Ranjith Ramasamy, M.D.1 University of Miami Miller School of Medicine, Miami, FL;1 University of Miami School of Medicine, Desai Sethi Urology Institute, Miami, FL;1 University of Miami, Desai Sethi Urology Institute, Miami, FL; Desai Sethi Urology Institute, Miller School of Medicine, University of Miami, Miami, FL;2 University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Despite the demonstrated safety of COVID-19 mRNA vaccines, a previous survey demonstrated that unknown long-term affects to fertility was a major reason for vaccine hesitancy. We conducted a single-center prospective study to investigate the long-term impact of COVID-19 vaccination on sperm parameters of healthy men. We hypothesized that COVID-19 vaccination (and booster doses) would not negatively impact sperm parameters in the long-term.

MATERIALS AND METHODS: Twelve healthy male volunteers between the ages of 18-50 years old with pre-vaccination semen analyses completed follow-up analyses between September 2021 - March 2022. Participants were required to provide documentation demonstrating at least two mRNA vaccine doses.

Semen analyses evaluated volume, sperm concentration, total motility, and TMSC. The number of days absent prior to sample collection was documented during the visit. The primary outcome was median change in the total motile sperm count at least 9 months following fully vaccinated COVID-19 status.

Individuals who admitted a history of infertility or previous azoospermia were excluded from study participation. After calculating data distribution on normality test, medians, and interquartile ranges (IQRs) were reported for all variables. The Wilcoxon rank sum test was used to compare pre- and post-vaccination semen parameters. A 2-tailed P < .05 was considered statistically significant.

RESULTS: A total of 12 men volunteered in our study median age 26 [25 - 30] years. Subjects provided follow-up semen samples at a median of 10.5 months following the second vaccine dose. There were no significant changes in any semen parameters at baseline, or months 3, 6, or 10 months following vaccination. Baseline samples demonstrated median sperm concentrations and TMSC of 29.5 million/cc [9.3 – 49] and 31 million [4-51.3], respectively. At follow-up, sperm concentration and TMSC were 43 [20.5 – 63.5] (p=0.407) and 43.5 [8.5 – 102.8] (p=0.519). Respectively. Of note, there were no significant changes in semen volume nor total motility (%) at follow-up. Two of the men were oligospermic at baseline. Of these two men, one was found to be normospermic at follow-up and the other remained oligospermic.

CONCLUSIONS: COVID-19 mRNA vaccines and boosters do not appear to negatively impact the semen parameters of healthy males even 10 months following vaccination. Our study and future studies should add to the growing body of evidence on the long-term safety of vaccines and potentially decrease vaccine hesitancy.

IMPACT STATEMENT: Vaccination against COVID-19 does not negatively impact the semen analyses of healthy young men.
RESULTS: A total of 8596 SA were included in the analysis (Table 1). Black men were significantly older (38.2 ±4.3 yrs, p=0.001) and had a higher BMI (30.1 kg/m², p= <0.001) than men in other groups. Most samples (97.9%) were collected through masturbation after a prior mean abstinence of 3.7±4.5 days. No differences were identified in azoospermia, asthenozoospermia and teratozoospermia diagnoses. However, Black men had the highest incidence of oligozoospermia among groups (38% vs White 17%, Asian 16%, Hispanic 11.2%, other 15%, non- specified 20%, p= <0.0001). In a logistic regression model adjusting for age and BMI, Black men had lower odds of having a normal SA compared to White men (aOR=1.06, 95% CI 1.05-1.08, p= .03).

CONCLUSIONS: To our knowledge, this is the largest study analyzing SA of men undergoing IVF of different racial groups. Our data indicates that Black men are more likely to have abnormal semen parameters when compared to other groups.

IMPACT STATEMENT: These data indicate that race remains a stratifying factor in reproductive health. Further studies underlying the mechanisms impacting male reproductive outcomes are warranted.

P-450 6:45 AM Wednesday, October 26, 2022

SOCIO-ECONOMIC STATUS IS ASSOCIATED WITH ASSISTED REPRODUCTIVE TECHNOLOGY (ART) UTILIZATION AND FERTILITY OUTCOMES IN A COHORT OF SUB-FERTILE MEN. Joshua J. Horns, PhD, Joshua A. Halpern, MD, MS, Kiarad Fendereski, MD, Joemy M. Ramsay, PhD, Tim G. Jenkins, PhD, James Hotaling, MD, Joseph M. Letourneau, MD, Lauren Elizabeth Verrilli, MD, Utah, Salt Lake City, UT; Department of Urology, Northwestern University Feinberg School of Medicine, Chicago, IL; University of Utah School of Medicine, Salt Lake City, UT; Brigham Young University, Provo, UT.

OBJECTIVE: To understand how socio-economic status (SES) impacts patterns of fertility and use of assisted reproductive technology (ART) in sub-fertile men.

MATERIALS AND METHODS: We identified all men in the Utah population database who underwent a semen analysis (SA) that met established oligozoospermic criteria for both count and concentration. We identified each person’s residential location at the time of their first SA and estimated their SES using state-level metrics of the area deprivation index (ADI). State-level ADI is measured on a discrete 1-10 scale (where 10 is the most deprived, lowest SES value) and we binned each subsequent pair of ADI scores (i.e. 1 and 2, 3 and 4, etc.) to create five levels of ADI. We also recorded age and semen.

RESULTS: A total of 8596 SA were included in the analysis (Table 1). Black men were significantly older (38.2 ±4.3 yrs, p=0.001) and had a higher BMI (30.1 kg/m², p= <0.001) than men in other groups. Most samples (97.9%) were collected through masturbation after a prior mean abstinence of 3.7±4.5 days. No differences were identified in azoospermia, asthenozoospermia and teratozoospermia diagnoses. However, Black men had the highest incidence of oligozoospermia among groups (38% vs White 17%, Asian 16%, Hispanic 11.2%, other 15%, non- specified 20%, p= <0.0001). In a logistic regression model adjusting for age and BMI, Black men had lower odds of having a normal SA compared to White men (aOR=1.06, 95% CI 1.05-1.08, p= .03).

CONCLUSIONS: To our knowledge, this is the largest study analyzing SA of men undergoing IVF of different racial groups. Our data indicates that Black men are more likely to have abnormal semen parameters when compared to other groups.

IMPACT STATEMENT: These data indicate that race remains a stratifying factor in reproductive health. Further studies underlying the mechanisms impacting male reproductive outcomes are warranted.

SUPPORT: None
THE IMPACT OF SMOKING ON SEMINAL BIO-MARKERS IN SUBFERTILE MEN. Sabrina Lasini Gruhl, MBBS, 1 Lee Mee Ho, BSc, 2 Marris Yin Xuan Sim, BSc, 3 Amy Shaw Ni Lee, MSc, 3 Serene Liqing Lim, MBBS, MRCOG, 3 Tze Tein Yeo, MBBS, MRCOG (UK), FAMS, 3 Su Ling Yu, MBBS, MMed, FRCOG, FAMS, Dr, 3 Harmeshree Rajesh, FRCOG 3 KK Women’s and Children’s Hospital, Singapore, Singapore; 2Singapore General Hospital, Singapore, Singapore.

OBJECTIVE: This study is to evaluate the effect of smoking on semen quality and the levels of seminal biomarker of the male accessory glands in subfertile men.

MATERIALS AND METHODS: A total of 200 male patients undergoing assessment for subfertility at Singapore General Hospital, Singapore, were recruited prospectively from June 2020 to August 2021. Samples of their semen were assessed for seminal parameters as well as biomarkers fructose, citrate and zinc, and compared against their smoking habits. Biomarker tests were performed on seminal plasma using a random-access automatic analyser, model A15 (BioSystems S. A., Spain). Patients were grouped as heavy-smokers (smoked ≥ 10 sticks of cigarette per day), light-smokers (<10 sticks/day) and non-smokers. Correlations between semen parameters and the biomarkers levels were assessed using non-parametric Spearman’s correlation coefficient, r, and these parameters were compared among the various smoker groups using non-parametric Mann-Whitney U test.

RESULTS: Seminal zinc (r = -0.163, P < 0.021) and citrate levels (r = -0.178, P = 0.013) were negatively correlated to the number of cigarette sticks smoked per day. 11% of the recruited patients were heavy-smokers (smoked median of 10 sticks/day), 10% were light-smokers (median 6 sticks/day) and the rest were non-smokers. Heavy-smokers had significantly lower sperm concentrations as compared to non-smokers and light-smokers, 35.3 vs 42.2 vs 73.2 million/mL, respectively. They also had lower total motile sperm count (TMSC), 30.9 vs 41.0 vs 103.6 million, respectively. Both heavy-smokers and light-smokers had similar zinc concentrations (4.9 and 4.6 μmol/ejaculate) and citrate levels (52.6 and 52.6 μmol/ejaculate), which were comparatively lower than the non-smokers, zinc levels of 6.8 μmol/ejaculate and citrate levels of 81.6 μmol/ejaculate, respectively, P < 0.05.

CONCLUSIONS: This study demonstrates that smoking has a negative effect on zinc and citrate levels, which therefore, significantly reduce sperm concentrations and TMSC.

IMPACT STATEMENT: Smoking has a deleterious effect on sperm health and in addition to standard fertility treatments, smoking cessation advice should be strongly recommended.

SUPPORT: 1. Education, Training and Research Fund from the Department of Obstetrics & Gynaecology, Singapore General Hospital.
2. Loan of random-access automatic analyzer, model A15 analyzer (BioSystems S.A., Spain), supply of reagents and consumables from BiomediX Singapore Pte Ltd, Singapore.


P-454 6:45 AM Wednesday, October 26, 2022

PROTEIN TYROSINE PHOSPHORYLATION MEASUREMENT THROUGH FLOW CYTOMETRY MAY BE A POTENTIAL NOVEL BIOMARKER OF HUMAN SPERMATOZOA CAPITATION AND FUNCTIONAL STATUS: A PILOT STUDY. Ana Ortiz Vallecillo, MSc, 1 Esther Santamaría-López, MSc, 2 Francisco María Pinto Pérez, PhD, 3 Luz Cadenas, PhD, 4 Manuel Fernández-Sánchez, MD, PhD, 5 Cristina González-Ravina, PhD 6 Seville, Sevilla, Spain; 1IVI-RMA Sevilla, Seville, Spain; 2Instituto de Investigaciones Químicas, CSIC, Seville, Spain; 3IVI-RMA Sevilla, Seville, Spain.

OBJECTIVE: To determine if the measurement of tyrosine phosphorylation (pTyr) could be validated as a novel biomarker of sperm capacitation that reflects the capacitation and functional status of a semen sample. Do pTyr levels differ among fertile and sub-fertile men?

MATERIALS AND METHODS: pTyr of 75 semen samples of fertile (F) (n=29) and sub-fertile (SF) (n=46) men was evaluated to assess the measurement of pTyr as a functional biomarker. Flow cytometry was used to quantify pTyr level before and after capacitation and at different incubation times (1 hour and 3 hours) after sample processing. Sperm concentrations and TMSC.
capacitation was performed using discontinuous density gradient centrifugation. T-Test was used to compare the age between the groups, Mann-Whitney U test was used to compare absolute capacitation rate (total progressive motile sperm after capacitation/total progressive motile sperm between the two groups) (SF= 22.2, IQR: 14.8-41.2; F= 30.2, IQR: 23.3-46.9; p>0.05). We found no statistically significant differences between pTyr before (SF= 1.2, IQR 0.7-2.1; F= 1.5, IQR: 0.9-2.5; p>0.05) and after capacitation (SF= 2.7, IQR 1.3-7.1; F= 2.8, IQR: 2.5-1.1; p>0.05) and after 1 (SF= 3.9, IQR 1.9-12; F= 4.9, IQR: 3.9-9; p>0.05) and 3 hours of incubation (SF= 6.5, IQR 3.2-16; F= 10.4, IQR: 5.18-8; p>0.05) post-capacitation between sub-fertile and fertile individuals. Although not statistically different, the median in the fertile group was slightly higher in all of the situations analyzed. Within each group, percentage of pTyr was significantly higher after capacitation compared to the fresh sample and after 1 and 3 hours of incubation compared to the capacitated sample (p<0.001 for all).

CONCLUSIONS: We have observed a significant increase in the percentage of pTyr in fertile and sub-fertile men after capacitation and after 1 and 3 hours of incubation. However, with the sample size included, we detected no significant differences in pTyr levels between the group of men with known fertility and the group of sub-fertile men.

IMPACT STATEMENT: pTyr is considered one of the most relevant intracellular signaling events in the capacitation process and in the regulation of sperm function. However, it is currently unknown whether determination of pTyr levels by flow cytometry could be established as a novel biomarker of sperm capacitation and functional status in human semen samples, which could have important implications for men with fertility problems. Our results show that no significant differences could be found between fertile and sub-fertile men, although study sample size has not yet been completed. Hence, we still cannot provide a final answer to the study question.

SUPPORT: The study was funded by The Centre for the Development of Industrial Technology, CDTI IDI-20200571 and supported by an FP19/03393 predoctoral program fellowship from the Ministry of Science, Innovation and Universities, Government of Spain (to A.O.V.).

P-455 6:45 AM Wednesday, October 26, 2022
RAISED SPERM DNA FRAGMENTATION INDEX, IS THERE AN EFFICIENT INTERVENTION TO OPTIMIZE REPRODUCTIVE OUTCOMES? – A FOUR ARM RANDOMIZED CONTROL TRIAL. Krishna Mantravadi, Dr., MBBS, PGD-HOM, Masters in clinical embryology, Durga Gudela Rao, Dr., MRCOG, Jagadeesh Kumar Manepalli Veera, Dr., BVSC, Priyadarshini Sunanda, DR, PhD, 1 1 Oasiss fertility, Hyderabad, India; 2 Oasiss Fertility, Hyderabad, India.

OBJECTIVE: To determine the best intervention that would reduce the raised SDF and evaluate their impact on outcomes.

MATERIALS AND METHODS: This prospective RCT approved by institutional Ethical Committee (IEC) done between October2020-January2022. Couples undergoing IVF with raised SDF were randomized into four arms i.e. TESA(n=10), MACS(n=10), Microfluidics(n=16) and Daily ejaculation(n=10) for sperm selection. Male with SDF>25% & Age 25-40yrs were included. Male Age >45yrs, Female >37yrs, BMI > 30 and men with history of smoking, Binge Alcohol, Varicocele were excluded. Couples who failed to conceive after one failed IVF cycle were offered testing for SDF. SDF>25% were included in the study. SDF for TESA arm was done by sperm chromatin dispersion assay and for other groups by sperm chromatin structural assay. TESA was done as per standard operating procedure of our clinic. MACS, Microfluidics & per the instruction from the manufacturer. Recruited subjects with high SF, after randomisation were subjected to oocyte retrieval, ICSI, Blastocyst Culture, Freeze all policy and Frozen Embryo Transfer in subsequent cycle with two good grade blastocysts.

Our primary outcome for this study was reduction of SDF value. We also evaluated Reproductive outcomes – Blastocyst Formation Rate (BFR), Clinical Pregnancy rates (CPR), Implantation rates (IR).

RESULTS: Mean Reproductive Outcomes for TESA, Microfluidics, MACS & Daily ejaculation were as follows:
- Mean of DFI on raw sample: 39.2vs 35.7vs 37.1 vs 37.1 (P = 0.827)
- Mean of DFI post intervention : 20.0 vs 10.56 vs 30.3 vs 19.8(P = 0.032)

Microfluidics seem to be a beneficial intervention to reduce the SDF in comparison with raw sample. MACS seemed to have offered the least reduction of SDF.

BFR: This was comparable between all groups with no statistical significance:
- IR: 68.8% vs 76.5% vs 53% vs 65% (p = 0.30)
- CPR: 90.0% Vs 75.0% vs 40% vs 80% (p = 0.110)

Of all arms, MACS seemed to have lesser CPR and IR. Microfluidics had the best IR and TESA had the best CPR. However, there was no statistical significance on the whole between the arms with reproductive outcomes.

Nevertheless, it’s worth noting that Daily ejaculation has equally managed to offer acceptable reduction in SDF and optimize reproductive outcomes.

This study still doesn’t prove the superiority of one intervention over the other. We need to be cautious while choosing the best intervention for couples undergoing assisted reproduction with a history of raised SDF.

Data of this study comes with few limitations. These are interim results of our pilot study with a small patient population. This is still an ongoing RCT and we intend to look at Live birth rates.

CONCLUSIONS: Interim data from this pilot RCT doesn’t seem to prove the superiority of one intervention over the other for couples with raised SDF. MACS seems to be offering guarded outcomes, while Microfluidics seems to offer the best outcomes.

Appropriate counselling is required before offering these interventions to the couples.

IMPACT STATEMENT: Efficient management of SDF is the need of the hour and data from this study doesn’t prove the superiority of one intervention over the other.

SUPPORT: Self Funded. No financial support taken.

P-456 6:45 AM Wednesday, October 26, 2022
PHOSPHATIDYLSERINE A BIOMARKER FOR FERTILIZATION COMPETENT SPERM. Ryan P. Smith, MD, Jeffrey J. Lysiak, PhD 1 University of Virginia, Crozet, VA; 2 Affiliation not provided.

OBJECTIVE: The premise for this study comes from our published studies (Rival et al., Nature Comm 2019) where we observed: (i) an unexpected exposure of the lipid phosphatidylserine (PtdSer) on the surface of viable and motile sperm; (ii) blockade of PtdSer on sperm significantly decreased fertilization; (iii) complementary expression of PtdSer receptors on the oocytes, and blocking/loss of some of these PtdSer receptors impairs fertilization and; (iv) we showed that sperm can fuse to myoblast cells in a PtdSer-dependent manner. Independent work in other laboratories have now also shown a role for PtdSer as a potential fusogen in muscle and trophoblast cells.

A basic semen analysis is often the first test of male infertility; however, it only provides information on sperm numbers, morphology, and motility, but yielding no data about the sperm’s ability to fertilize an oocyte. With the high incidence of male infertility and lack of biomarkers to assess a sperm’s fertilization competency, urologic and fertility experts would welcome new diagnostic biomarkers that could provide valuable additional information about male infertility. This study aims to address the role of PtdSer on sperm as potential biomarker for fertilization competent sperm.

MATERIALS AND METHODS: Human semen samples were retrieved from a Cryobank. For this initial study all samples were from males with known paternity and normal semen analysis (n=10). PtdSer surface expression on sperm was determined using fluorescently tagged annexin V, while 7AAD was used to determine dead cells, and staining quantitated using Flow Cytometry. Using our novel sperm-myoblast fusion assay (Rival et al Nature Comm 2019) we were able to assess human sperm myoblast fusion. Briefly sperm were washed and labeled with a red-fluorescent cytoplasmic dye (Calcine-AM) and incubated with C2C12 mouse myoblasts. After incubation we assessed myoblasts that acquire the sperm-derived Calcine-AM staining.
RESULTS: The average percentage of live PtdSer positive 7AAD negative sperm in the samples was 42.3%±3.8. Results from sperm-myoemblast fusion assays revealed a fusion index of 7.8±0.93 and this was blocked with annexin as well as cytochalasin B. 2.7% ± 2.5% for annexin B.

Our previous studies in the mouse show that PtdSer on sperm plays an important role in sperm-egg fusion. Results from these studies demonstrate that PtdSer is expressed on live human sperm and that human sperm can fuse to myoblasts cells in a PtdSer-dependent manner. It is now recognized that PtdSer plays an essential role in myoblast as well as trophoblast cell fusion. We suggest that PtdSer can be an important biomarker to assess pre-implantation.

IMPACT STATEMENT: These results support the premise that PtdSer is an important biomarker for assessing sperm-egg fusion.

P-457 6:45 AM Wednesday, October 26, 2022

OXIDATIVE STRESS IN THE NATIVE AND PROCESSED SEMEN AS PREDICTORS OF FERTILIZATION AND PREGNANCY IN THE IVF MODEL. Hassan Sallam, MD, PhD, FRCOG, Noorman Sallam, MD, MCh, Ashraf Farrag, MD, MCh Alexandria University Faculty of Medicine, Alexandria, Egypt; 3 Alexandria Fertility Center, Alexandria, Egypt.

OBJECTIVE: We have previously shown that oxidative stress (OS) in the native semen is a good predictor of fertilization and pregnancy in the IVF model. The aim of the current work was to compare OS in the native versus the processed semen as predictors of fertilization and pregnancy in the IVF model.

MATERIALS AND METHODS: This prospective cohort study was conducted between September 2017 and December 2018. In order to study the fertilizing capacity of the sperm, couples with unexplained infertility treated with combined IVF/ICSI were recruited but only IVF results were analyzed in this current work. Couples in their first cycle of treatments from whom at least 12 oocytes were retrieved were included in the study. Three of these oocytes were inseminated by conventional IVF and the rest by ICSI for fear of total fertilization failure. If good embryos resulted from IVF, 2 were transferred. If no fertilization occurred from IVF, 2 embryos resulting from ICSI were transferred. All remaining embryos were frozen. OS was determined in native semen and in processed semen by measuring oxidative reduction potential (ORP) using the MoXYS system and the results correlated with the fertilization (FR) and clinical pregnancy rates (CPR).

RESULTS: A total of 107 couples were enrolled but only 25 fulfilled the criteria. A total of 575 oocytes were retrieved from the 25 patients (mean ± SD = 20.5 ± 5.6 oocyte/cycle). Out of the 108 oocytes inseminated with conventional IVF, 36 reached the 2PN stage (FR = 33.3%). The mean (±SD) ORP in the processed semen was 3.05 (±1.86) mV/10⁶ sperm/ml, which was significantly higher than the mean (±SD) ORP in the native semen (1.0723 ± 1.2984) mV/10⁶ sperm/mL (P < 0.0001). The mean (±SD) ORP in the native semen and in processed semen with >50% IVF fertilization was 1.02 ± 0.1 mV/10⁶ sperm/mL, which is significantly lower than in couples with <50% fertilization (2.05 ± 0.7 mV/10⁶ sperm/mL) (P < 0.02). On the contrary, there was no significant difference between the mean (±SD) ORP in the processed semen in couples with >50% fertilization rate [2.9490 (± 1.7345) mV/10⁶ sperm/ml] and those with <50% fertilization rate [3.2077 (± 2.0020) mV/10⁶ sperm/ml] (P = 0.8129). The ORP in the native semen was evaluated as a predictor of fertilization in IVF. A receiver operating characteristic (ROC) curve was constructed and the area under the curve (AUC) was found to be equal to 0.854167 with a cut-off point at 1.57 mV/10⁶ sperm/ml. On the contrary, the ROC curve for the processed semen had an AUC equal to 0.5267 with a cut-off point at 2.75 mV/10⁶ sperm/ml. The ORP in the native semen was also evaluated as a predictor of pregnancy in IVF. The ROC curve showed an AUC equal to 0.800 with a cut-off point at 0.75 mV/10⁶ sperm/ml, while the AUC for the processed semen was equal to 0.1800.

CONCLUSIONS: It is concluded that ORP in the native semen but not in the processed semen is a good predictor of the fertilizing capacity of the sperm and of clinical pregnancy in IVF treated couples.

IMPACT STATEMENT: In couples with unexplained infertility all oocytes should be treated with ICSI if the ORP in the native semen is >1.57 mV/10⁶ sperm/ml.

SUPPORT: None

P-458 6:45 AM Wednesday, October 26, 2022

GEOGRAPHIC VARIATION IN SEMEN PARAMETERS FROM DATA USED FOR THE WORLD HEALTH ORGANIZATION SEMEN ANALYSIS REFERENCE RANGES. Ido Feferkorn, MD, Liat Azani, MSC, Einav Peero Dr, MD, Ranit Hizkiyahu, MD, Guy Shrem, MD, Mali Salmon-Divon, Ph.D., Michael H. Dahan, M.D. Division of Reproductive Endocrinology and Infertility, McGill University Health Care Center, Montreal, Canada; 2 McGill University Health Center, Montreal QC, Canada; 3 McGill University Health Care Center, Montreal, QC, Canada; 4 Ariel University, Israel; 5 McGill University Health Center, Montreal QC, Canada; 6 McGill University Health Care Center, Montreal, QC, Canada.

OBJECTIVE: To study geographic variations in sperm parameters using data from the trials that defined the reference ranges of the World Health Organization (WHO) 2021 manual.

MATERIALS AND METHODS: Retrospective evaluation of the data used to define the WHO reference ranges. The data from 11 studies, including 3484 participants across five continents, were divided according to geographic locations. Sperm parameters’ distribution were presented using boxplot as a function of location. P-values were calculated by the Kruskal Wallis rank-sum test followed by Dunn post-hoc test. Analyses were conducted using the R programming language.

RESULTS: Semen volume was significantly lower in samples from Asia and Africa than in other regions. Sperm concentration in the USA was significantly lower than in Europe and highest in Australia. Total motile count (TMC) and total progressive count (TPC) were significantly lower in Asia as compared to other regions. TMC and TPC were lowest in Africa (median 126.1 and 97.2 million) and in the USA (median 142.8 million and 133.2 million) were significantly lower than in Europe (median 160.6 million and 142.9 million) and Australia (median 179.6 million and 162.7 million). The 5th percentile of sperm concentration was the lowest in the USA (12.5x10⁶/ml) and highest in Australia (21.4x10⁶/ml). The 5th percentile for TMC and TPC were lowest in Africa (TMC 15.08 million, TPC 12.06 million) and the USA (TMC 18.05 million, TPC 16.86 million) and highest in Australia (TMC 29.61 million, TPC 25.80 million).

CONCLUSIONS: Significant geographical differences in sperm parameters exist, regional fertility societies should consider adding their own reference limits based on local experience.

IMPACT STATEMENT: The geographical differences in sperm parameters noted questions the generalizability of the WHO reference ranges.

SUPPORT: none
time as the initial semen analysis (performed within 3-4 months of IVF cycle start) by processing part of the semen sample and shipping the same day to Androvia Life Sciences. The localization patterns of the ganglioside GM1 within the plasma membrane was examined and the percentage of capacitated sperm determined. For those couples undergoing IVF, ICSI was performed routinely. The fertilization rates were compared between those with normal and low Cap-Scores, and the euploidy rate of those undergoing PGT-A was also assessed. In addition, the outcome of the first Frozen Embryo Transfer (FET) in 121 patients was compared between the two groups.

RESULTS: 76 men had low Cap-Scores (76/236, 32.2%). The ICSI fertilization rates were not different between those with normal or low Cap-Scores (84.3% vs 84.7%, P = 0.88), nor were the euploidy rates (39.1% vs 38.9%; P = 0.90). Of the 121 women who underwent a FET, 31 did not undergo PGT-A, and 90 did. There was no difference in first cycle live birth rates between those with normal or low Cap-Scores.

CONCLUSIONS: The Cap-Score identifies men with capacitation abnormalities which impacts their chances at natural conception and conception with IUI. However, once these men undergo IVF and ICSI is performed, they have equivalent fertilization rates, euploidy rates, and FET success rates as men with normal scores. Men with low Cap-Scores should therefore be counselled that their ART outcomes are as good as men with normal scores.

IMPACT STATEMENT: Men with low Cap-scores do not have worse outcomes to men with normal scores when ICSI is performed.

SUPPORT: None


THE ASSOCIATION BETWEEN A HISTORY OF ABORTION.

OBJECTIVE: To investigate the effects of smoking and smoking methods on male fertility. MATERIALS AND METHODS: Semen samples were collected from 84 men (36.2±4.7 years old). Each patient was divided into non-smokers (n=34), regular smokers (n=12), e-cigarettes smokers (n=14), regular smokers / e-cigarette smokers (n=28). After semen liquefaction (30-60 minutes), semen analysis and halo-test (HT-HS10 kit) were performed. For statistical analysis, One-way ANOVA was done.

RESULTS: Semen analysis results and testosterone levels did not differ between groups. Sperm DFI was significantly different between groups. Sperm DFI was not statistically significant (p=0.474), but non-smokers (13.2±5.5) were lower than regulars (19.7±2.88), e-cigarettes (27.7±16.6), and regular/e-cigarette smokers (26.6±16.1, p<0.001). Although not statistically significant, it was confirmed that the sperm DFI in e-cigarettes was higher than in regular cigarettes.

CONCLUSIONS: The difference in sperm DFI was not statistically significant between nonsmokers and regular smokers, but the sperm DFI of smokers was higher than that of nonsmokers. However, the sperm DFI of non-smokers was significantly lower than that of e-cigarettes (27.7±16.6, p<0.01) and regular/e-cigarette smokers (26.6±16.1, p<0.01). It was considered that smoking, and smoking methods could be a factor more affecting sperm DFI than regular cigarettes, and it became evidence that e-cigarettes could have a detrimental effect on human reproductive organs like regular cigarettes. This shows that e-cigarettes cannot be considered an alternative to regular smoking. It is considered that additional research should be conducted on the correlation between the difference in DNA fragmentation by smoking type and embryonic development.

IMPACT STATEMENT: In this study, we confirmed that e-cigarettes are just as harmful as regular cigarettes and might be more harmful when used with regular cigarettes together.
OBJECTIVE: Combustible tobacco smoking leads to significant health deficits including reproductive morbidity. Paternal smoking has been shown to increase the risk of spontaneous abortion (SAB). Vaping may be a potentially safer alternative for nicotine consumption; however, limited studies exist regarding both. The current study evaluated the association between paternal vaping and SAB.

MATERIALS AND METHODS: We analyzed data from 1,446 males aged ≥21 years participating in Pregnancy Study Online (PRESTO), a preconception cohort study in North America of pregnancy planners. On baseline questionnaires completed during the preconception period, male participants and their female partners reported information about demographics, tobacco product use and other lifestyle characteristics. Female partners completed bimonthly follow-up questionnaires to update their data on pregnancy status and SAB. We used Cox regression models with multiple imputation to estimate hazard ratios (HRs) and 95% confidence intervals for the associations of ever use of nicotine vaping with SAB, while adjusting for male and female factors including cigarette smoking.

RESULTS: The mean age for the males and females was 32 years and 30 years, respectively, with over 85% self-identifying as white. 72% of the cohort had completed college. 19% of males reported ever vaping, 10% reported current smoking, and 10% reported ever use of chewing tobacco. In all, there were 339 SABs. The prevalence of male ever vaping was 21% among the couples who experienced a SAB and 24% among the couples without a SAB. In multivariable models, male ever vaping was not materially associated with SAB (HR 1.05, 95% CI 0.77-1.43). In addition, no associations were apparent for male ever chewing tobacco, female ever vaping, or combinations of male and female ever vaping (i.e. M+P+, M+P-, M-P+, M-P-) with no patterns identified.

CONCLUSIONS: The current report suggests that a history of paternal vaping is not associated with SAB.

IMPACT STATEMENT: While the current report did not find an association between paternal vaping and pregnancy loss, further assessment of current vaping during preconception will be required to better assess safety.

SUPPORT: This work was supported by the National Institutes of Health:
R21-HD094322; R01-HD086742; R01-HD105863.

VARIATION IN THE SEMEN MICROBIOME OF FERTILE MEN VERSUS MEN WITH IDIOPATHIC INFERTILITY: A SINGLE-INSTITUTION COHORT STUDY. John Tucker Sigalos, M.D.,1 Thomas W. Gaither Castellanos, B.A., B.S.,1 Michelle K. Li, B.A.,1 Dar Yoffe, B.S.,1 Ming-Yeah Hu, B.S.,1 Tommy Jiang, B.A.,1 Srimat V. Eleswarapu, M.D., Ph.D.,1 Jesse Mills, M.D.,1 David Geffen School of Medicine at UCLA, Los Angeles, CA; 2University of California, Los Angeles, Los Angeles, CA.

OBJECTIVE: Next-generation sequencing (NGS) has enabled robust characterization of environmental microorganism diversity, which may play a role in semen quality and male fertility. Few studies have employed NGS to evaluate semen. We sought to characterize the semen microbiome of fertile and infertile men.

MATERIALS AND METHODS: Men with idiopathic infertility or proven proven infertility were recruited from 8/2021-3/2022. Men underwent history and physical exam, urine and semen analysis, and bloodwork. Urine and semen underwent PCR and NGS (16S rRNA). Prevalence of the top 3 principle organisms were recorded. Descriptive statistics and t-tests were performed.

RESULTS: 71 men (43 infertile, 28 fertile) were enrolled, mean age 36.8y and 40.7y. Sperm concentration, motility, and morphology were significantly different between fertile compared to infertile men (Table). There were 39 unique principal organisms, with the most represented microbes presented in the Table. There was no difference in comorbidity rates, nor circumcision or varicocele status.

CONCLUSIONS: Diverse microbial populations may represent potential targets for mechanistic exploration and therapeutic intervention in men with idiopathic infertility. These data contribute to the growing evidence for microbial composition in fertility and infertile men.
P-466 6:45 AM Wednesday, October 26, 2022

DEVELOPMENT OF A NOVEL ROBUST ARTIFICIAL INTELLIGENCE DEVELOPED Sperm DNA FRAGMENTATION TEST – PRELIMINARY FINDINGS. Shinnosuke Kuroda, MD, PhD, 1 Keshab Kumar Karna, PhD, 1 Raneen Sawaid Kaiyal, MD, 2 Sajal Gupta, MD, 2 Rakesh Sharma, PhD, 2 Ashok Agarwal, PhD, 3 Cleveland Clinic Foundation, Cleveland, OH; 2American Center for Reproductive Medicine, Cleveland, OH.

OBJECTIVE: Sperm DNA fragmentation (SDF) is examined by multiple techniques (SCSA, TUNEL, SCD and COMET) while the sperm chromatin dispersion (SCD) test using Halosperm is a popular commercial test used by many IVF clinics. The SCD technique has the advantage of being inexpensive as it does not require advanced equipment or reagents. The main shortcoming of this method is its poor sensitivity due to the limited counting of a small number of sperm with the current Halosperm G2 test. The Lenshooke R10 test can be used for male infertility evaluation due to its objective and robust.

RESULTS: Sperm concentration, motility and morphology in a population of known fertile men. The WHO guidelines have progressively decreased the percentage of semen samples with normal sperm parameters. However, the reliability of SCD test is still under question. %DFI evaluated by LensHooke R10 both manually and by automated X12 are significantly correlated with Halosperm G2. AI-aided instrument has the advantage of analyzing larger number of spermatozoa objectively and thereby reducing the subjectivity of manual counting of a small number of sperm with the current Halosperm G2 test. This makes the X12 SCD technique faster, objective and robust.

IMPACT STATEMENT: LensHooke R10 test combined with novel X12 AI-aided instrument has the advantage of analyzing larger number of spermatozoa objectively and thereby reducing the subjectivity of manual counting of a small number of sperm with the current Halosperm G2 test. The Lenshooke R10 test can be used for male infertility evaluation due to its acceptable agreement with Halosperm G2 test. Furthermore, the R10 test is approved by the US-FDA and CE marked for EU.

P-467 6:45 AM Wednesday, October 26, 2022

THE QUESTIONABLE CLINICAL UTILITY OF SPERM MORPHOLOGY: RATE OF ISOLATED TERATOSPERMIA IN A POPULATION OF FERTILE MEN. David Miller, MD, Lucille Cheng, BA, Kathleen Hwang, MD UPMC, Pittsburgh, PA.

OBJECTIVE: The assessment of sperm morphology remains a standard component of the semen analysis however its clinical utility is not well-defined. The WHO guidelines have progressively decreased the percentage of normal morphology over the years and currently normal is 4% or greater. Despite these increasingly strict criteria for the assessment of morphology the clinical implications remain questionable. Furthermore, accurate repeatability of sperm morphology assessment has been shown to be low due to differences in proficiency between labs and technicians themselves. To better understand the impact of sperm morphology on fertility we assessed sperm morphology in a population of known fertile men.

MATERIALS AND METHODS: Healthy men over 18 years of age were recruited to provide one semen sample prior to vasectomy from March 2020 through April 2022. To be included in the study participants were required to have biological children under the age of 5 years old, with no history of difficulty achieving pregnancy, and had undergone no prior fertility procedures. Sperm morphology was analyzed using Papanicolaou stain with Kruger strict criteria by two technicians in an Andrology specialty laboratory per the WHO 5th edition manual.
RESULTS: There were 54 men who participated in the study, of which there was a morphology assessment available for 52 patients. The average age of participants was 36 and the mean BMI was 27.9 (20.4–37.3). Of those with smoking history available (n = 48), 61% of men were non-smokers (n = 30), 20% were former smokers (n = 10), and 19% were current smokers (n = 8). Patients had an average of 2.7 children with a mean age of the youngest child of 15 months old. The mean sperm density was 58.5 mil/ml, the mean motility was 61%, and mean progressive motility was 76%. The median morphology was 3%. There were 29 patients (58%) with 3% or lower sperm morphology including one patient who had 0% normal morphology (Figure 1). The most common morphologic abnormalities were head shape defects (n = 51), followed by coiled tails (n = 14) with some patients having both abnormalities.

CONCLUSIONS: Over half of fertile male patients (58%) had lower than normal sperm morphology in our study. The results of our study further question the clinical relevance of sperm morphology on fertility outcomes and if the current approach in assessing morphology is too strict.

IMPACT STATEMENT: Our results further question the clinical utility of sperm morphology due to the high percentage of known fertile males with lower than normal morphology. Additionally, this test may lead to undue patient anxiety as well as couples who are fast tracked to IVF and IVF/ICSI purely based on the male partner’s isolated teratospermia

P-468 6:45 AM Wednesday, October 26, 2022

DESIGN AND VALIDATION OF A 3D PRINTED VAS DEFERENS MODEL FOR MALE FERTILITY VASOSOMATIC TRAINING. Michael Tradewell, M.D., M.S., Rohit Reddy, B.S., Mehul S. Patel, M.D., Ranjith Ramasamy, M.D.1 University of Miami, Miami, FL; 1University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: To develop a 3D printed model that is substantially equivalent in size, shape, and tissue properties to human vas deferens for use as a vasosomatic microsurgical trainer.

MATERIALS AND METHODS: Through an iterative design process we developed a 3D printed vas deferens model. Solidworks was used for computer-aided design (Dassault Systemes, Velizy-Villacoublay, France). Stereolithography 3D printing was completed with a Form 3 printer and elastic resin with a durometer of 50A (Formlabs, Somerville, MA, USA). Formlabs elastic resin 3D prints are not rated to print internal channels below 1.5 mm. We were able to reliably print a patent 300μm lumen via a tapered end design and with post-processing pumping isopropyl alcohol through the lumen prior to UV curing the prints. As a comparator, discarded human vas deferens samples were collected during vasovasostomy or vasoepididymostomy under an IRB approved protocol. For biosafety these samples were preserved in formaldehyde. To assess face validity, the 3D printed vas deferens models and discarded human vas deferens samples were quantitively compared by urology residents, fellows and attendings.

RESULTS: A 3D printed model of the vas deferens designed for vasovasostomy simulation. Future efforts will quantify and criterion validity to determine whether practicing microsurgical technique on the synthetic vas deferens translates to practical microsurgical skill acquisition.

IMPACT STATEMENT: Microsurgical skill acquisition is challenging and training availability is limited. We have developed a high-fidelity 3D printed model of the vas deferens designed for vasovasostomy simulation.

SUPPORT: The American Urologic Association Urology Care Foundation 2021 Residency Research Award awarded to MT.

REFERENCES: None
OBJECTIVE: Varicocele is a common condition amongst infertile men. Varicocele repair (VR) is frequently performed to improve semen quality, sperm DNA fragmentation, and the chances of pregnancy. However, there is a lack of consensus about the diagnosis, indications, and outcomes for VR. The aim of this study was to explore global practice patterns among practicing male infertility clinicians on the management of varicocele in the context of couple infertility.

MATERIALS AND METHODS: Sixty practicing urologists/andrologists from 23 countries initially designed 382 multiple-choice questions pertaining to varicocele management. These were finally condensed into an online questionnaire survey consisting of 55 questions, that was forwarded to male infertility clinicians through direct email invitations. The results were analyzed for similarities and discrepancies in practice patterns, compared and contrasted to the latest guidelines of international professional societies (American Urological Association (AUA), American Society for Reproductive Medicine (ASRM), and European Association of Urology (EAU), as well as with evidence emerging from recent systematic reviews and meta-analyses. Additionally, an expert opinion on each topic was provided based on the consensus of 16 experts in the field.

RESULTS: The questionnaire survey was answered by 574 clinicians from 59 countries, mainly from Asia (n=277, 48.3%) and Africa (n=134, 23.3%). The majority of respondents were urologists (n=227, 39.7%) and uro-andrologists (n=226, 39.5%). A wide diversity of opinion was seen in every aspect of varicocele diagnosis, indications for repair, choice of technique, management of sub-clinical varicocele, and the role of VR in azospermia. A significant proportion of the responses conflicted with the recommendations of AUA, ASRM, and EAU, ranging from the diagnosis of varicocele, to symptoms, indications for VR, VR prior to assisted reproductive techniques (ART), contraindication to VR, predictors of VR outcome, techniques used for VR, VR in patients with non-obstructive azoospermia (NOA), recurrence of varicocele and subclinical varicocele. A large number of clinical scenarios was identified where no guidelines were available.

CONCLUSIONS: The survey highlights several areas where there is inconclusive data and the need for more research, and also identifies numerous gaps in the management guidelines issued by professional bodies (ASRM, AUA, EAU), which need to be addressed in future guidelines.

IMPACT STATEMENT: This study is the largest global survey performed to date on the clinical management of varicocele for male infertility. It demonstrates: 1) a wide variation in the approach to varicocele management among clinicians, 2) large gaps between the real-life clinical practice patterns and the guidelines from professional societies, 3) the need for guidelines that are less generic and closer to real-life, and for further studies on several aspects of varicocele management in infertile men.

SUPPORT: None

P-472 6:45 AM Wednesday, October 26, 2022

A COMPARISON OF THE EFFECTS OF ANTIOXIDANT THERAPY IN INFERTILE MEN WITH VARICOCELE FOLLOWING VARICOCELE REPAIR VERSUS NO REPAIR: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.

Ashok Agarwal, PhD,1 Rossella Cannarella, MD, PhD,1 Ramadan Saleh, MD,2 Florence Boitrelle, MD, PhD,3 Gianmario Salvio, MD,4 Ahmed Harraz, MD,5 Amarnath Rambhatla, M.D.,67 Parviz K. Kavoussi, MD,8 Ramdan Saleh, MD,9 Giovanni M. Colpi, MD,10 Rupin Shah, MD1 Cleveland Clinic, Cleveland, OH; 2Sohag University, Sohag, Egypt; 3ART Center - Andrology - CECOS, France; 4Department of Endocrinology and Metabolic Diseases, Polytechnic University of Marche, Ancona, Italy; 5Mansoura University, Mansoura, Egypt; 6Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI; 71Department of Urology, Lilavati Hospital and Research Centre, Mumbai, India.

OBJECTIVE: Few studies to date have evaluated the effects of antioxidants (AOXs) in infertile patients with varicocele who underwent repair or no repair. This present systematic review and meta-analysis (SRMA) was conducted to assess and compare the impact of using AOXs in the population of infertile men with varicocele who underwent either varicocele repair (VR) versus no repair (nVR). This meta-analysis aims to determine the non-inferiority/or superiority of VR+AOXs versus nVR+AOXs among the target population.

MATERIALS AND METHODS: Literature search was performed using Scopus, PubMed, Ovid, Embase and Cochrane databases. Eligible randomized controlled trial (RCT) studies were selected following the model of Population-Intervention-Comparison-Outcome (PICO); where P=infertile men with varicoceles, I=AOXs therapy, C=VR+AOXs versus nVR+AOXs. The primary outcome of this study was spontaneous clinical pregnancy rate (odds ratio [OR] and 95% CI). The secondary outcomes were conventional sperm parameters (mean difference [MD] and 95% CI). A meta-regression analysis was performed to determine the between-group differences in the pooled effect size.

RESULTS: 1307 abstracts were initially extracted, to finally include 66 RCTs. Overall, treatment with AOXs improved pregnancy rate in patients with varicocele, independent of varicocele repair [OR 1.97 (1.28-3.04), p = 0.002]. When compared according to VR or nVR [VR: OR 2 (0.84-4.76), p=0.05, and nVR: OR 2.12 (1.23-3.65), p=0.007] there was no evidence of between-group difference (Q = 0.01, p=0.9). Similarly, sperm concentration significantly improved after AOXs treatment in...
overall subjects [MD 5.77 (4.28-7.25), p < 0.001] and within each group [VR: MD 5.93 (3.44-8.42), p < 0.001; and nVR: MD 5.36 (3.71-7.02), p < 0.001], with non-significant between-group difference (Q = 0.14, p = 0.7). Similar results were obtained for progressive sperm motility [MD 7.21 (2.4-17), p < 0.001; and VR: MD 7.35 (0.8-9.3), p = 0.03; nVR: MD 7.7 (2.73-12.67), p = 0.002] with non-significant between-group difference (Q = 3.4; p = 0.8). Improved sperm morphology was similarly significantly demonstrated in overall subjects [overall: MD 7.52 (3.11-11.94), p < 0.001; VR: MD 7.11 (4.12-10.11), p < 0.001; nVR: MD 7.7 (2.73-12.67), p = 0.03] with non-significant between-group difference (Q = 0.04; p = 0.8). IMPACT STATEMENT: The results of this study suggest that men with varicocele and OAT should receive AOXs as their primary therapy, and additional benefit from VR is likely to be limited.

SUPPORT: None

**P-473** 6:45 AM Wednesday, October 26, 2022

**EFFECT OF VARICOCELE REPAIR ON CONVENTIONAL SPERM PARAMETERS IN INFERTILE PATIENTS WITH CLINICAL VARICOCELE: A SYSTEMATIC REVIEW AND META-ANALYSIS.**

**AnalySIS:** Ashok, Agarwal, PhD,1 Rossella Cannarelli, MD, PhD,2,3 Ramadan Saleh, MD,4 Florence Boitrelle, MD, PhD,5 Taha Abdel-Meguid Hamoda, MD, MSc, MBBS,4 Murat Gül, MD,4,5 Giannaria Salvi, MD,4,6 Mohamed Arafa, MD,4,7 Giorgio Ivan Russo, MD,4,8 Tuncay Toprak, MD,2,9 Ahmed Harraz, MD,10 Ralf Henkel, PhD,11 Rajender Singh, PhD,12,13 Nicolas Garrido Puchalt, PhD,14 Shinnosuke Kuroda, MD, PhD,15 Andrea Crafa, MD,16,17 Amarnath Rambhala, MD,18 Ayad Palami, PhD,19,20 Christopher Ho, MD,21 Mesut Berkman Duran, MD,22 Eran Ceyhan, MD,22 Fotos Dimitriadis, MD,23,24 Emine Sâıs,22,24 Marlon Bendayan, MD,25 Mahsa Darbandi, B.S.C., M.P.HL, M.S.C., P.H.D.,25,26 Tan Le, MD,27,28 Szegn Gunes, P.H.D.,28 Petroula Tsiroulo, MD,29,30 Kadir Bocu, MD,31 Parisa Dolati, PhD,32,33 Berk Hazir, MD,34 Herik Acosta Acosta Gonzalez, MD,35,36 Gökhan Çeker, MD,37 Abdullah Alarbid, MD,38 Sara Darbandi, PhD,39 Damayanthi Durairajayagam, PhD,24 Carlo Gialloni, MD,33 Vilnapathy Senguttuvan S. Karthikeyan, MD,40 Azin Aghamajidi, PhD,41 Noora Al Khalidi, PhD,31 Gokhan Calik, MD,32 Enurullah Sogutdelan, MD,32 Marco Falcone, MD,33 Vineet Malhotra, M.B.B.S.,34 Federica Finocchi, PhD,35 Raghavender Goud Kosi SR, M.B.B.S., M.D.,36,37,38 Rupin Shah, MD,39 Cleveland Clinic, Cleveland, OH;39 Sohag University, Sohag, Egypt;40 ART Center - Andrology - CECSO, France;41 King Abdulaziz University, Jeddah, Saudi Arabia;42 Department of Andrology, Selcuk University, Konya, Turkey;43 Department of Endocrinology and Metabolic Diseases, Politechnic University of Marche, Ancona, Italy;44 Hamad Medical Corporation, Doha, Qatar;45 University of Catania, Catania, Italy;46 Department of Urology, University of Health Sciences, Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Turkey;47 Mansoura University, Mansoura, Egypt;48 University of the Western Cape, Bellville, South Africa;49 CSIR-Central Drug Research Institute;50 IVF Foundation, Varanasi, India;51 Cleveland Clinic Foundation, Cleveland, OH;52 Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy;53 Department of Urology, Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI;54 College of Medicine, University of Garmian, Kalar, Iraq;55 Department of Surgery, School of Medicine, Faculty of Health and Medical Sciences, Taylor’s University, Malaysia;56 Department of Urology, Denizli State Hospital, Denizli, Turkey;57 Department of Urology, Baskent University Faculty of Medicine, Ankara, Turkey;58 School of Medicine, Aristotle University, Thessaloniki, Greece;59 Department of Reproductive Biology, Fertility Preservation, Andrology, CECSO, Poissy Hospital, Poissy, France;60 Fetal Health Research Center, Hope Generation Foundation, Tehran, Iran (Islamic Republic of);61 Department of Andrology, Bing Dan Hospital, Ho Chi Minh City, Vietnam;62 Department of Urology, Dokuy, Mayis University, Faculty of Medicine, Samsun, Turkey;63 Department of Physiology, Group of Reproductive and Clinical Embryology, Medical School, National and Kapodistrian University of Athens, Greece;64 American Center for Reproductive Medicine, Cleveland Clinic, Cleveland;65 Lund University, Malmö, Skåne Laen, Sweden;66 Başakşehir Çam and Sakura City Hospital, Istanbul, Turkey;67 Department of Surgery, Urology Unit, Farwaniya Hospital, 68 Hope Generation Foundation, Tehran, Iran (Islamic Republic of);69 Department of Physiology, Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh Campus, Sungai Buloh, Malaysia;70 Department of Urology, Politechnic University of Marche Region, Ancona, Italy;71 Apollo Hospitals, Greens Road, Chennai, India;72 Department of Immunology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran (Islamic Republic of);73 Department of Urology, Faculty of Medicine, Istanbul Medipol University, Istanbul, Turkey;74 Department of Urology, Boğ Antab Izzet Bayal University;75 Department of Urology, Molinette hospital, AOI “Città della Salute e della Scienza”, University of Turin, Italy;76 SCM clinic and hospital, New Dehi, India;77 Politechnic University of Marche, Ancona, Italy;78 Department of Urology and Andrology, AIG Hospitals, Hyderabad, India;79 Department of Urology, Lilavati Hospital and Research Centre, Mumbai, India.

**IMPACT STATEMENT:** To the best of our knowledge, this is the first SRMA evaluating the impact of VR on conventional semen parameters in infertile patients with clinical varicocele and infertility. Despite the significant role of varicocele in the pathogenesis of male infertility, the impact of varicocele repair (VR) on conventional semen parameters remains controversial. To the best of our knowledge, only a few systematic reviews and meta-analyses (SRMA) have evaluated the impact of VR on sperm concentration, total motility, and progressive motility using a before–after analytic approach for analyzing 22, 17, and 5 prospective uncontrolled trials, respectively. Indeed, the majority of SRMAs have focused on pregnancy rate as an outcome. This study aimed to evaluate the effect of VR on conventional semen parameters in infertile patients with clinical varicocele compared to untreated controls.

**MATERIALS AND METHODS:** Literature search was performed in Scopus, PubMed, Ovid, Embase, and Cochrane databases using the PICO model (Population: Infertile patients with clinical varicocele; Intervention: Varicocele repair; Comparison: No treatment; Outcomes: Sperm concentration, sperm total count, sperm progressive motility, sperm total motility, and semen volume). Both randomized-controlled trials (RCTs) and observational studies were included.

**RESULTS:** 1632 abstracts were initially assessed for eligibility, 16 studies were finally included with a total of 2420 infertile patients with clinical varicocele (1424 patients treated with VR vs. 996 untreated controls). The analysis showed significantly improved post-operative sperm parameters in the VR group compared to controls: sperm concentration [standardized mean difference (SMD) 1.87 (95% CI: 1.25, 2.48); p<0.01; I²=97.6%], total sperm count [SMD 1.89 (95% CI: 0.57, 3.22); p<0.05; I²=97.8%], sperm progressive motility [SMD 3.30% (95% CI: 2.16, 4.44); p<0.01; I²=98.4%], total sperm motility [SMD 0.89% (95% CI: 0.04, 1.74); p=0.04; I²=97.4%] and normal sperm morphology [SMD 1.68% (95% CI: 0.88, 2.47); p<0.05; I²=97.4%]. All the outcomes had a high level of inter-study heterogeneity, but sensitivity analysis showed that no study was sensitive enough to change these results. Publication bias was present only in the analysis of sperm concentration and progressive motility. No significant difference was found in semen volume [SMD 0.13 ml (95% CI: -0.24, 0.87); p=0.27; I²=89.7%].

**CONCLUSIONS:** This study provides evidence in favor of a positive effect of VR in improving conventional semen parameters in patients with clinical varicocele and infertility.

**SUPPORT: None**

**P-475** 6:45 AM Wednesday, October 26, 2022

**COVID-19 IS UNLIKELY TO AFFECT MALE FERTILITY: RESULTS OF HISTOPATHOLOGIC AND RT-PCR ANALYSIS.**

**John M. Masterson, MD,1 Chau M. Bui, MD,1 Yi Zhang, MD,1 Carissa Huynh, BS,1 Daniel A. Luthringer, MD,2 Warren Tourtelotte, MD,2 Maurice Marcel Garcia, MD1 1Cedars Sinai Medical Center, Los Angeles, CA;2 Cedars-Sinai Medical Center, Los Angeles, CA.

**SUPPORT:** None

**Vol. 118, No. 4, Supplement, October 2022**
OBJECTIVE: Male sex is an independent risk factor for death from COVID19. The ACE2 receptor is a known entry mechanism of SARS-CoV-2 into cells and is present within testicles. There is limited and conflicting data as to whether COVID19 infects the testes. We sought to identify evidence of COVID19 within the testes of men who died with active COVID19 infection.

MATERIALS AND METHODS: We performed autopsy of 8 consecutive men who died of COVID19 pneumonia and whose families provided consent to harvest testicle tissue. Lung and testis tissue of all men were stained for SARS-CoV-2 nucleocapsid, ACE2 receptor IHC, H&E IHC was performed to assess for spermatogenesis and evidence of testicular tissue damage. RTPCR analysis for SARS-CoV-2 was performed on matched lung and bilateral testicular tissue samples from all men.

RESULTS: Patient age ranged 50 to 79 years. The average time from COVID19 diagnosis to death was 21 days. SARS-CoV-2 viral RNA was detected by RTPCR in testis tissue in one man, and in pulmonary tissue of all men. The man with RTPCR positivity in testis tissue (left testicle, CT 39.23 in 1/5 runs; CT 39.63 in 2/5 runs) had the highest RTPCR positivity in lung (CT 37.55 in 3/5 runs). All 8 testicle specimens that underwent ACE2 IHC showed uniformly strong immunoreactivity against all testicle cell populations. By H&E, no testis specimens showed inflammation, vascular thrombosis, vasculitis, or morphologic evidence of viral changes. One case showed diminished but present spermatogenesis, consistent with patient age (Table 1).

CONCLUSIONS: Our RTPCR results suggest that while SARS-CoV-2 is not common in testes at time of death, it can infect the testes. We believe our IHC results were similar to others’ findings, but inconclusive based on a lack of a standardized control. Contrary to all prior histologic studies, our results showed no evidence of damage to reproductive tissues that might impair fertility.

IMPACT STATEMENT: Our results suggest that SARS-CoV-2 infection likely does not adversely affect male fertility.

P-476 6:45 AM Wednesday, October 26, 2022
EVALUATION OF ANDROGEN SATURATION IN HUMAN CORPUS CAVERNOSUM. Kajal Khodamoradi, PhD,1 Alexandre Dullea, MS,1 Roei Golan, BS,2 Daniel E. Nassau, MD,1 Jesse Ory, MD,1 Himanshu Arora, B.SC., M.SC., PH.D.,1 Ranjith Ramasamy, M.D.1 1University of Miami Miller School of Medicine, Miami, FL; 2Florida State University College of Medicine, Tallahassee, FL.

OBJECTIVE: Testosterone (T) plays an essential role in properly developing and maintaining male reproductive tissues (1). The normal serum testosterone levels can vary between 300 to 1000 ng/dL. However, it is unclear whether androgen receptor signaling can vary based on serum T levels. What remains unknown is whether there is a consistent serum T level above which androgen receptor signaling within the tissue remains similar. Therefore, we evaluated whether varying serum levels of T alter androgen receptor (AR) signaling in human penile tissue.

MATERIALS AND METHODS: We obtained human corpus cavernosum (CC) tissue biopsies during penile implant surgery from 17 men. We recorded their serum T levels one week before surgery. After mechanical dispersion of CC tissue with a homogenizer, the total protein was extracted using RIPA buffer, and quantitative detection of vascular endothelial growth factor (VEGF) was evaluated by western blot.

RESULTS: The mean age of participants was 64 ± 10, and the mean T level was 487 ng/dL ± 377. The western blot results showed that all corpus cavernosum samples in men with T >200 ng/dL expressed similar levels of VEGF in men. However, men with a low serum T level (<200 ng/dL) had decreased expression of VEGF.

CONCLUSIONS: Even with a wide range of serum T levels (200-1594 ng/dL), androgen receptor signaling was similar in penile tissue. This data suggests that the saturation value for penile androgen receptors could be approximately 200ng/dL.

IMPACT STATEMENT: Understanding the androgen receptor saturation hypothesis provides the vital context necessary for appropriately prescribing exogenous T to optimize patient outcomes.

P-477 6:45 AM Wednesday, October 26, 2022
DYSPERGULATION OF THE HUMAN B-DEFENSIN 128 GENE IMPACTS SPERM FUNCTION. Shruti Kane, B.SC., M.SC.,1 Sarah Martins da Silva, M.B.B.CH., M.D.,2 Sean Brown Dr, PhD3 1University of Aberty Dundee, Dundee, Angus, United Kingdom; 2University of Dundee, NHS Tayside; 3University of Aberty.

OBJECTIVE: Male infertility is a global issue and many of the cases of male infertility have unknown causes. Genetic mutations may be a causative factor in a significant number of idiopathic cases. We conducted Whole Exome Sequencing (WES) analysis in men undergoing assisted conception and identified a genetic mutation in the β-defensin 128 (DEFB128) gene. The DEFB128 gene is explicitly expressed in the male reproductive tract, where it forms part of the sperm glycocalyx and protects sperm cells in the female reproductive tract.

MATERIALS AND METHODS: DNA was extracted from the blood of 26 men attending the assisted conception unit and sequenced using WES. A pathogenic variant in the β-defensin 128 gene was identified using bioinformatics analysis and validated using Sanger sequencing. Enzyme-linked immunosorbent assay (ELISA) was used to detect the presence of the DEFB128 protein on sperm cells. wvDEFB128 recombinant protein was brought commercially and anti-microbial assays against a range of control strain Gram-positive and Gram-negative bacteria commonly found in the female reproductive tract were performed.

RESULTS: Based on bioinformatics analysis, we identified a novel pathogenic homozygous frame-shift insertion causing a premature stop codon in the DEFB128 gene from one patient. Sanger sequencing was used to confirm the pathogenic mutation in the patient. DEFB128 has been shown in literature to be highly and exclusively expressed in the male tissue, presence of DEFB128 on sperm was investigated using ELISA assays. In order to identify the functional significance of this protein, antimicrobial assays were performed using the commercially available DEFB128 recombinant protein.

Based on our results, we hypothesise that the loss of the DEFB128 protein reduced the competence of the patients sperm cells by making them more prone to infections in the female reproductive tract.

CONCLUSIONS: The identified DEFB128 mutation (rs11396059) has not been associated with any disease to date. Reduced antimicrobial activity due to the pathogenic mutation may render sperm cells with less protection against pathogens in the female reproductive tract. As the patient with the DEFB128 mutation has no other medical condition we predict that it is the cause of infertility. However, the exact physiological impairment in vivo needs to be confirmed.

Furthermore, like the human DEFB126 protein, the DEFB128 may contribute to the formation of the sperm glycocalyx and hence it may be involved in the efficient movement of sperm in the female reproductive tract. Sperm penetration assays will need to be performed on affected patients sperm cells to provide further evidence of functional failure.

IMPACT STATEMENT: Many cases of idiopathic male infertility remain a mystery. This may be in-part due to the lack of understanding of the physiological regulation of sperm cells. The DEFB128 gene is exclusive expressed in the male reproductive tract and forms part of the sperm glycocalyx. Understanding the sperm glycocalyx and its functional significance will help in understanding the cause of dysfunction in many cases of idiopathic male infertility.

P-478 6:45 AM Wednesday, October 26, 2022
IMPACT OF COMORBIDITIES ON MALE TESTOSTERONE LEVELS WITH AGE: RESULTS FROM THE BALTIMORE LONGITUDINAL AGING STUDY. Joshua Theodore White, MD,1 Chase Carto, BS,1 Maria Camila Suarez Arbelaez, MD,1 Ranjith Ramasamy, M.D.1 1Dalphous University, Halifax, NS, Canada; 2University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: To evaluate the longitudinal impact of additive comorbidity burden on testosterone levels in aging males. We hypothesized that age alone in the absence of comorbidities would not predict a significant decline in testosterone level, but development of comorbidities would lead to testosterone decline with aging.
MATERIALS AND METHODS: Patients were selected from the Baltimore Longitudinal Study on Aging (BLSA), an ongoing continuous enrollment study created to investigate the physiology of aging. Participants that received at least one testosterone laboratory measurement were included in this analysis, with conditions consistent at every visit to track development of comorbidities over time in each patient. All patients on any form of testosterone replacement therapy or with negative testosterone levels due to documentation error were identified and removed from the analysis. Additionally, patients with total testosterone level below 50 ng/dL (cstrate) were removed from the analysis. Panel regression analysis was performed in R to assess the impact of the following variables on testosterone levels: age, anemia, depression, obesity, cancer, hypertension, diabetes mellitus, heart disease, heart failure, stroke, peripheral artery disease, COPD, chronic kidney disease, and joint disease. Statistical significance was assessed at p < 0.05.

RESULTS: After removal of the aforementioned patients, 758 men with 2264 total visits remained for statistical analysis. The number of testosterone measurements per patient varied from one to ten. Panel regression analysis did not reveal a significant negative relationship between age and testosterone level in the overall cohort (p = 0.11). However, significant decline in testosterone level was observed in men who developed anemia (coefficient = -38.83, p < 0.001), obesity (coefficient = -44.78, p < 0.001), cancer (coefficient = -32.67, p = 0.013), and diabetes mellitus (coefficient = -44.44, p = 0.006). Surprisingly, development of COPD was associated with a significant increase in testosterone levels (coefficient = 32.13, p = 0.016). We also found that aging alone in the absence of comorbidities does not have a significantly negative association with testosterone level. However, subsequent development of comorbidities including anemia, obesity, cancer, and diabetes may lead to significant decline in testosterone with aging.

IMPACT STATEMENT: Additive comorbidity burden with aging may predict significantly lower testosterone levels compared to healthy aging without development of comorbidities. Management by physicians aimed at mitigating risk factors of chronic health conditions could help decrease the likelihood of developing symptoms of testosterone deficiency with aging.

P-479 6:45 AM Wednesday, October 26, 2022

HYPOGONADISM AND TESTOSTERONE THERAPY AMONG MEN WITH KLINEFELTER SYNDROME: ANALYSIS OF A GLOBAL FEDERATED RESEARCH NETWORK. Joshua Theodore White, MD, Chase Carro, BS, Justin Loloi, M.D., Ranjith Ramasamy, M.D. Dalhousie University, Halifax, NS, Canada; University of Miami Miller School of Medicine, Miami, FL; Great Neck, NY.

OBJECTIVE: Klinefelter syndrome (KS) is one of the on-label indications for testosterone therapy. The prevalence of testosterone deficiency in men with KS is estimated to be 65-85%. Klinefelter syndrome is underdiagnosed in affected men, as men don’t often seek care and clinical presentation is highly variable. However, KS is associated with several comorbidities. Therefore, we hypothesized that men with KS are undertreated for testosterone deficiency. We used a national database to report the rates of prescription of testosterone replacement therapy (TRT) in men with KS.

MATERIALS AND METHODS: We queried TriNetX, a large, multicenter electronic health record database, to identify all men with a diagnosis of Klinefelter syndrome (ICD-10-CM Q98.0). The primary outcome of the study was prescription of any of the following forms of TRT on the day of diagnosis or later using associated medication codes: testosterone, testosterone 17-phenylpropionate, testosterone enanthate, testosterone cypionate, testosterone undecanoate. Secondary analysis was performed comparing TRT prescription in men with KS to a control cohort of men with diagnosis testicular hypofunction (ICD-10-CM E29.1) in the absence of KS. Cohorts were balanced for age, race, and ethnicity as well as preexisting hypertension, CKD, overweight or obesity, and diabetes mellitus using propensity score matching. Men with prescription of TRT prior to the time window or diagnosis of KS or testicular hypofunction more than 20 years ago were excluded from analysis. Statistical significance was assessed at p < 0.05.

RESULTS: There were 4,652 total men with diagnosis of KS. Mean age at diagnosis was 44 years (range 16 - 51), and mean testosterone level was 371 ng/dL [68 – 674]. Overall, only 35.10% of men with KS were given prescription for TRT at any time following diagnosis Interestingly, secondary analysis revealed that men with KS were prescribed TRT at significantly higher rates than hypogonadal men without KS (OR = 1.17; 95% CI: 1.095 – 1.239; p < 0.0001).

CONCLUSIONS: To the knowledge of the authors, this is the first study to evaluate TRT prescribing habits in men with KS. In this large, retrospective study, TRT was under-prescribed in men with KS. Further studies are needed to corroborate these findings and to evaluate the complexities recognizing symptoms and receiving care in this population.

IMPACT STATEMENT: Just over 35% of men with Klinefelter syndrome received prescription of TRT for associated hypogonadism in this study of a large, electronic health record network. Increased awareness of this trend is important in ensuring proper management and appropriate referral to male reproductive specialists for these patients.

P-480 6:45 AM Wednesday, October 26, 2022

THE IMPACT OF PREIMPLANTATION GENETIC TESTING ON MENTAL HEALTH OF COUPLES UNDERGOING ASSISTED REPRODUCTION TREATMENT: AFFECTIVITY AS AN INDICATOR OF QUALITY OF LIFE. Victor Zalai, PhD, Denise Christofolini, MSc., PH.D., Caio Barbosa, MD, PhD, Bianca Bianco, PH.D. Instituto Ideia Fertil, Santo Andre, Brazil; Faculdade de Medicina do ABC, Brazil; Instituto Ideia Fertil de Saude Reproductiva, Santo Andre, Brazil; Faculdade de Medicina do ABC, Sao Paulo, Brazil.

OBJECTIVE: About 20% of the causes of infertility are genetic. Preimplantation genetic testing (PGT) is an early form of prenatal diagnosis that aims to prevent genetic diseases through embryo selection. Due to the complex nature of a follow-up in genetics the involvement of a multiprofessional healthcare team is needed, with a prominent role of the psychological support. There is an inverse relationship between mental health and infertility, with general well-being impairment. Most patients undergoing PGT may have experienced miscarriages, to have a children affected by genetic disease, themselves to be affected by a genetic disease, and/or have experienced previous in vitro fertilization (IVF) treatment failures, which can increase the level of negative affects and impact on quality of life. Therefore, couples referred to PGT are considered vulnerable due to the impact on mental and social health. Here we aimed to identify and compare the levels of affect and quality of life in patients undergoing IVF treatments with and without indication for PGT.

MATERIALS AND METHODS: Qualitative study comprising 375 patients undergoing IVF treatment. The patients were divided into two groups: 'PGT' (n=73) and 'Non-PGT' (n=302). Participants filled the Positive and Negative Affect Schedule (PANAS) and Fertility Quality of Life (FERTIQOL) scales. The Spearman Correlation test was used to verify relationships between continuous variables and the Mann-Whitney U Test for group comparison.

RESULTS: Sex, type and cause of infertility, and psychotropic use were not different between groups. Regarding the affectivity and quality of life, the non-PGT group presented better positive affect and quality of life scores (all domains) when compared to the PGT group (p<0.001). Negative affect was inversely related to quality of life, especially the social domain.

CONCLUSIONS: Patients referred to PGT required more attention from the healthcare team than those that did not performed the test. We suggest that the first ones experienced higher levels of negative affects from the very beginning of the treatment, presenting substantial impairment in the quality of life domains.

IMPACT STATEMENT: Patients undergoing assisted reproduction treatments that require PGT must be closely followed by the multidisciplinary healthcare team, especially genetic counseling and psychological support. The goal is to develop adaptive strategies for the improvement of positive affects and quality of life in order to preserve and improve the mental health status of these patients.

OBJECTIVE: Several patient populations prefer to avoid TV monitoring for comfort or to prevent dysphoria. The purpose of this study is to compare TA and TV ultrasound as a means of determining cycle trigger timing and predicting oocyte maturity based on scans performed during ART cycles in this patient population.

MATERIALS AND METHODS: This was a retrospective cohort study of 59 patients who underwent ≥1 ART cycle at a single academic center. The study group consisted of patients who preferred TA monitoring based on any of 3 following inclusion criteria: 1) if they were virginal, 2) identified as transgender or 3) had a diagnosis of vaginismus. The control group included patients within this cohort that had no preference for TA imaging and thus underwent TV imaging. Demographics and variables included age, body mass index (BMI), antral follicle count (AFC) and anti-mullerian hormone (AMH), day 2 estradiol (D2 E2) and follicle-stimulating hormone (FSH) levels, # scans per cycle, # stimulations per day, estimated # follicles at trigger and # oocytes retrieved.

RESULTS: There was no significant difference between estimated # follicles at trigger and # oocytes retrieved. There was no significant difference between estimated # follicles at trigger and # oocytes retrieved. There was no significant difference between estimated # follicles at trigger and # oocytes retrieved. There was no significant difference between estimated # follicles at trigger and # oocytes retrieved. There was no significant difference between estimated # follicles at trigger and # oocytes retrieved. There was no significant difference between estimated # follicles at trigger and # oocytes retrieved. There was no significant difference between estimated # follicles at trigger and # oocytes retrieved. There was no significant difference between estimated # follicles at trigger and # oocytes retrieved. There was no significant difference between estimated # follicles at trigger and # oocytes retrieved.

CONCLUSIONS: TA and TV imaging do not differ in their ability to predict FC cycle characteristics, oocytes retrieved or oocyte maturity rate. TA imaging may offer an acceptable alternative for patients uncomfortable with TV imaging during FP.

IMPACT STATEMENT: The prolonged nature of the COVID-19 pandemic continues to be associated with high rates of depression amongst women currently considering or undergoing fertility treatments. Although anxiety scores were generally low, higher anxiety (and depression) scores are associated with medical mistrust. This highlights the importance of providing psychological support to this group of patients in order to better care for this population.

P-483 6:45 AM Wednesday, October 26, 2022

EMOTIONAL ASPECTS ASSESSED BY THE DASS-21 SCALE IN PREGNANT WOMEN CONCEIVED BY IN VITRO FERTILIZATION DURING THE COVID-19 PANDEMIC. Camilla C. A. Motta, MD, student, 1 João D. R. Duk, MD, student, 1 Livia Oliveira O. Munhoz Soares, MD, 2 Flavia Rocha Torelli, MD, MSc, 3 Mauricio B. Chehin, MD, PhD, 4 Aline R. Lorenzo, PhD, 5 Eduardo L. A. Motta, MD, PhD, 4 Renato Fraietta, MD, PhD, 6 Santa Casa de Sao Paulo, Sao Paulo, Brazil; 7Huntington Medicina Reprodutiva - Eugin Group, Brasilia, Brazil; 8Huntington Medicina Reprodutiva - Eugin Group, Campinas, Brazil; 9Huntington Medicina Reprodutiva - Eugin Group, Sao Paulo, Brazil; 10Huntington Medicina Reprodutiva - Eugin Group, Sao Paulo, Brazil; 11Federal University of Sao Paulo, Sao Paulo, Brazil.

OBJECTIVE: The COVID-19 pandemic has brought new challenges to infertile couples: the fear and uncertainty of potential SARS-CoV-2 infection effects during pregnancy. The present study aims to evaluate depression, anxiety and stress parameters in pregnant women conceived by IVF, during the coronavirus outbreak.

MATERIALS AND METHODS: This prospective cohort study included 109 clinical pregnant women (fetal heart beat) that consecutively underwent embryo transfer after an IVF treatment during the coronavirus outbreak between Jun/20 to Feb/21 in a private ART (assisted reproductive technology) clinic. Patients were evaluated through telephonic interview at the end of each trimester of pregnancy (12, 24 and 34 weeks) by the DASS-21 questionnaire, an internationally validated scale to track the severity of depression, anxiety and stress symptoms. Clinical variables such as age, obstetric history, clinical comorbidities and years of infertility were also included. Comparison statistical tests were applied accordingly to normal distribution of values. A p value <0.05 was considered significant.

RESULTS: The mean age was 38.9±5.02 years old. The majority of patients had never been pregnant before (67%) and reported other complications (75.2%). The mean infertility time was 3.76±2.38 years. Singleton pregnancies represented 83.5%. During the follow-up, two patients had late miscarriage at 21 weeks of singleton pregnancies (1,8%) and one had a fetal demise at 26 weeks of a singleton pregnancy (0,9%). Four patients (3,7%) had very preterm labor (between 28-32 weeks), seven (6,4%) had preterm labor (between 33-35 weeks) and one (0,9%) had a late preterm labor (36th week). In general, there were no differences in any of the emotional aspects evaluated (depression, anxiety and stress) along first, 2nd and 3rd trimesters (p=0.13, p=0.93 and p=0.55, respectively). However, when patients were separated by groups of age (<38 yo and ≥38 yo), means 34,8±4.90 and 42,35±4.69, (p=0.007), older patients presented higher levels of stress (p=0.007) compared to the younger. Furthermore,

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patients with history of previous pregnancy loss presented higher levels of anxiety and stress (p = 0.037 and 0.036 respectively) compared to the nulliparous. In addition, when comorbidities were associated with infertility, patients also presented higher levels of anxiety and stress (p = 0.03 and 0.002, respectively). Years of infertility (≤3 or >3 years) was not associated with aggravation in DASS scores during pregnancy.

CONCLUSIONS: Our data demonstrated that patients who conceived during the pandemic by IVF showed higher levels of anxiety and stress throughout their pregnancy, as assessed by the DASS-21 scale, mainly if they are greater than 38y/o, had previous pregnancy loss or presented other comorbidity associated.

IMPACT STATEMENT: COVID-19 pandemic brought new challenges to our society. Infertile women are probably highly vulnerable to stress and anxiety mainly during pregnancy and demand a proper psychological support to alleviate those symptoms, in order to promote a better environment to the binomial mother-baby.

P-484 6:45 AM Wednesday, October 26, 2022

ONE EPISODE OF SEVERE OVARIAN HYPERSTIMULATION SYNDROME (OHSS) IN AN OOCYTE DONOR INDICATES HIGH RISK FOR REOCCURRING SEVERE OHSS IN SUBSEQUENT OOCYTE DONATION CYCLES. Diane M. Tober, D.PHIL., M.A.1, Kevin S. Richter, PhD.2, Shannon Koljohn, MS.c, Said Daneshmand, MD.3, UCSF, Tuscaloosa, AL; 1Fertility Science Consulting, Silver Spring, MD; 2San Diego Fertility Center, San Diego, CA.

OBJECTIVE: While it is generally accepted that a prior history of severe OHSS is a risk factor for OHSS in subsequent cycles of ovarian hyperstimulation for in vitro fertilization (IVF), empirical evidence for this conjecture is lacking. Our objective was to evaluate OHSS risk according to the degree of OHSS experienced in initial cycles among donors undergoing multiple donation cycles.

MATERIALS AND METHODS: Oocyte donors (n=218) who donated multiple times were surveyed retrospectively. Donors reported the severity of OHSS associated with each cycle, along with specific symptoms (e.g., severe bloating, bed rest, hospitalization, nausea/vomiting, difficulty breathing, fluid drainage aka paracentesis). For analysis, OHSS severity was categorized according to standard SART/ASRM classification (none, mild, moderate, or severe). Spearman’s Rank-Order Correlation was used to nonparametrically evaluate the association between OHSS severity experienced in 2nd versus 1st donation cycles.

RESULTS: The degree of OHSS experienced by donors in 1st cycles was highly predictive of the severity of OHSS they experienced in 2nd cycles (correlation coefficient r = 0.608, p < 0.0001). The same degree of OHSS was reported for both cycles among 155 of the participating donors (71%). Two-thirds of all donors reporting moderate OHSS symptoms in 1st cycles also reported moderate OHSS in 2nd cycles, and three-quarters of all donors reporting severe OHSS in 1st cycles also reported severe OHSS in 2nd cycles. Among the 14 donors who donated again after experiencing severe OHSS in 1st cycles, five (36%) experienced severe OHSS again, and more than half (57%) had at least moderate OHSS symptoms in 2nd cycles.

<table>
<thead>
<tr>
<th>Degree of OHSS experienced with 1st donation cycle</th>
<th>No OHSS</th>
<th>Mild OHSS</th>
<th>Moderate OHSS</th>
<th>Severe OHSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>51</td>
<td>100</td>
<td>53</td>
<td>14</td>
</tr>
<tr>
<td>No OHSS in 2nd Cycle</td>
<td>75%</td>
<td>5%</td>
<td>2%</td>
<td>7%</td>
</tr>
<tr>
<td>Mild OHSS in 2nd Cycle</td>
<td>12%</td>
<td>77%</td>
<td>25%</td>
<td>36%</td>
</tr>
<tr>
<td>Moderate OHSS in 2nd Cycle</td>
<td>10%</td>
<td>13%</td>
<td>66%</td>
<td>21%</td>
</tr>
<tr>
<td>Severe OHSS in 2nd Cycle</td>
<td>4%</td>
<td>5%</td>
<td>8%</td>
<td>36%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: This is the first definitive evidence confirming that a history of severe OHSS is a significant risk factor for additional episodes of severe OHSS. Our results suggest that donors who experience an episode of severe OHSS associated with one cycle of oocyte donation have a very high risk of severe OHSS if they continue to undergo additional donation cycles.

IMPACT STATEMENT: Given such high estimated chances of recurrent severe OHSS, it could be argued that a single episode of severe OHSS should disqualify a person from any further oocyte donations.

SUPPORT: University of California, San Francisco National Center of Excellence in Women’s Health National Science Foundation Grant #1828783

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OBSTETRIC OUTCOMES FOLLOWING OVARIAN HYPERSTIMULATION SYNDROME IN IVF – A COMPARISON WITH UNCOMPLICATED FRESH AND FROZEN TRANSFER CYCLES. Hadas Ganer Herman, MD.1, Yossi Mizrachi, MD.2, Eran Horowitz, MD, Dr.3, Ariel Weissman, M.D.1, Ben Sabbah, MD.1, Ohad Gluck, MD.3, Arieh Raziel, MD.3, Michal Kovo, MD Prof.3 Montréal, QC, Canada; 3Edith Wolfson Medical Center, affiliated with the Sackler Faculty of Medicine, Holon, Israel.

OBJECTIVE: We aimed to assess the correlation between ovarian hyperstimulation syndrome (OHSS) in the early course of in vitro fertilization (IVF) pregnancies and obstetric outcomes.

MATERIALS AND METHODS: We identified records of patients admitted due to OHSS following IVF treatment at our institution between 2008 and 2020. Cases were included if pregnancy resulted in a live singleton delivery (OHSS group). OHSS cases were matched at a 1:5:5 ratio with live singleton deliveries following IVF with fresh embryo transfer (fresh transfer group) and frozen embryo transfer (FET group), according to maternal age, parity, and 220 FET pregnancies. Patient demographics were similar between the groups, including body mass index (BMI) less than 40, and a diagnosis of PCOS, undergoing oral OI followed by timed intercourse (TIC) or intrauterine insemination (IUI). The same degree of OHSS was highly predictive of the severity of OHSS they experienced in 2nd cycles (correlation coefficient r = 0.608, p < 0.0001). The same degree of OHSS was reported for both cycles among 155 of the participating donors (71%). Two-thirds of all donors reporting moderate OHSS symptoms in 1st cycles also reported moderate OHSS in 2nd cycles, and three-quarters of all donors reporting severe OHSS in 1st cycles also reported severe OHSS in 2nd cycles. Among the 14 donors who donated again after experiencing severe OHSS in 1st cycles, five (36%) experienced severe OHSS again, and more than half (57%) had at least moderate OHSS symptoms in 2nd cycles.

RESULTS: Overall, 44 OHSS cases were matched with 220 fresh transfer and 220 FET pregnancies. Patient demographics were similar between the groups, including body mass index, smoking and comorbidities. Gestational age at delivery, the rate of preterm births, preeclampsia and cesarean delivery were similar between the groups. Placental abruption occurred in 6.8% of OHSS pregnancies, 1.4% of fresh transfer pregnancies and 0.9% of FET pregnancies (p = 0.02). On post-hoc analysis, the rate of placental abruption was significantly higher in OHSS pregnancies, compared with the two other groups, and this maintained significance after adjustment for confounders. Birthweights were 3057 ± 483, 3057 ± 545 and 3213 ± 542 grams in the OHSS, fresh transfer and FET groups, respectively (p = 0.004), although the rate of small for gestational age neonates was similar between the groups.

CONCLUSIONS: OHSS in the early course of IVF pregnancies is associated with an increased risk of placental abruption.

OBJECTIVE: To study how anti-mullerian hormone (AMH) level in patients with polycystic ovary syndrome (PCOS) affects ovulation induction (OI) cycle cancellation rates. Pregnancy and live birth rates were secondarily analyzed.

MATERIALS AND METHODS: A multicenter, retrospective study of OI cycles conducted from September 1, 2018 through December 31, 2021 was performed. Patients included were infertile, 18-35 years old, with a body mass index (BMI) less than 40, and a diagnosis of PCOS, undergoing oral OI followed by timed intercourse (TIC) or intrauterine insemination (IUI). Patients with a coexisting infertility diagnosis were excluded. The data
was summarized using descriptive statistics for continuous variables (mean, standard deviation, and percentages) with Excel version 16.54. Statistical Analytics Software (SAS) version 9.4 was used to analyze continuous data by way of a mixed model logistic regression with covariates when necessary, while patient age and BMI were adjusted for via a multivariable regression model. A p-value < 0.05 was considered statistically significant.

RESULTS: A total of 420 cycles completed by 109 patients were included. AMH levels ranged from 0.92-54.8 ng/mL with an average of 10.4 ng/mL (SD 8). Clinical pregnancy was achieved in 47% of patients (n=52) and a live birth in 34% (n=37). A total of 6% (n=24) of OI cycles were cancelled for lack of ovarian response. Eighty-seven patients with an AMH level below 16 ng/mL completed 328 cycles of OL, averaging 3.7 OI cycles per patient. Of these 328 cycles, 4.6% (n=15) were cancelled and 10.4% (n=34) were redosed. Twenty-two patients with an AMH level above 16 ng/mL completed 90 cycles of OL, averaging 4.1 cycles per patient. In this group, 11.1% (n=10) of OI cycles were cancelled and 14.4% (n=13) were redosed. Patients with an AMH level above 16 ng/mL were significantly more likely to encounter cycle cancellation (p<0.05) and achieve a clinical pregnancy (p<0.05). These findings remained significant after adjusting for age and BMI (p<0.05).

CONCLUSIONS: PCOS patients with a high AMH level are at an increased risk of OI cycle cancellation despite an increased clinical pregnancy rate.

IMPACT STATEMENT: Patients with PCOS and a high AMH level should be counseled on the risks of OI cycle cancellation based on their ovarian reserve. Fertility strategies, regardless of age or BMI, should be individualized.

P-488 6:45 AM Wednesday, October 26, 2022
OUTCOMES FOLLOWING RANDOM START PLUS PROGESTIN PRIMED OVARIAN STIMULATION IN AN OOCYTE DONATION PROGRAM. Juan C. Farfan, MD PhD,1 Jaime Guerrero, MSc,2 Andrea Bernabeu García, PhD3 Alicante/Alacant, Alicante, Spain; 2Instituto Bernabeu, Alicante, Spain.

OBJECTIVE: Random-start ovarian stimulation protocols have emerged allowing treatment to begin at any day of the menstrual cycle. Concomitantly, in what is called progestin primed oocyte stimulation (PPOS), the use of progestins seem similarly as effective as GnRH antagonists in preventing LH surge. If ovarian stimulation can be initiated randomly together with the advantages of PPOS, without adversely impacting oocyte yield or quality, the approach may facilitate tasks in oocyte donation (OD) units.

MATERIALS AND METHODS: Retrospective analysis of 1765 OD cycles performed in 2020-2021. Donors started stimulation with 150-300 IU FSH on day 1-3 of the menstrual cycle (Group 1, n=363) and were compared to donors initiating in the mid (day 4-9) (Group 2, n=1243) and late follicular phase (day 10-14) (Group 3, n=139). Ovarian stimulation was not initiated in a post ovulatory phase due to concerns in the eventuality of an (unnoticed) early pregnancy. Natural micronized progesterone 200 mg/daily/oral beginning on the first day of stimulation was used to prevent LH surge until the administration of a GnRH agonist trigger. Recipients used a sequential estrogen/progesterone endometrial preparation for embryo transfer.

The cycle and laboratory outcomes were analyzed; clinical outcomes per fresh embryo transfer in recipients (n=909) were also assessed. Continuous variables were compared with ANOVA test and categorical variables with Chi-square.

RESULTS: Ovarian stimulation lasted less and required lower doses of FSH when initiated in the mid follicular phase. A lower number of and meta-phase II oocytes were collected when ovarian stimulation was initiated in the early follicular phase (Table). Overall, recipients received 9.5 ± 1.4 oocytes, fertilization rate was 82% (ICSI), number of usable blastocyst embryos was 4.4 ± 1.9, and after a fresh embryo transfer of 1.09 ± 0.3 embryos the clinical pregnancy rate was 49.4%.

CONCLUSIONS: These data, from a retrospective study design, shows that the oocyte yield and competence from random-start plus PPOS throughout the follicular phase is not negatively affected in oocyte-donors.

IMPACT STATEMENT: With this protocol, ovarian stimulation can be initiated at any moment during the follicular phase without adversely impacting oocyte yield or competence; the approach may facilitate schedules and provide convenience for oocyte donation programs.

SUPPORT: None

P-489 6:45 AM Wednesday, October 26, 2022
THE USE OF A LEUPROLIDE ACETATE (LA) TRIGGER DURING OVARIAN STIMULATION FOR A TRANSGENDER (TG) PERSON ON LONG TERM TESTOSTERONE (T): A CASE REPORT AND LITERATURE REVIEW. Arri Taggar, M.D., M.P.H., Reeva B. Makhijani, MD, Daniel R. Grow, MD, MHC, David W. Schmidt, M.D. University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT.

OBJECTIVE: To highlight a TG fertility preservation case in a patient on long term T with a LA trigger minimizing the risk of ovarian hyperstimulation syndrome, and to review pertinent literature.

A 33-year-old non-binary person with ovaries presented for care seeking fertility preservation for a future shared conception cycle with their cisgendered female partner. The patient had been on T gel for over four years. They had not had any pelvic surgery and had no pertinent medical conditions. They were amenorrheic with a levonorgestrel intrauterine device in place. Their BMI was 27 kg/m2, their anti-Mullerian hormone was 3.34 ng/ml, their baseline follicle stimulating hormone was 7.8 mIU/mL, their baseline luteinizing hormone was 4 mIU/mL, their baseline estradiol was 39 pg/ml, and their baseline antral follicle count was 21.

The couple planned to use sperm from an anonymous donor and desired embryo cryopreservation with use of preimplantation genetic testing for aneuploidy (PGT-A). Transabdominal scans were preferably used for assessment and cycle monitoring. T gel was stopped five days prior to the start of stimulation, and letrozole was not used during the cycle. A standard antago-nist stimulation protocol was used. The peak estradiol was 1510 pg/ml. The patient was triggered with 1mg of LA. Fourteen metaphase II oocytes were retrieved vaginally, 12 fertilized, and 7 blastocysts were biopsied and cryo-preserved. Three embryos resulted euploid after the use of PGT-A. A few months later, one was transferred to the patient’s partner and resulted in a suc-cesful ongoing pregnancy.

MATERIALS AND METHODS: The case was reviewed. A review of the literature was performed. The search terms “Transgender” or “gender nonconforming,” and “fertility preservation” or “ovarian stimulation,” and “Leuprolide Acetate,” or “Lupron,” or “Testosterone,” on PubMed and Google Scholar were used, with articles limited to English through March 2022. Duplicate, psychological only, pediatric and sperm preservation pieces were excluded.

RESULTS: 172 unique publications were screened, and two were found relevant. Both were case reports. One case reported continued use of T through ovarian stimulation and used a LA trigger for final oocyte maturatin.1 The second case reported stopping T for 24 days prior to ovarian stimulation and used a human chorionic gonadotropin trigger.2 All other literature reported stopping T 3-6 months prior to stimulation and were therefore excluded.

CONCLUSIONS: To our knowledge, this is the first reported case of ovarian stimulation and embryo cryopreservation after such a length and temporal relation to T use. This is the first reported use of PGT-A in a TG patient on long term T. This is the second reported case of the use of a LA trigger for ovarian stimulation in this type of patient scenario. There is a dearth of literature around this subject, and additional publications could enhance the care of gender nonconforming patients seeking fertility preservation.
IMPACT STATEMENT: Clinicians should consider that ovarian stimulation on long term T use is certainly possible and is shown to be successful and safe with a LA trigger.

SUPPORT: None


P-489 6:45 AM Wednesday, October 26, 2022

A PROSPECTIVE STUDY ON THE VALUE OF MONITORING EXTRACULAR SERUM HUMAN CHORIONIC GONADOTROPIN LEVELS DURING IVF STIMULATION: LESSONS LEARNED FROM 2,257 CYCLES. Cheri K. Margolis, MD, 1 Danielle Gallo, MD, 2 Leah M. Roberts, MD, 1 Amber M. Klimczak, MD, 1 Nola Herlihy, MD, 1 Pavan Gill, MD, 1 Andres Reig, MD, 1 Christine V. Whitehead, BSN, RN, 1 Emre Seli, MD 1 IVIRMA New Jersey, Basking Ridge, NJ; 2 Saint Peter’s University Hospital, New Brunswick, NJ.

OBJECTIVE: Adding an LH component to IVF stimulation has previously been reported to improve retrieval outcomes in certain populations, when compared to follicle stimulating hormone (FSH) alone. Consequently, IVF cycles routinely utilize human chorionic gonadotropin (hCG) as a means of luteinizing hormone (LH) replacement throughout stimulation, either through use of human menopausal gonadotropin (hMG) or low dose hCG (ldHCG). The influence of these medications is reflected in serum hCG levels. The aim of this study is to determine if serum hCG levels during the follicular phase of IVF stimulation are associated with improved embryologic outcomes.

MATERIALS AND METHODS: A prospective, observational study of patients undergoing IVF stimulation with protocols utilizing hMG or ldHCG at a large infertility practice. hCG was measured from otherwise discarded serum on stimulation days (SD) 5-6, and on the day of trigger. hCG was measured on the ROCHE immunooassay system, calibrated to detect levels as low as 0.1 mIU/mL. ANOVA and linear regression testing were used to determine the relationship between serum hCG values and the numbers of oocytes retrieved, mature oocytes (M2’s), pronuclear (2PN) and blastocyst stage embryos.

RESULTS: In total, 2,257 IVF cycles from 01/2019-01/2022 were analyzed. Results for serum hCG levels on SD5-6 and on the day of trigger were distributed in to four quartiles (Q1 having the lowest levels). On SD5-6, when controlling for age, AMH, and BMI, there was a persistently significant difference seen in that the lowest quartiles had progressively more oocytes retrieved (p=.001), M2’s (p=.005), 2PN’s (p=.002), and blastocysts (p=.003). When looking at a subset of 1,024 cycles of patients who received a consistent dose of 150 IU/day hMG or 20 IU/day ldHCG throughout stimulation, the same statistically significant trend persisted when controlling for age, AMH, and BMI for oocytes retrieved (p=.011), M2’s (p=.020), and 2PN’s (p=.024), but not blastocysts obtained (p=.059). When looking at serum hCG levels on the day of trigger, when controlling for age, AMH, and BMI, there was no statistically significant difference seen in embryologic outcomes between the different quartiles when looking at all cycles, as well as those on a consistent dose of 150 IU/day hMG or 20 IU/day ldHCG.

CONCLUSIONS: When controlling for age, AMH, and BMI, lower serum hCG levels on SD5-6 are associated with improved embryologic outcomes in IVF protocols utilizing hMG or ldHCG. This holds true for patients on a consistent dose of hMG or ldHCG throughout stimulation, indicating that an effect on embryologic outcomes remains when factoring in the patient’s capacity for hCG absorption and clearance. There was no difference in embryologic outcomes between day of trigger serum hCG quartiles, highlighting the value of monitoring serum hCG throughout stimulation, rather than solely at the time of trigger.

IMPACT STATEMENT: When using hMG or ldHCG in IVF stimulation, lower SD5-6 serum hCG levels are associated with more oocytes retrieved, M2’s, 2PN’s, and blastocyst stage embryos. Trigger day serum hCG levels had no effect on these outcomes.

P-490 6:45 AM Wednesday, October 26, 2022

THE USE OF BIOSIMILAR OR ORIGINATOR FOLLITROPIN ALFA PREPARATIONS IN PROGESTIN PRIMED OVARIAN STIMULATION PROTOCOLS (PPOS) RESULT IN SIMILAR CLINICAL OUTCOMES. María Cruz, PhD, 1 Vanessa Vergara-Bravo, MD, 2 Antonio Requena, MD 1 IVIRMA Global Headquarters, Madrid, Spain; 2 Reproductive Medicine Specialist, Madrid, Spain.

OBJECTIVE: To assess clinical outcomes using different follitropin alfa preparations in the context of a progestin primed ovarian stimulation (PPOS) protocol and to identify confounding factors attributable to the success of the cycle.

MATERIALS AND METHODS: Women accepted as oocyte donors and undergoing ovarian stimulation with 3 different follitropin alfa preparations (Ovaleap® (Theramex Spain); n=3231, Bemfola® (Gedeon Richter Iberica); n=3542 or Gonal-F® (Merck SL) n=616. Ovaleap® and Bemfola® are both biosimilars to the originally approved biological product, Gonal-F®. On day cycle 2 or 3, donors started to administered daily 150-225 IU of one of the 3 different follitropin alfa preparations. On the first FSH stimulation day, 10 mg acetate of medroxyprogesterone (MPA) was administered daily and then continued until GnRH agonist trigger (triptorelin). Finally, a single dose of 0.2 mg GnRH agonist was administered to trigger final oocyte maturation. Transvaginal oocyte retrieval was performed 36 hours later. The oocytes were fertilized and, in all cases, a single embryo transfer was performed. Statistical analysis was performed by ANOVA and Chi-squared; and a logistic regression analysis was performed with the ongoing pregnancy rate as the dependent variable

RESULTS: There were some significant differences in stimulation characteristics such as age, days of stimulation, and number of retrieved oocytes, which were higher in the Gonal-F-stimulated donor group; however, regarding clinical variables analyzed, there were no significant differences found between the three study groups. This was further confirmed on applying a linear regression model, which used the ongoing pregnancy rate as the explanatory variable. Both age 0.986 (0.974-0.999, p=0.033) and the number of mature oocytes 1.027 (1.007-1.047, p=0.008), significantly affected the chances of achieving an ongoing clinical pregnancy while the type of follitropin alfa 1.048 (0.956-1.149, p=0.317) and the fact of having taken contraceptives prior to treatment cycle 1.046 (0.934-1.173, p=0.436) did not influence the success rate.

CONCLUSIONS: As biosimilars have minor variations in sialylation from the originator, it is very reassuring that these small differences had no clinical impact when compared with the reference product. The different types of follitropin alfa are interchangeable in PPOS.

IMPACT STATEMENT: No differences were found between different types of follitropin alfa when compared in PPOS.

SUPPORT: Not apply

REFERENCES: Not apply

E-POSTER ABSTRACT STATION: W6

P-491 6:45 AM Wednesday, October 26, 2022

DOES THE USE OF CLOMIPHENE CITRATE DURING GONADOTROPIN STIMULATION IMPACT ENDOMETRIAL THICKNESS AND CLINICAL PREGNANCY RATE DURING FRESH TRANSFER CYCLES. Lauren Ursillo, M.D., 1 Alexandra Peyser, M.D., 2 Randi H. Goldman, M.D. 1 Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, New York, NY; 2 Northwell Health Fertility, Zucker School of Medicine at Hofstra Northwell, Manhasset, NY; 3 Northwell Health Fertility, Northwell Health, Manhasset, NY.

OBJECTIVE: Clomiphene citrate (CC) has been used as an adjunct to gonadotropin administration during fresh in vitro fertilization (IVF) cycles in patients with diminished ovarian reserve. As CC is a selective estrogen receptor modulator that has antiestrogenic properties at the level of the endometrium, use of CC could potentially have a detrimental effect on outcomes.
following fresh embryo transfer. The objective of this study was therefore to
determine the impact of CC on endometrial lining thickness and pregnancy
outcomes in women undergoing a fresh autologous embryo transfer.

MATERIALS AND METHODS: A retrospective chart review examined all
stimulation cycles that resulted in autologous fresh embryo
transfer performed at a single academic medical center between October
2019 and January 2022. Patients in the clomiphene citrate group took
100mg on day 1 through day 5 of stimulation. The primary outcomes were
endometrial thickness and ongoing pregnancy (CIG). Chi-squared test and
logistic regression were used to compare endometrial thickness and preg-
nancy outcomes among cycles with and without CC, with p < 0.05 defining
significance. Regression models were adjusted for age.

RESULTS: One hundred seventy-three cycles were included, of which 27
utilized CC. Patients in the CC group were older (mean 39.5 vs. 37.9 years),
had a lower AMH (0.91 vs. 2.45), lower estradiol on day of trigger (1619 vs.
2248 pg/mL), fewer number of eggs retrieved (7.3 vs. 11.8), and fewer 2PNs
(4.9 vs. 6.0) than patients whose cycles did not include CC. There was no dif-
ference in endometrial thickness between patients who did and did not use
CC (10.3 vs. 11.1mm respectively, p = 0.16). Four of the 27 cycles (14.8%) that
utilized CC resulted in ongoing pregnancy, while 48 of the 146 cycles
(32.9%) without CC resulted in CIG. In the unadjusted model, use of CC ap-
ppeared to have a significant negative impact on CIG (p = 0.04), however, after
adjusting for age, CC no longer remained a significant predictor of outcome
(p = 0.14). There was no difference in SAB or biochemical pregnancy rate be-
tween the two groups (p = 0.09).

CONCLUSIONS: Use of CC was associated with older patient age and
lower levels of AMH, estradiol on day of trigger, number of eggs retrieved
and number of 2PNs, but did not independently impact endometrial thickness or
pregnancy outcomes during fresh transfer cycles.

IMPACT STATEMENT: Clomiphene citrate does not impact endometrial
thickness or ongoing pregnancy in patients undergoing fresh embryo transfer.

P-492 6:45 AM Wednesday, October 26, 2022

CAN THE DUAL TRIGGER PROTOCOL IMPACT EM-
BRYO PLOIDIA? Fernanda Rodrigues Bernarder, MS, Silvia Morales Jau, MD, Amanda Faria Lino, MD, Marcelo Lucchesi Lucchesi Montenegro, MD, Edson G. Lo Turco, PhD, Fernando Prado Ferreira, MD, PhD São Paulo Federal University; 2Medical Doctor; 3Medical doctor; 4Sao Paulo Federal University, Department of Surgery, Division of Urology, Human Reproduction Section, Sao Paulo, Brazil; 5Neo Vita Reprodução Humana, Sao Paulo, Brazil.

OBJECTIVE: To evaluate the impact of the induction of final follicular matu-
rative by the dual trigger protocol on the euploidy of in vitro cultured embryos.

MATERIALS AND METHODS: Data were collected from 1102 patients for
36 months who were splitted into 5 groups according to the trigger protocol. The
Groups were Chorionom group with 18 patients (CG), Gonapetbyl group with 452
patients (GG), Lupron group with 67 patients (LG), Ovidrel group with 87 pa-
tients (OG), Gonapetbyl plus Chorionom group with 478 patients (GCG). All pa-
tients were randomized into 2 groups of 40 each by a computer generated program.

RESULTS: One hundred seventy-three cycles were included, of which 27
utilized CC. Patients in the CC group were older (mean 39.5 vs. 37.9 years),
had a lower AMH (0.91 vs. 2.45), lower estradiol on day of trigger (1619 vs.
2248 pg/mL), fewer number of eggs retrieved (7.3 vs. 11.8), and fewer 2PNs
(4.9 vs. 6.0) than patients whose cycles did not include CC. There was no dif-
ference in endometrial thickness between patients who did and did not use
CC (10.3 vs. 11.1mm respectively, p = 0.16). Four of the 27 cycles (14.8%) that
utilized CC resulted in ongoing pregnancy, while 48 of the 146 cycles
(32.9%) without CC resulted in CIG. In the unadjusted model, use of CC ap-
ppeared to have a significant negative impact on CIG (p = 0.04), however, after
adjusting for age, CC no longer remained a significant predictor of outcome
(p = 0.14). There was no difference in SAB or biochemical pregnancy rate be-
tween the two groups (p = 0.09).

CONCLUSIONS: Use of CC was associated with older patient age and
lower levels of AMH, estradiol on day of trigger, number of eggs retrieved
and number of 2PNs, but did not independently impact endometrial thickness or
pregnancy outcomes during fresh transfer cycles.

IMPACT STATEMENT: Clomiphene citrate does not impact endometrial thickness or ongoing pregnancy in patients undergoing fresh embryo transfer.

P-493 6:45 AM Wednesday, October 26, 2022

PROGESTERONE PRIMED OVARIAN STIMULATION
PROTOCOL (PPOS) VS GNRH ANTAGONIST FOR PA-
TIENTS OF FREEZE ALL CYCLES: A PROSPECTIVE
RANDOMISED CONTROLLED TRIAL. Kanad Dev Nayar, M.D., DGO, Dip. Obst (Ireland), FICOG, Shweta Gupta, MD, MRCOG, Sabina Sanan, MS, FNB, MRCOG, Sumita Agarwal, MD, DNB, Garima Kaur, MS, MRCOG, Kanika Sharma, MBBS, MS, Gaurav Kant, M.Sc, Kapil Dev Nayar, MBBS Akanksha IVF Centre, Delhi, India.

OBJECTIVE: To compare effectiveness of Progesterone vs GnRH Antag-
ons for pituitary suppression in controlled ovarian stimulation for patients of
Freeze all IVF/ICSI cycles.

MATERIALS AND METHODS: Prospective Randomised controlled trial conducted from 1st January 2021 to 31st December 2021 at a ter-
tiary care infertility centre Akanksha IVF centre, New Delhi. Eighty-
in fertile patients aged between 23-37years with normal antral follicular
count and normal uterine caviness by 2D ultrasound were enrolled and ran-
domized into 2 groups of 40 each by a computer generated program.
Study Group (n=40) patients were given Tab medroxyprogesterone ac-
etate (MPA) 10mg once daily from day 1 of stimulation. Control
Group(n=40) received GnRH Antagonist Inj. Cetrorelix 0.25mg s/c
on Day 6 of stimulation according to fixed protocol. TVS monitoring started
on day 2 of menses along with gonadotropins. When > 2 follicles
reached the size of 18 mm, all patients received Inj Leupride 2mg submu-
taneously as trigger for final oocyte maturation. Oocyte retrievals were
performed at 35 - 36 hours. Day 3 Frozen embryo transfers (3x 8cellA)
was performed for all cases. The luteal phase support was with vaginal supple-
mintion of 800 mcg micronized progesterone. Serum beta hCG was
performed after 14 days of embryo transfer. Primary outcome: Num-
ber of oocyte retrieved and clinical pregnancy rate. Secondary outcomes:
incidence of ovarian hyperstimulation syndrome (OHSS), implantation rate
and miscarriage rate. Data analyzed using SPSS version-17 and us-
ing chi-square test for categorical variables and unpaired t-test for contin-
uous variables.

RESULTS: The number of oocyte retrieved were slightly more in PPOS
group (12.4 ± 2.6) than in antagonist group (11.8 ± 2.2) although difference
was not statistically significant. But clinical pregnancy rate (38.6% in the
PPOS group vs. 40.2%) were similar between two groups. No premature
ovulation was observed in either group. Although one patient in the antago-
nist group had symptoms of mild OHSS.
Implantation rate (29.67% in the PPOS group vs. 26.08% in the antagonist
group) and miscarriage rate (10.8% in the PPOS group vs. 11.4% in the
antagonist group) were comparable.

CONCLUSIONS: PPOS can achieve similar implantation and clinical
outcomes while reducing the incidence of ovarian hyperstimulation
syndrome (OHSS) as compared to fixed antagonist protocol. Hence,
PPOS with MPA seems to be a patient friendly and cost effective
choice for women undergoing ovarian stimulation without affecting
ovarian reserve.

IMPACT STATEMENT: Progesterone can independently prevent premature
ovulation in ART cycles, with the additional benefit of having no OHSS.

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WHAT EFFECTS THE NEW MARKERS OF OVARIAN
STIMULATION: FOLLICULAR OUTPUT RATE (FORT),
FOLLICULAR TO-OOCYTE INDEX (FOI) AND
OOCYTES RETRIEVED PER FOLLICLES
(OPF)? Kubra Boymakalin, MD, 1 Meral Gultomruk, BSc, 2 Zalihe Yarkiner, PhD 3 1Bahceci Health Group, Fulya IVF Center, Istanbul,
Turkey; 2Bahceci Fulya IVF Center, ISTANBUL, Turkey; 3Cyprus Interna-
tional University, Faculty of Arts and Sciences, Kyrenia, Cyprus.

OBJECTIVE: To evaluate the factors affecting FORT, FOI and OPF
who triggered with gonadotrophin releasing hormone (GnRH) agonist in hyperres-
ponders.

RESULTS: The number of oocyte retrieved were slightly more in PPOS
group (12.4 ± 2.6) than in antagonist group (11.8 ± 2.2) although difference
was not statistically significant. But clinical pregnancy rate (38.6% in the
PPOS group vs. 40.2%) were similar between two groups. No premature
ovulation was observed in either group. Although one patient in the antago-
nist group had symptoms of mild OHSS.
Implantation rate (29.67% in the PPOS group vs. 26.08% in the antagonist
group) and miscarriage rate (10.8% in the PPOS group vs. 11.4% in the
antagonist group) were comparable.

CONCLUSIONS: PPOS can achieve similar implantation and clinical
outcomes while reducing the incidence of ovarian hyperstimulation
syndrome (OHSS) as compared to fixed antagonist protocol. Hence,
PPOS with MPA seems to be a patient friendly and cost effective
choice for women undergoing ovarian stimulation without affecting
ovarian reserve.

IMPACT STATEMENT: Progesterone can independently prevent premature
ovulation in ART cycles, with the additional benefit of having no OHSS.

P-494 6:45 AM Wednesday, October 26, 2022

SUPPON: NONE

MATERIALS AND METHODS: This study is a prospective cohort study including 84 hyperresponder patients undergoing GnRH antagonist cycles in which GnRHa trigger was used. The study performed between April 2021 and December 2021. The primary outcome measure was the FORT (number of pre-ovulatory follicles (≥15 mm)/AFCs 100), FOI (number of oocytes retrieved/AFCs 100) and OPF (number of oocytes retrieved/number of follicles aspirated during oocyte retrieval100).

To evaluate the factor affecting FORT patients were divided into three FORT groups: <35th percentile (low FORT: <41%, n=26), 35th-66th percentile (medium FORT: 41–57%, n=28), >67th percentile (high FORT: >57%; n=28). FOI ≤ 50% indicated low ovarian sensitivity (LOS) (n=20) and those >50% indicated normal ovarian sensitivity (NOS) (n=64). OPF values <80% indicated low ORF group (n=57) and those ≥ 80% indicated normal OPF group (n=27). Patient, OS and endocrinologic parameters were compared regarding these groups and correlation analysis were performed.

RESULTS: The mean age, body mass index (kg/m²), AFC and anti-mullerian hormone (AMH) were 3152±3.4, 24.80±5.06, 3154±13.56, and 5.94±4.92 respectively. The mean FORT, FOI and OPF levels were 67±±2.12, 32.6%, 52.1±20.3%, and 71.39±18.14%. The three FORT groups were comparable in terms of age, BMIs, AMH, total gonadotrophin dosage used, estradiol(E2) and progesterone(P4) levels on trigger day and oocyte retrieval day. Conversely, AFC and duration of stimulation showed decrease from the low to the high FORT groups (p<0.01, p=0.006 respectively). Correlation analysis revealed that FORT was correlated with AFC (r=0.53, P<0.001) and duration of stimulation (r=-0.266, p=0.016). Comparing LOS and NOS group showed no significant difference in ages, BMIs, AMH, total gonadotrophin dosage used, duration of stimulation, E2 levels on trigger day and oocyte retrieval day. AFC was significantly lower (p=0.003) and P4 on oocyte retrieval day was significantly higher in NOS group. AFC was found to be significantly correlated with FOI (r=0.53, p<0.001). No noteworthy differences were noted regarding any parameters between low OPF and normal OPF. In addition, the correlation analysis identified no factor for OPF.

CONCLUSIONS: FORT and FOI is negatively and independently related to antral follicle count, whereas OPF is not related.

IMPACT STATEMENT: FORT, FOI and OPF can be used as surrogate measures to identify women with ovarian resistance to gonadotropin stimulation. The factors effecting these parameters should be highlighted. These results may guide possible to how to manage the most optimal ovarian stimulations by using higher dosage of gonadotrophin or addition of LH.

REFERENCE:

P-496 6:45 AM Wednesday, October 26, 2022

DOES LUTEAL ESTRADIOL PRIMING (E2P) IMPROVE EUPLOIDY IN PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGTA) IN VITRO FERTILIZATION (IVF) IN SOCIETY FOR ASSISTED REPRODUCTIVE TECHNOLOGY (SART) AGES? 1 Aquelyn Shaw, MD, 2 James A. Grifo, MD, PhD, 3 Jennifer K. Blakemore, MD, MS 4 NYU Langone Fertility Center, New York, NY; 5NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: E2P is a technique for IVF protocols in poor responders to reduce cycle cancellation due to elevated FSH as well as increase stimulation response. Yet data is inconsistent on the impact on clinical pregnancy rates. 1 We sought to evaluate if E2P increases euploidy rates in IVF with PGTA.

MATERIALS AND METHODS: This is a retrospective cohort study of IVF cycles with PGTA from 3/2020-12/2021 at a single academic fertility center. E2P cycles were compared to age and AMH matched controls (CON) (1:2 ratio). The primary outcome was number of euploid embryos. Secondary outcomes were cycle start follicle stimulation hormone level (FSH), total gonadotrophin (GDN) dose, number oocytes, mature oocytes (MI), fertilization rate (2PN), and number of embryos biopsied (BX). Mann Whitney and Chi-square tests were performed (p<0.05 significant). Data is reported in median (range) and percentages.

RESULTS: 337 E2P cycles were compared to 674 CON. There were fewer microdose lupron (MCD) cycles in E2P patients (E2P: 88% antagonist (ANT), 12% MCD vs CON: 76% ANT, 24% MCD, p<0.01). Similar cancellation rates [E2P: 14% (47/337) vs CON: 12% (82/674), p=0.42] and poor blast formation (defined as nothing for biopsy) [E2P: 18% (60/337) vs CON: 15% (103/674), p=0.24] were seen between groups. Number of euploid embryos were similar across all SART age groups except for 38-40 years (y), with fewer euploids in E2P (Table). Cycle start FSH was lower and total GDN dose was higher for E2P (p<0.05). Other cycle outcomes were not different.

CONCLUSIONS: E2P is a viable tool for PGTA freeze all cycles, but does not improve euploidy rate; larger studies are necessary to determine if E2P produces fewer euploids in >38y.

IMPACT STATEMENT: E2P cycles require higher GDN dose without increased yield in euploid embryos.
confirm its clinical efficacy with solid evidence.

be considered as a treatment option in women with POI and POR. Prospective alternative for restoring ovarian function and resumption of ovulation in

In all patients, the embryo quality score was improved after PRP injection. Nine

data, and the time to ovulation resumption was 34.5 days (10-117). Among the 12

OBJECTIVE: As the age of women undergoing IVF increases, the most common cause of repeated implantation failure has become ovarian dysfunction. A breakthrough treatment is needed to restore decreased ovarian function, improve oocyte quality and quantity, or resume ovulation in premature ovarian insufficiency (POI). The purpose of this study was to determine the efficacy of intraovarian autologous platelet-rich plasma (PRP) on ovarian folliculogenesis in women with poor ovarian responder (POR) and POI.

MATERIALS AND METHODS: A prospective clinical study was conducted with women diagnosed with POI (N=19) and POR (N=20). In POI patients, hormone level, ultrasound, and result of menstruation were observed every two weeks after intraovarian injection of PRP. If the evidence of ovulation resumption was observed, controlled ovarian stimulation (COS) was started to get oocytes. In POR, intraovarian PRP injection was done on COS start day, and the COS was performed with GnRH antagonist protocol.

RESULTS: The mean age of the POI patients was 35.5±4.6 months. The duration of amenorrhea was 42.5±6.0 months, the basal FSH level was 104.7±37.5 (IU/L), and the ovarian volume was 1.2±0.3 and 1.5±1.3 cm3 for right and left ovary, respectively. The injection was successful in 208 women that underwent dual triggering constituted the study group with hCG only triggering, in antagonist cycles.

OBJECTIVE: To compare the clinical outcomes of dual triggering with gonadotropin releasing hormone (GnRH) agonist and human chorionic gonadotropin (hCG) in POSEIDON groups 3 and 4 low prognostic women with hCG only triggering, in antagonist cycles.

MATERIALS AND METHODS: This study was a retrospective analysis of patients with expected poor ovarian response (POR), namely POSEIDON groups 3 and 4 who underwent fresh embryo transfers following antagonist cycles triggered either with dual triggering with GnRH agonist of 0.2 mg triptorelin acetate (Gonapeptyl, Ferring Pharmaceuticals) and 250 mcg recombinant human chorionic gonadotropin (Ovitrelle, Merck Serono) or hCG-only (250 mcg recombinant human chorionic gonadotropin; Ovi-trelle, Merck Serono) trigger between January 2010 and April 2020. A total of 1068 women that underwent dual triggering constituted the study group and 1931 that underwent hCG-only triggering were included in control group.

RESULTS: Within the study group, 315 (29.4%) were classified as POSEIDON group 4 poor responders. Within the control group, 637 (32.9%) were classified as POSEIDON group 3, whereas 1294 (67%) were POSEIDON group 4. Peak estradiol levels (1059.43±645.87 pg/ml vs 929.20±459.14 pg/ml; p<0.001), endometrial thickness (10.32±1.83 mm vs 9.99±1.93mm; p=0.006), mean number of frozen embryos (1.18±0.86 vs 0.73; p<0.001), clinical pregnancy rate (130(41.3%) vs 208(32.7%); p=0.009), implantation rate (0.36±0.45 vs 0.26±0.39; p=0.003) and live birth rates (123(39%) vs 163(25.6%); p<0.001) were observed to significantly higher in dual-triggering group compared to hCG-only group in POSEIDON group 3 women. Nevertheless, no differences in these parameters were observed between dual-triggering and hCG-only group in POSEIDON group 4 women, except for a higher live birth rate in favor of dual triggering that reached statistical significance (143(19%) vs 188(14.5%); p=0.008).

CONCLUSIONS: Although the advantages of dual-triggering have been well-reported in high- and normo-responders, the currently available literature is controversial about the exact impact in poor responders and not sufficient to make robust evidence based recommendations. Contradictory results of former studies primarily arise from discrepancies in proper categorization of poor responders. Result of this study indicated that dual trigger with GnRH agonist and hCG appears to improve IVF outcomes, and increase live birth rates in women with expected POR, in POSEIDON group 3 and 4 women.

IMPACT STATEMENT: This study demonstrated that dual triggering improves live birth rates in POSEIDON group 3 and group 4, expected POR women along with addressing the probable importance of categorization of “poor responders” to determine the exact subgroup of patients who will benefit from a particular treatment.

SUPPORT: None

REFERENCES: None
OBJECTIVE: To evaluate the effectiveness and safety of biosimilar Folli-tropin alpha preparations for controlled ovarian stimulation in ovulatory women undergoing IVF, as compared to the originator.

MATERIALS AND METHODS: Systematic review and meta-analysis of randomized controlled trials (RCTs). Infertile women undergoing in vitro fertilization (IVF). We followed the PRISMA guidelines for systematic reviews and meta-analysis in the conduct of this study. Five databases were searched through 22 August 2021 for RCTs comparing the biosimilar Folli-tropin alpha to the originator for controlled ovarian stimulation and reporting clinical IVF outcomes, not restricted by language. We excluded quasi- and non-randomized designs. We used The Cochrane Risk of Bias 2 tool was used to assess the quality of the included studies.

RESULTS: The search retrieved 111 records. Five studies met the eligibility criteria and were included in the qualitative synthesis and the meta-analysis. Compared to the originator Folli-tropin alpha, biosimilars are probably associated with lower pregnancy rates (RR 0.79, 95% CI 0.67 to 0.92, I² = 0%, 5 RCTs, 1353 participants, moderate-quality evidence), but there was no evidence of a difference in the number of retrieved oocytes (MD 0.71, 95% CI -0.09 to 1.52, I² = 5%, 5 RCTs, 1353 participants, moderate-quality evidence). We are uncertain of the effect of biosimilar preparations on live birth which may indicate no difference or serious harm (RR 0.83, 95% CI 0.68 to 1.02, I² = 0%, 4 RCTs, 878 participants, low-quality evidence). Both preparations were similar in terms of OHSS (RR 1.25, 95% CI 0.89 to 1.76, 5 RCTs, 1353 participants, moderate-quality evidence) and adverse events (RR 1.09, 95% CI 0.92 to 1.30, 4RCTs, 981 participants, moderate-quality evidence).

CONCLUSIONS: Biosimilar preparations of Folli-tropin alpha are probably associated with lower clinical pregnancy and ongoing pregnancy rates than the originator, while there was insufficient evidence in terms of live birth rates. Both treatments are probably similar in OHSS and adverse events rates.

IMPACT STATEMENT: couples should be counseled for the possible inferiority of these preparations compared to the originator. More RCTs are required to confirm these results, and these RCTs should consider the cost-effectiveness outcomes in their designs and analyses.

SUPPORT: none

REFERENCES: none

TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>PRP (n=38)</th>
<th>Controls (n=35)</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>34.4 ± 2.7</td>
<td>34.6 ± 2.0</td>
<td>0.69</td>
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<tr>
<td>AMH (ng/ml)</td>
<td>1.02 ± 1.00</td>
<td>0.75 ± 0.59</td>
<td>0.17</td>
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<td>Day 3 FSH (mIU/ml)</td>
<td>9.4 ± 4.6</td>
<td>8.7 ± 3.1</td>
<td>0.47</td>
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<td>MII oocytes</td>
<td>3.7 ± 3.3</td>
<td>3.0 ± 2.5</td>
<td>0.64</td>
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<td>2PN</td>
<td>2.6 ± 2.8</td>
<td>2.3 ± 2.2</td>
<td>0.63</td>
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<tr>
<td>Euploid blastocysts</td>
<td>1.0 ± 1.7</td>
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<td>Implantation rate</td>
<td>10/10</td>
<td>9/12</td>
<td>0.22</td>
</tr>
<tr>
<td>Clinical pregnancy</td>
<td>9/9</td>
<td>9/12</td>
<td>0.22</td>
</tr>
<tr>
<td>Ongoing pregnancy</td>
<td>7/8</td>
<td>6/10</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>88%</td>
<td>60%</td>
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</table>

SUPPORT: This study was funded by a grant from the Foundation for Embryonic Competence.
CHANGING STIMULATION PROTOCOL FROM A STANDARD GNRH ANTAGONIST TO CLOMIPHENE OR LETROZOLE WITH LOW DOSE GONADOTROPINS FOR SECOND STIMULATION CYCLE IN WOMEN 40 AND OLDER DOES NOT IMPROVE CYCLE OUTCOMES. Nissiya Adjie, BS,1 Pietro Bortoletto, MD, MSc,2 Phillip A. Romanski, MD, MSc,3 Steven D. Spandorfer, MD4 The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; 5NewYork-Presbyterian/Weill Cornell Medical Center, New York, NY; 6New York, NY.

OBJECTIVE: To evaluate if the addition of clomiphene citrate (CC) or letrozole (LTZ) to a GnRH antagonist protocols improves cycle and fresh transfer outcomes compared to repeat use of a GnRH antagonist protocol in women 40 and older.

MATERIALS AND METHODS: We retrospectively reviewed our single center experience between 2010 and 2020. We identified a total of 844 women 40 and older undergoing their first GnRH antagonist stimulation cycle with a second stimulation cycle initiated within 6 months. Patients were dichotomized by which protocol was utilized for their second stimulation cycle: 1) repeat use of GnRH antagonist or 2) switch to CC or LTZ with low dose gonadotropin (i.e. <300 IU total gonadotropin dose) with GnRH antagonist. The outcomes of interest were number of mature oocytes retrieved, number of embryos transferred, cycle cancellation rate, and fresh transfer outcome.

RESULTS: Of the 844 women included, 77.7% (n=656) repeated the same GnRH antagonist protocol whereas 22.3% (n=188) switched to a CC/LTZ low dose protocol. Despite similar ages, parity, BMI, and infertility diagnosis, AMH levels were lower in those that switched protocols (median: 0.8 [IQR: 0.5-1.3] versus 1.1 [0.6-2.1], p<0.001). Patients who switched protocols had longer median days of stimulation (13 [11-14] versus 10 [9-11]), utilized less gonadotropins (3213 [2250-4725] versus 4350 [3250-5400] IU), and had fewer mature oocytes retrieved (4 [3-7] versus 7 [4-9], p<0.001). Of the 59% of patients who underwent fresh embryo transfer, cleavage stage transfer was more common in those that switched protocols (98.4 versus 93.1%, p=0.029). Despite fewer embryos being transferred in the group that switched protocols (mean: 2.9 [SD: 1.3] versus 3.4 [1.3], p=0.002) there were no differences in cycle outcomes (clinical IUP: 30.7 versus 30.3%, not pregnant: 61.6 versus 63.9%; biochemical: 7.1 versus 4.9%, p=0.825). Cycle cancellation rate was similar between both groups (3.2 versus 1.5%, p=0.140).

CONCLUSIONS: In women 40 and older who have undergone stimulation with a GnRH antagonist protocol, switching to a CC/LTZ low dose gonadotropin protocol was associated with fewer mature oocytes retrieved, fewer embryos transferred, but no difference in cycle outcome or cycle cancellation rate. For women over 40, a switch to, a CC/LTZ low dose gonadotropin protocol may present an opportunity for reducing gonadotropin consumption without sacrificing clinical outcomes.

IMPACT STATEMENT: In women 40 and older who have previously undergone IVF with a GnRH antagonist protocol, a switch to CC/LTZ low dose gonadotropins does not negatively impact cycle or transfer outcomes.

P-502 6:45 AM Wednesday, October 26, 2022

ANTAGONIST VERSUS SHORT AGONIST PROTOCOL IN POSEIDON-4 CATEGORY UNDERGOING FRESH ICSI CYCLES. Tarek K. Al-Hussaini, MD, Ahmed Aboelafelde Mohamed, MD, Ayman Askar, MD, Yousra M. Othman, MD, Ahmed A. Abden, MD, Reda S. Hussein, MD Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: Recently POSEIDON (Patient-Oriented Strategies Encompassing IndividualizEd Oocyte Number) criteria were for defining cases with predicted poor response to conventional stimulation (1). Our study’s aim is to compare the GnRH-antagonist and GnRH-agonist short protocols in IVF/ICSI cycles for the POSEIDON-3 group. MATERIALS AND METHODS: This is a retrospective cohort study conducted in a tertiary infertility unit for infertile women who met the criteria of the POSEIDON-3 group and underwent ovarian stimulation using GnRH-agonist and GnRH-antagonist short protocols between January 2016 and December 2020. The POSEIDON 4 includes patients ≥ 35 years with poor ovarian reserve markers; AFC < 5 and/or AMH < 1.2 ng/ml. Exclusions were cycles with uterine factor abnormality, surgically retrieved embryos, frozen embryo transfer, and cycles of pre-implantation genetic testing. Ovum pickup was done when there was a prediction of ≥ 2 oocytes retrieval. The baseline clinical characteristics and cycle outcomes were compared between both groups. Thereafter, a multivariate logistic regression model was performed for adjusting the effect of baseline cycle covariates on clinical pregnancy rate.

RESULTS: One hundred ninety fresh ICSI cycles were analyzed. Of the total cohort, 41.6 % (79) patients pursued antagonist protocol compared to 58.4% (111) who underwent short agonist protocol. Fresh embryo transfer was accomplished in 55.7 % (44/79) vs. 61.3 % (68/111), P = 0.44 in antagonist vs. short protocol respectively. Cycle cancellation due to poor ovarian response was encountered in (32.9% vs. 27.9%, P=0.50) in the antagonist and short groups, whereas no good-quality embryos were developed after ovum pickup in 11.4% vs. 10.8%, P<0.05. The antagonist group had statistically, yet non-clinically significant, lower age [median (IQR); 38 (3) vs. 39 (4), P < 0.001] and higher AFC [4 (2) vs. 3 (2), P<0.001] than short protocol. Both groups achieved similar total gonadotropins dose, good-quality embryos, implantation rate, number of retrieved and mature oocytes. The two groups had a comparable clinical pregnancy rate; 11/79 (13.9%) vs. 20/111 (18%), P=0.45 for the antagonist and short groups. The protocol type does not significantly affect clinical pregnancy after adjusting to age and AFC in a multivariate analysis (aOR: 0.43, 95%CI 0.17-1.08, P=0.07).

CONCLUSIONS: Our study exhibits comparable pregnancy outcomes for the antagonist and short agonist protocols in IVF/ICSI cycles for POSEIDON 4 category.

IMPACT STATEMENT: For POSEIDON-4 IVF/ICSI patients, clinicians can choose from both antagonist and short agonist protocols based on their convenience.

REFERENCES:
gonadotropins dose, good-quality embryos, implantation rate, and the number of retrieved and mature oocytes. The two groups had a comparable clinical pregnancy rate; 21/102 (20.6%) vs. 19/65 (29.2%), P=0.20 for the antagonist and short groups. In the multivariate binary logistic regression model, the protocol type still does not significantly affect clinical pregnancy after adjusting to AFC and AMH (aOR: 0.56, 95%CI 0.25-1.28, P=0.17).

CONCLUSIONS: Our study shows no significant superiority for short over antagonist protocol in IVF/ICSI cycles for POSEIDON 3 category or vice versa. A large-scale randomized trial is needed to validate such results.

IMPACT STATEMENT: For POSEIDON-3 IVF patients, both short and antagonist protocols have fair comparable results.

REFERENCES:

P-506 6:45 AM Wednesday, October 26, 2022
IMPACT OF ESTROGEN SUPPLEMENTATION ON INTRAUTERINE INSEMINATION PREGNANCY SUCCESS RATES. Sereena Jivraj, B.S., Robert A. Kaufmann, M.D., Mackenzie Kahroff, B.S. Texas Christian University.

OBJECTIVE: To compare the pregnancy success rate and endometrial thickness of patients undergoing intrauterine insemination (IUI) with or without exogenous estrogen supplementation.

MATERIALS AND METHODS: This retrospective data analysis used data collected by an independent clinic. The dataset included patients who underwent IUI between January 2019 and April 2022. Cohorts were separated by use of Estrace (exogenous estrogen) prior to ovulation induction (Group A: 2mg dose vaginally or orally daily until a heartbeat was detected; Group B: non-treatment controls). Patients that had a history of thin endometrium were given Estrace. Those who smoked, were older than 40 years, had a BMI greater than 36, diminished ovarian reserve, defined as an AMH less than 1.0, or male factor, defined as less than or equal to 5 million motile sperm, were excluded from the study. Endometrial thickness before and after Estrace supplementation as well as cycle outcomes were recorded. Logistic regression analysis was utilized for statistical analysis.

RESULTS: A total of 157 patients were included in the analysis. 57 patients who underwent IUI with estrogen supplementation were compared against 100 controls. There were 11 clinical pregnancies in the estrogen supplementation group and 16 in the control groups. There was no statistical difference in pregnancy rates comparing both groups (P=0.4). There was also no difference in pregnancy rates with respect to comparing age (P=0.8) or endometrial thickness (P=0.4). There was a higher AMH (P=0.04) and number of motile sperm (0.03) in the pregnancy groups.

CONCLUSIONS: There does not appear to be a significant difference between pregnancy success rates in patients receiving exogenous estrogen for thin endometrium compared to those pursuing natural IUI. In addition patients with a thinner endometrium continued to have similar success rates with ovulation induction and insemination.

IMPACT STATEMENT: This study may alter current practices regarding estrogen supplementation for ovulation induction and insemination. Endometrial thickness may not be an indicator of success with ovulation induction.

SUPPORT: None

REFERENCES:

P-508 6:45 AM Wednesday, October 26, 2022
PATIENTS WHO CHOOSE IN PERSON VS TELEHEALTH FIRST VISIT APPOINTMENTS: DIFFERENCES IN BASELINE CHARACTERISTICS AND ENGAGEMENT IN CARE. Leah M. Roberts, MD, Cherri K. Margolis, MD, Andrea Reig, MD, Nola Herlihy, MD, Amber M. Klimczak, MD, Pavan Gill, MD, Emre Seli, MD, Thomas Molinardo, MD, MSCE IVIRMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: To evaluate if there are differences in baseline characteristics or engagement patterns of patients who choose telehealth (audio and video) first visit compared to those who are seen in person.

MATERIALS AND METHODS: A retrospective cohort study of all new patient visits between April of 2020 and March of 2021 at a university-affiliated fertility center was performed. Patients who engaged in a telehealth new patient visit were compared to those with an in-person new patient visit. Outcomes were divided into those who presented pregnant (Group A), did not complete diagnostics (Group B), completed diagnostics and did not pursue treatment (Group C), presented with a pregnancy diagnosis (Group D), underwent oocyte retrieval without success (Group E), and with successful discharge to obstetrical care (Group F). Statistical analyses were performed using SPSS.

RESULTS: A total of 5678 patients were included in the analyses. Of those, 4291 had an in person first visit and 1387 had a telehealth visit. Patients who had a telehealth first visit were older (35.4 vs.53.1, p=0.018), had a lower BMI (26.9 vs. 27.6, p=0.001), and lower AMH (3.4 vs. 4.0, p=0.018) when compared to those who had an in-person first visit. There was no difference between the groups in having a partner, having a same sex partner, or baseline serum FSH. Patients who had an initial telehealth visit were slightly less likely to complete diagnostics, move on to treatment, or proceed to IVF, however were slightly more likely statistically to have a successful discharge to obstetrical care after frozen embryo transfer (see Table).

MATERIALS AND METHODS: The method of quantitative research of women’s awareness using a structured anonymous questionnaire (20 polytomy questions) was chosen. Out of the total number of 64 respondents, 31 women (36.9 %) underwent IBR due to BRCA 1,2 mutations and 53 women (63.1 %) due to breast cancer. Before the mastectomy, all respondents already knew what IBR meant, as well as about the payment of IBR by the health insurance company. When asked whether there is sufficient information about IBR in the Czech Republic, answer “no” 61.9 % of women, resp. “I don’t no” 28.6 % of women. All respondents would choose the IBR option. 94.0 % of women cited body integrity as a reason. 88.1 % of women knew about the possibility of performing IBR with their own tissues. There was also excellent information about IBR by foreign material (100 %). There were differing views on the harmfulness of the silicone implant. Only 4.8 % of women said “yes”, 73.8 % of answers “no”, resp. 13.1 % “I don’t know”. All respondents had knowledge and information about different sizes and shapes of silicone implants. Opinions and wishes for breast size after reconstruction differed. 79.8 % of women chose the same breast size, 9.5 % wanted bigger and 6.0 % smaller breasts, 93 % of women were informed about possible complications. Considering the above, there was a fundamental difference in awareness of the fact that postoperative complications in IBR are more common than in delayed reconstructions.

CONCLUSIONS: Women who have breast cancer or have an increased risk of breast cancer and undergo mastectomy should have a choice nowadays. Whether to accept only wearing an epithesis or undergoing breast replacement surgery. There are few specialized centers with a team of experts in reconstructive breast surgery in the Czech Republic, especially those performing IBR. Research has shown that all patients were well informed about IBR, but the vast majority did not just before the surgical procedure was planned. All women wished to maintain body integrity, and if there was a possibility of IBR, they all underwent it.

IMPACT STATEMENT: This study showed that all patients were well informed about immediate breast reconstruction, but the vast majority were just about to plan their operation.

SUPPORT: Dedication: The work was carried out with institutional support of Masaryk University Brno.

P-508 6:45 AM Wednesday, October 26, 2022
IMMEDIATE BREAST RECONSTRUCTION AFTER MASTECTOMY FROM THE PATIENT’S POINT OF VIEW. Tomás Ventruta, MD, Pavel Ventruta, Ph.D., Prof., Michal Jeseta, PhD, Faculty of Medicine, Masaryk University and University Hospital Brno, Brno, Czech Republic.

OBJECTIVE: The aim of the study was to find out the awareness of women about immediate breast reconstruction (IBR) with mastectomy at one time, which these operations have already undergone. The indication was a proven genetic mutation BRCA 1 and 2 and/or breast cancer. Four sub-objectives were set with hypotheses for two variables.

P-505 6:45 AM Wednesday, October 26, 2022
ENGAGEMENT IN CARE. Leah M. Roberts, MD, Cherri K. Margolis, MD, Andrea Reig, MD, Nola Herlihy, MD, Amber M. Klimczak, MD, Pavan Gill, MD, Emre Seli, MD, Thomas Molinardo, MD, MSCE IVIRMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: To evaluate if there are differences in baseline characteristics or engagement patterns of patients who choose telehealth (audio and video) first visit compared to those who are seen in person.

MATERIALS AND METHODS: A retrospective cohort study of all new patient visits between April of 2020 and March of 2021 at a university-affiliated fertility center was performed. Patients who engaged in a telehealth new patient visit were compared to those with an in-person new patient visit. Outcomes were divided into those who presented pregnant (Group A), did not complete diagnostics (Group B), completed diagnostics and did not pursue treatment (Group C), presented with a pregnancy diagnosis (Group D), underwent oocyte retrieval without success (Group E), and with successful discharge to obstetrical care (Group F). Statistical analyses were performed using SPSS.

RESULTS: A total of 5678 patients were included in the analyses. Of those, 4291 had an in person first visit and 1387 had a telehealth visit. Patients who had a telehealth first visit were older (35.4 vs.35.1, p=0.018), had a lower BMI (26.9 vs. 27.6, p=0.001), and lower AMH (3.4 vs. 4.0, p=0.018) when compared to those who had an in-person first visit. There was no difference between the groups in having a partner, having a same sex partner, or baseline serum FSH. Patients who had an initial telehealth visit were slightly less likely to complete diagnostics, move on to treatment, or proceed to IVF, however were slightly more likely statistically to have a successful discharge to obstetrical care after frozen embryo transfer (see Table).
CONCLUSIONS: Although we identified statistically significant differences between patients choosing telehealth first visits compared to those choosing in person first visit, these are unlikely to be clinically significant. No specific factors were noted that should make the practitioner more wary of offering telehealth visits.

IMPACT STATEMENT: Telehealth became increasingly utilized and accepted during the Covid-19 pandemic, and should be continued to be offered to our patients, as there is little difference in how patients engaged in care compared to those who underwent an in person new patient visit.

SUPPORT: None

REFERENCES: None

P-507 6:45 AM Wednesday, October 26, 2022

INSTAGRAM CYSTERS: WHAT'S AVAILABLE ON POLYCYSTIC OVARIAN SYNDROME? Janet Cruz, MD, Zahab Qazi, Alsheta Vasireddy, BS, Kaleigh Amanda Vilchez-Russell, PhD, Mallory A. Stuparchik, MD, Samar Naas, MD, Sadikah Bebehania, M.D. 1 University of California Riverside, Riverside, CA; 2 UC Riverside School of Medicine, Riverside, CA; 3 University of California, Riverside, School of Medicine, Riverside, CA.

OBJECTIVE: To describe and categorize the content available to patients with PCOS on the Instagram social media platform and assess how post content relates to user engagement.

MATERIALS AND METHODS: This is a retrospective content analysis, where the five most commonly used PCOS hashtags on Instagram were analyzed: #PCOS, #PCOSinfertility, #PCOSweightloss, #PCOSdiet, and #PCOSAwhered. Only English language posts were included. For every hashtag, the first 25 posts were reviewed daily for 30 days. Posts were reviewed for: type of post (picture, video, reel), type of account by user profile (account dedicated to only PCOS, nutritionist account, physician account, lifestyle coach, fitness trainer), post engagement (measured by number of likes), and post category (advertisement, motivational content, including posts containing messages of support and encouragement for patients with PCOS, and educational content).

Differences between number of posts by hashtag and category were analyzed using a one-way analysis of variance (ANOVA). Post hoc analyses were done using Tukey’s HSD. All statistical analyses were done in R version 1.3.1093.

RESULTS: A total of 3801 posts were recorded during the sampling period, with 5.4% (204 posts) categorized as advertisements, 29.7% (1130 posts) as educational, and 64.9% (2467 posts) as motivational posts. There was no significant difference in the number of posts by hashtag ($F_{4,10}=0.001$, $p=1.00$). There was a significant difference in number of posts by category ($F_{2,12}=175.7$, $p<0.001$), with motivational as the most posted category, educational the second most posted, and advertisements the least posted. Motivational posts were most common and also had the most engagement. Regarding type of accounts, the most engaging posts were from accounts dedicated to only PCOS, nutritionist account, physician account, and PCOS awareness. Post engagement on posts containing messages of support and encouragement for patients with PCOS, and educational content.

CONCLUSIONS: Most PCOS content shared on Instagram is considered motivational and is related to health and wellness as the post were from fitness coaches, dietitians and nutritionists. Accounts dedicated to PCOS were engaged the most whether the content was educational or motivational, and likely means that patients with PCOS opt to follow accounts dedicated to PCOS. Given the high dedication to motivational and educational posts, patients with PCOS may be encouraged by physicians to use Instagram for support and information related to the disease.

IMPACT STATEMENT: Social media has been welcomed in different sectors, however it has not been fully adapted into the healthcare sector. Because Instagram posts are less likely to be from physicians, it is important for medical providers to be aware of the information being gathered by our patients and how to better engage them. Most importantly, to foster healthy relationships with our patients’ positive motivation and education will get the most engagement.

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ACOG Committee Opinion 653, Feb 2016. Concerns regarding social media & health issues adolescents and young adults

P-508 6:45 AM Wednesday, October 26, 2022

IMPACT OF DECLINING FERTILITY RATES ON US STATE POLICIES. Katherine Bogaard, BA, Sarah K. Darmon, PhD, Vitaly A. Kushnir, MD, Pasadena, CA; Center for Human Reproduction, New York, NY; University of California Irvine, CA.

OBJECTIVE: To determine whether rapid decline in General Fertility Rate (GFR) in various US states prompts policy changes and to attempt to identify a threshold fertility rate below which states mandate fertility benefits.

MATERIALS AND METHODS: We used annual data from the CDC National Vital Statistics Reports for years 1990 through 2020. Specifically, we analyzed the GFR defined as the total number of births per 1,000 women aged 15-44 for each US state for all years. During the study period nine US states passed legislation related to insurance coverage for infertility treatment. New York state passed two distinct sets of policies during this time interval; both were analyzed separately. Type of statistical tests used in analysis include Fisher test, one sample t-test and two sample t-test.

RESULTS: Across the 50 US states, the GFR during the 30-year study period showed a significant decline from 70.9 to 55.8. For each state that passed policies, we compared the preceding 5-year GFR to the 5-year GFR for the remaining states during the same time interval, no statistical differences were found.

To investigate whether threshold GFR exists below which states mandate fertility benefits, the states were stratified presence (n=9) or lack of policy (n=41) and whether the state went below the threshold GFR during the same time period. Various GFR values were compared ranging between 50 and 65; however, no statistically significant threshold value was identified.

CONCLUSIONS: Declining fertility rates, population growth and aging of the population have negative future economic implications. Accordingly, governments are incentivized to implement pro-fertility policies to improve the economic trajectory.

Our data confirms decreasing fertility rates in all 50 US states between 1990 and 2020. Despite this, we were not able to identify a statistically significant threshold GFR that triggers policy changes or establish differences in GFR between states that have passed fertility insurance mandates and those that have not.

IMPACT STATEMENT: Given our knowledge of the negative economic implications of declining fertility rates, future studies should evaluate for correlation between factors beyond fertility rates which may influence policy decisions. One potential direction is an analysis of working-age population ratios for states with and without mandated fertility benefits.

P-509 6:45 AM Wednesday, October 26, 2022

LEGAL, ETHICAL AND REGULATORY CHALLENGES OF ASSISTED REPRODUCTIVE TECHNOLOGY IN DEVELOPING COUNTRIES – THE CASE OF GHANA. Promise E. Setogah, MD, MPH, DLSHTM, FWACS, Gordon Abekah-Nkumah, PhD, Oboshie Anim-Boamah, MPhtl, MED, PGDE, RN, FWACN, Theresa Barnes, MPhtl, BSc, PON, Promise E. Sefogah, MD, MPH, DLSHTM, FWACN, Theresa Barnes, MPhtl, BSc, PON, Promise E. Sefogah, MD, MPH, DLSHTM, FWACN, Theresa Barnes, MPhtl, BSc, PON, Promise E. Sefogah, MD, MPH, DLSHTM, FWACN, Theresa Barnes, MPhtl, BSc, PON, Promise E. Sefogah, MD, MPH, DLSHTM, FWACN, Theresa Barnes, MPhtl, BSc, PON, Promise E. Sefogah, MD, MPH, DLSHTM, FWACN, Theresa Barnes, MPhtl, BSc, PON, Promise E. Sefogah, MD, MPH, DLSHTM, FWACN, Theresa Barnes, MPhtl, BSc, PON, Promise E. Sefogah, MD, MPH, DLSHTM, FWACN, Theresa Barnes, MPhtl, BSc, PON.
BACKGROUND: Infertility remains a challenge globally and assisted reproductive technology (ART) progressively gaining relevance in developing countries including Ghana. However, associated ethical, legal and regulatory challenges have not like to meet the child, even if only the recipient had become pregnant. Approximately 0.05). Approximately 71% of women do not want any contact with the child born from their eggs; 69% of them would not like to meet the recipients and 75% would not like to meet the child, even if only the recipient had become pregnant.

OBJECTIVE: Genetics-related indications are increasingly occupying clinic’s time in assisted reproduction clinics. Genetic counselors (GCs) are uniquely equipped to address genetic aspects of reproductive care; however, few fertility clinics employ genetic counselors, often relying on laboratory-based GCs instead. This study aimed to evaluate if loss of egg donor anonymity could affect access to reproductive technology but the opinion or behaviour of this population about the presence or absence of anonymity is limited to a few studies. This study aimed to evaluate if loss of egg donor anonymity could affect shared donation programs in Brazil.

MATERIALS AND METHODS: An anonymous survey was constructed and administered to practice managers of assisted reproduction clinics who employ one or more genetic counselors. Respondents were recruited through their GC colleagues who are members of the Genetic Counseling Professional Group of the American Society for Reproductive Medicine and/or the Assisted Reproductive Technologies and Infertility Special Interest Group of the National Society of Genetic Counselors. Survey questions assessed the clinicians’ reasons for hiring an in-house genetic counselor, the relationship between the clinic and the in-house GC, the GC’s scope of practice, the GC’s impact on quality of care, and overall satisfaction with the in-house GC.

RESULTS: Eleven practice managers were surveyed. When asked why the clinic opted to include a GC in their practice, 10/11 respondents selected “to align clinical practice with the rapidly-changing advancements in reproductive genetics.” 9/11 respondents also indicated they employ a GC to improve patient care and patient experience, to remain informed of genetic testing recommendations and regulations, and because other staff are unable to address patients’ genetics questions and concerns. The roles of genetic counselors within these practices were varied, with the majority of respondents indicating their GC’s role includes explaining test results, evaluating family medical histories, coordinating genetic testing, serving as a liaison between the clinic and genetic testing labs, developing standard operating procedures for genetic testing and services, educating other staff on testing regulations and guidelines, and developing consent forms, patient information sheets, and website content. 4/11 respondents stated their clinic bills insurance for genetic counseling services. Nearly all respondents reported their genetic counselors have improved the clinic’s quality of care by a great amount.

CONCLUSIONS: Genetic counselors’ formal training in medical genetics allows them to appropriately address genetics-related issues and indications in the fertility setting. GCs in the fertility clinic improve quality of care according to fertility practice managers.

IMPACT STATEMENT: Assisted reproduction clinics find clinical and monetary value in the services in-house genetic counselors provide. One respondent stated “I wouldn’t feel comfortable working in a clinic without [a genetic counselor].” However, genetic counselors remain absent from most fertility clinics. Further research should explore the barriers preventing clinics from hiring a genetic counselor and how those barriers can be overcome.

SUPPORT: Assisted Reproductive Technologies/Infertility Special Interest Group of the National Society of Genetic Counselors

REFERENCES:

E-POSTER ABSTRACT STATION: W8

P-510 6:45 AM Wednesday, October 26, 2022

THE IMPACT OF GENETIC COUNSELORS IN ASSISTED REPRODUCTION CLINICS: A SURVEY OF PRACTICE MANAGERS. Jenna Miller, MS, CGC, Pamela Callum, MS, CGC, Lauren Isley, MS, CGC. Cooper-Surgical, Livingston, NJ. Generate Life Sciences, Los Angeles, CA.

OBJECTIVE: Genetics-related indications are increasingly occupying clinicians’ time in assisted reproduction clinics. Genetic counselors (GCs) are uniquely equipped to address genetic aspects of reproductive care; however, few fertility clinics employ genetic counselors, often relying on laboratory-based GCs instead. The objective of this study was to evaluate the current scope of practice and impact of genetic counselors employed by assisted reproduction clinics.

MATERIALS AND METHODS: A multi-centered qualitative exploratory phenomenological approach was employed to examine Assisted Reproductive Technology across 8 facilities in Ghana, focusing on ethics, law and regulation for this practice. A semi-structured interview guide was used to collect data from ART practitioners, practice managers, facility owners, surrogate/gamete donor agencies, and regulatory bodies’ representatives. The interview responses were recorded and transcribed for on and analysis. Subsequent coding and generation of themes was performed from the data. This was presented narratively using themes and sub-themes, and supported by verbatim quotes from respondents.

RESULTS: No public health facilities provide ART services in Ghana, all ART Centers in Ghana are privately owned, with 78.6% (11/14) located in the capital city. Ethical challenges identified included border on inequity, lack of access, informed consent, client’s priority, protection of clinical data, donor gametes, multiple gestations, single parenting, and social and religious issues. The legal challenges identified are: the non-existence of a legal regime for regulating ART practice, and the absence of professional body with clear-cut mandate for regulating ART practice. There are no ethical and legal framework on ART practice in Ghana, and this affects ART practice adversely. In the absence of legal and ethical frameworks in Ghana, practitioners are guided by guidelines from ESHRE and ASRM, and principles and general medical ethics.

CONCLUSIONS: Significant inequity, ethical, legal and regulatory challenges are associated with ART practice in Ghana, with no existing ethical, legal regulatory framework. Regulation is essential for the provision of safe and successful ART practice to protect providers and users. Governmental efforts at regulation in Ghana need to be prioritized.

IMPACT STATEMENT: This study highlights the major ethical, legal and regulatory challenges in ART needing prioritised national policy attention in developing countries.

SUPPORT: No financial support was received for this research.

P-511 6:45 AM Wednesday, October 26, 2022

ENDING THE ANONYMITY OF EGG DONORS IN SHARED DONATION PROGRAMS COULD REDUCE THE NUMBER OF PARTICIPANTS. Elisangela Vigil Vigil, B.S.c., Claudia G. Petersen, Ph.D., Fabiana C. Massaro, B.S.c., Brunna Petersen, B.S.c., Laura D. Vagnini, M.Sc., Andreia Nicoletti, R.N., Juliana Ricci, R.N., Camila Zamar, R.N., Felipe Dieamant, M.D., Antonio Helio Oliani, M.D., Ph.D., Joao B. A. Oliveira, M.D., M.Sc., Ph.D., Jose G. Franco, Jr., M.D., Ph.D. Center for Human Reproduction Prof. Franco Jr, Ribeirao Preto, Brazil, Center for Human Reproduction Prof. Franco Jr/ Paulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; Paulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; Sao Jose do Rio Preto School of Medicine FAMERP, Sao Jose do Rio Preto, Brazil.

OBJECTIVE: The Brazilian Federal Council of Medicine seems to be increasingly flexible with regard to maintaining mandatory secrecy on the identity of donors. The resolution regarding assisted reproduction techniques, approved in 2021, concerns the possibility of donation between family members, up to fourth degree relatives not consanguineous. The possibility to know and have access to this identity or even the search for half-brothers can be a reality in many countries for children born through access to reproductive technology but the opinion or behaviour of this population about the presence or absence of anonymity is limited to a few studies. This study aimed to evaluate if loss of egg donor anonymity could affect shared donation programs in Brazil.

MATERIALS AND METHODS: Women (n=800) who applied for enrolment in the shared egg donation program at a private IVF clinic were invited to participate in an electronic survey developed using the online Survio® tool. The invitation to participate was sent by email from June to November 2021. The invitation to participate was sent to 800 women (34.8% response rate) responded to the survey. The information was obtained through questioning and gaining information about: socioeconomic profile of the donors, their motives, ambivalence in relation to the sharing of eggs and feelings about a possible end of anonymity. Thereafter, answers given to 10 specific questions were recorded. Furthermore, a correlation analysis was performed to assess the relationship between acceptance of the end of donor anonymity and various study parameters.

RESULTS: Approximately 61% of participants would want to become egg donors for two reasons: to reduce IVF costs and to help another woman. However, significantly younger women want to be part of the egg donation program just to reduce their treatment costs (P < 0.05). Approximately 71% of women do not want any contact with the child born from their eggs; 69% of them would not like to meet the recipients and 75% would not like to meet the child, even if only the recipient had become pregnant.
If donors lost a child, they would not even want to meet the child who was born with their donated eggs (76%). Most participants also responded that they would be in the program even if the anonymity was not maintained (80%). However, women with higher income would drop out of the program if donor anonymity was not maintained (56.3%) compared to women with lower income (13.5%; P < 0.001).

CONCLUSIONS: Approximately 20% of the women who participated in this study would drop out of the program, especially those with higher incomes.

IMPACT STATEMENT: A possible end to the anonymity of egg donors in Brazil would pose numerous challenges to the current practice of gamete donation. These concerns give rise to a broad discussion in society about how best to safeguard and promote the interests of donor-conceived children and protect the rights of donors.

P-512 6:45 AM Wednesday, October 26, 2022

A SURVEY OF VIRGINITY TESTING IN THE UNITED STATES. Eden Sheinin, BS,1 James H. Segars, MD,2 Bhuchitra Singh, MD, MPH, MS, MBA2 3Alexandria, VA; 2Johns Hopkins School of Medicine, Baltimore, MD.

OBJECTIVE: The aim of the study was to determine the prevalence of virginity testing and evaluate the attitudes and effects of virginity testing in the United States, as reported by the general population and healthcare providers.

MATERIALS AND METHODS: After IRB approval, a 19-item anonymous electronic survey was developed using Qualtrics and distributed online via email, Reddit, Facebook, and Twitter. The survey contained questions specific to females, males, and healthcare providers to assess the prevalence, attitudes and effects of virginity testing. Survey responses were captured in Qualtrics and exported for analysis using Microsoft Excel version 16.33 (Microsoft Corporation, Redmond, WA). Descriptive statistics were used to report the findings.

RESULTS: One thousand and seventy-two survey responses were received, consisting of 274 males and 798 females. One hundred and sixty-five respondents identified as healthcare providers and the remainder (n=907) identified as part of the general population. The majority of respondents (86%) felt negatively about virginity testing. The average age of respondents who reported virginity testing was 15-17 years old, legally considered minors in the United States. Out of the 156 healthcare providers polled, 5% (7) reported performing virginity testing whereas 9% (14) reported being requested to perform such testing. Only 12% (19) of providers reported encountering virginity testing during their medical training.

CONCLUSIONS: The prevalence of virginity testing in the United States is high, and the majority of providers felt negatively about virginity testing. Further research is warranted to better understand the prevalence, attitudes, and impact of virginity testing in the United States.

IMPACT STATEMENT: The study aimed to assess the availability and amount of LGBTQ+ content on sperm and egg provider websites. Kyle Nguyen Le, MD,1 Aditi Trivedi, MD,2 Andrew Needleman, MD,1 John Gaughan, PhD,1 Jacqueline Guttman, M.D.1 Richard Fischer, MD1 Philadelphia, PA; 1Cooper Medical School of Rowan University, Camden, NJ; 1RMA of Philadelphia, King Of Prussia, PA; 2Cooper University Health Care, Camden, NJ.

OBJECTIVE: The study aims to assess the availability and amount of LGBTQ+ content on sperm and egg provider websites.

MATERIALS AND METHODS: A search of the Food and Drug Administration’s (FDA) human cell and tissue establishment registry (https://www.accessdata.fda.gov/scripts/cber/CFAppsPub/tiss/Index.cf?fuseAction=fuse_DisplaySearchResults) was performed to identify registered sperm/egg providers. 720 establishments were identified. Websites were then found via Google search using the facility name and address for verification. International, inactive, and no website establishments were excluded. Websites were evaluated for presence and amount of LGBTQ+ content. Content was categorized into none, minimal, moderate, and significant (Table 1). LGBTQ+ content was evaluated in relationship to geographic region and IVF cycles/year.

RESULTS: Overall, 57.1% of sperm and egg provider websites had LGBTQ+ content. The northeast and west (NE-W) were more likely to have LGBTQ+ website content (62.6%) compared to the south and midwest (S-MW) (51.7%, P = 0.02) and also had a higher amount of content (P = 0.02). Websites in the NE-W were more likely to have moderate (32.3%) and significant (22.6%) content compared to the S-MW with 27.1% and 14.2%, respectively. Lastly, for each increase in 100 cycles/year, the probability of any content increased by 8.1% (OR = 1.08).

CONCLUSIONS: Websites in the NE-W were more likely to have LGBTQ+ content and a greater amount of LGBTQ+ content. As IVF cycles/year rose, so did the probability of having LGBTQ+ content on these establishments’ websites.
PATIENT’S OPINION ON THE MAINTENANCE OF P-515 fertility websites.

knowledge, this study is the first to quantify amount of LGBTQ+ content on how the LGBTQ+ community interacts with infertility sites. To the author's

TILIDAD Y GENETICA REPRODUCTIVA, CORDOBA, Argentina; change their clinic or doctor to support the possibility of using telemedicine, (18.25%). Of all those surveyed, 83.51% stated that they would like telemedicine during the pandemic, valuing the experience on average mostly between 21 and 40 years old (49.49%). 59.27% stated that they had practiced telemedicine as a safe and beneficial way for both, patients and doctors, 17 provinces of Argentina. All responses were collected using the Survey...

The survey was answered by people of both sexes over 16 years of age from

reasons why they use/do not use the tool, predisposition to continue using this type of medical care, and 52.53% would be willing to pay for the consultation outside of their traditional medical coverage (private/private), regardless of the channel used to make it (phone call/video call).

CONCLUSIONS: Telemedicine represents a valuable tool for communication between patients and doctors. In general, the majority of patients value the experience as positive and express a clear intention to continue using this modality even when face-to-face care is once again allowed. A significant percentage of patients are willing to pay more to obtain this service or even change their doctor and primary institution to maintain it. These data are extremely important when making institutional decisions on how to maintain the continuity of telemedicine and which are the points that should be improved.

IMPACT STATEMENT: Maintaining the telemedicine modality represents an added value to patient care that all health institutions should evaluate.

P-M516 6:45 AM Wednesday, October 26, 2022

P-516 PATIENT’S OPINION ON THE MAINTENANCE OF THE TELEMEDICINE MODALITY IN THE POST-PANDEMIC TIME. Marcelo Herran, Sr., BAcc, Marcela Cullere, PhD, Natalia Reyna Dezotti, Attty, Cesar Sanchez Sarmiento, PhD1 NASCENTIS. ESPECIALISTAS EN FERTILIDAD Y GENETICA REPRODUCTIVA, CORDOBA, Argentina; NASCENTIS, ESPECIALISTAS EN FERTILIDAD Y GENETICA REPRODUCTIVA, Argentina.

OBJECTIVE: During the COVID-19 pandemic, telemedicine became the most widely used medical care modality. Carrying out a “stay at home” medical consultation was a safe and beneficial way for both, patients and doctors, to maintain health controls. With the end of the pandemic, it is necessary to define whether this tool can continue to be used and how it will be implemented by health institutions. We aimed to determine how patients value telemedicine, and to investigate the reasons that influence the decision to continue using this type of medical care definitively.

MATERIALS AND METHODS: A mixed-type questionnaire of 17 questions was designed (segmentation and questions about preferences of use, reasons why they use/do not use the tool, predisposition to continue using it) that was distributed to different sectors of society through social networks. The survey was answered by people of both sexes over 16 years of age from 17 provinces of Argentina. All responses were collected using the Survey-Monkey platform and analyzed using calculation programs and statistical tools (Excel, Statistica 8.0) and the results processed using graphic programs (Excel, Power Point, Sigma Plot).

RESULTS: A total of 491 responses were obtained, 77.39% were women, mostly between 21 and 40 years old (49.49%). 59.27% stated that they had used telemedicine during the pandemic, valuing the experience on average 4/5. Currently, 47.33% continue to use it, while the remaining 52.67% no longer do so. The reasons why people stopped using this tool were: the social insurance no longer pays for this type of care (31.39%), the perception of a lower quality of attention when it is done through video calls (21.9%) and the lack of offer from the doctor or the institution for this type of modality (18.23%). Of all those surveyed, 83.51% stated that they would like telemedicine to be permanently installed. In this sense, 38.48% would be willing to change their clinic or doctor to support the possibility of using telemedicine, and 52.53% would be willing to pay for the consultation outside of their traditional medical coverage (private/private), regardless of the channel used to make it (phone call/video call).

CONCLUSIONS: Telemedicine represents a valuable tool for communication between patients and doctors. In general, the majority of patients value the experience as positive and express a clear intention to continue using this modality even when face-to-face care is once again allowed. A significant percentage of patients are willing to pay more to obtain this service or even change their doctor and primary institution to maintain it. These data are extremely important when making institutional decisions on how to maintain the continuity of telemedicine and which are the points that should be improved.

IMPACT STATEMENT: Maintaining the telemedicine modality represents an added value to patient care that all health institutions should evaluate.
TELEMEDICINE HAS MADE ASSISTED REPRODUCTIVE TECHNOLOGY FAR MORE CONVENIENT FOR PATIENTS, WITH HIGH PATIENT SATISFACTION AND SUCCESS RATES. Louisa Drake, D.O., Katherine Koniaris, MD, Alison Bartolucci, PhD, Evelyn Neuber, PhD HCLD, Michael Yohe, BA, Daniel R. Grow, MD, MHC M University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT.

OBJECTIVE: To enhance patient and staff safety during the Covid-19 pandemic, we implemented video based telemedicine for all new patient visits and follow up consults at our academic medical center. This review is to determine the effects of telemedicine on patient volumes, patient satisfaction, and IVF outcomes.

MATERIALS AND METHODS: This is a retrospective cohort study of all patients who received care at an academic infertility center during 2019 and 2021, the year before and after the implementation of telemedicine. The number of IVF cycles initiated, vaginal oocyte retrievals and embryo transfers performed, as well as the number of patient visits during the two years was compared. Patient satisfaction, as measured by Press Ganey scores was examined, with 500 patients surveyed each year.

RESULTS:

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>2019</th>
<th>2021</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVF Cycles and Appointments for All Age Groups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of new patient appointments</td>
<td>1473</td>
<td>1827</td>
<td></td>
</tr>
<tr>
<td>Number of follow up appointments</td>
<td>1208</td>
<td>1857</td>
<td></td>
</tr>
<tr>
<td>Number of intruterine inseminations</td>
<td>1316</td>
<td>1505</td>
<td></td>
</tr>
<tr>
<td>Number of IVF cycles initiated</td>
<td>1173</td>
<td>1258</td>
<td></td>
</tr>
<tr>
<td>Number of vaginal oocyte retrievals</td>
<td>1017</td>
<td>1110</td>
<td></td>
</tr>
<tr>
<td>Number of fresh embryo transfers</td>
<td>336</td>
<td>365</td>
<td></td>
</tr>
<tr>
<td>IVF Outcomes for Patients &lt;35 Years of Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ongoing primary ET rate (fresh + first FET after freeze all)</td>
<td>58%</td>
<td>56%</td>
<td></td>
</tr>
<tr>
<td>Ongoing pregnancy rate of first FET after freeze all</td>
<td>67%</td>
<td>76%</td>
<td></td>
</tr>
<tr>
<td>Fresh implantation rate</td>
<td>47%</td>
<td>42%</td>
<td></td>
</tr>
<tr>
<td>Average number of embryos transferred</td>
<td>1.1</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Percent of singleton pregnancies</td>
<td>94%</td>
<td>94%</td>
<td></td>
</tr>
<tr>
<td>Press Ganey Scores (Scale of 0-100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ease of scheduling appointments</td>
<td>86.59</td>
<td>90.03</td>
<td></td>
</tr>
<tr>
<td>Care provider overall</td>
<td>94.94</td>
<td>95.09</td>
<td></td>
</tr>
<tr>
<td>Likelihood of recommending care provider</td>
<td>95.51</td>
<td>95.37</td>
<td></td>
</tr>
<tr>
<td>Overall assessment</td>
<td>95.21</td>
<td>95.09</td>
<td></td>
</tr>
<tr>
<td>Care received during visit</td>
<td>95.69</td>
<td>95.12</td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS: Patient visits and procedures of all types increased in 2021 compared to 2019. Telemedicine has provided a helpful, efficient way to provide patient care. IVF outcomes at an academic institution were found to be similar before and after the implementation of telemedicine. Patients also continued to have high satisfaction rates with their care during the implementation of telemedicine.

IMPACT STATEMENT: Virtual visits are a sustainable method of providing patient care as evidenced by continued excellent Press Ganey scores and IVF outcomes. Patient visits increased after telemedicine, perhaps reflecting increased convenience and the perception of safety during a pandemic.

P-518 6:45 AM Wednesday, October 26, 2022

SOCIAL, CLINICAL AND LABORATORY PREDICTORS OF PATIENT ENGAGEMENT IN WOMEN UNDERGOING INFERTILITY TREATMENT. Leah M. Roberts, MD, Cheri K. Margolis, MD, Andres Reig, MD, Nola Herlhy, MD, Amber M. Klimeczak, MD, Pavan Gill, MD, Michael R. Drews, M.D., Emre Seli, MD, Thomas Molinaro, MD, MSCE IVIRMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: To assess the clinical and insurance coverage characteristics of patients who engage in fertility care.

MATERIALS AND METHODS: A retrospective cohort study was performed consisting of all new patient visits between January of 2017 and April of 2021 at a single fertility center. Insurance coverage, age, BMI, AMH, FSH, and relationship status for 23,033 patients were analyzed. Patients with insurance coverage (n=22138) were compared to those without (n=895). Outcomes were divided into those who presented pregnant (A; n=657), did not complete diagnostics (B; n=7959), completed diagnostics but did not pursue treatment (C; n=468), proceeded with diagnostics and treatment but did not proceed to IVF (D; n=2138), underwent oocyte retrieval without successful (E; n=4585), and those completed treatment with successful discharge to obstetrical care (F; n=7351).

RESULTS: Patients with insurance had a significantly higher BMI (27.4 vs 26.7; p=0.005) and were more likely to have a partner (93.3% vs 91.2%; p=0.01). Patients without insurance coverage were more likely to discontinue care prior to completing diagnostics (51.4% vs 33.3%; p<0.01) and less likely to proceed to IVF (37.3% vs 52.4%; p<0.01). Only 21.2% of self-pay patients successfully completed IVF and were discharged pregnant versus 32.3% of insured patients (p<0.01).

When subgroup analysis was performed, the difference between insured and self-pay patients who had BMI <40 but >18.5, AMH more than 1.2, were partnered (regardless of gender of the partner), and all ages except 41-42 persisted.

CONCLUSIONS: Patients with insurance are more likely to complete diagnostic evaluation, pursue treatment, and achieve a pregnancy from frozen embryo transfer than those without coverage.

IMPACT STATEMENT: It is ultimately unclear why some patients continue to engage in care and some do not, however lack of insurance coverage is a clear barrier to completing diagnostic testing, and continuation to every further stage in an infertility journey.

SUPPORT: None

REFERENCES: None
GONADOTROPIN UTILIZATION DATA CAN BE USED AS AN INDICATOR OF US ASSISTED REPRODUCTIVE TECHNOLOGY (ART) MARKET DYNAMICS. Fady I. Sharara, M.D.,1 Lindsay Kelly, PhD,2 Andi Luca, MBA,3 Sasminia I. Lalwani, M.D.,1,3 Patrick W. Heiser, PhD1,3 Virginia Center for Reproductive Medicine, Reston, VA; 2Ferring Pharmaceuticals, Parsippany, NJ.

OBJECTIVE: National summaries produced by the Centers for Disease Control (CDC) and Society for Assisted Reproductive Technology (SART) are instructive in highlighting ART use trends but lag the market by 2-years. Here we explore gonadotropin utilization metrics as a surrogate and more proximate marker to assess US ART utilization. Resultant forecasts may be valuable for anticipating demand and better ensuring availability of resources.

MATERIALS AND METHODS: We conducted an analysis of national summaries of U.S. gonadotropin utilization as compared to CDC data. Gonadotropin market data were provided by a private database compiled from four sources: syndicated (general market) data providers; specialty pharmacies not reporting to a syndicated source; outlet data not contained with the syndicated source; direct purchases of customers of Ferring gonadotropin product. Gonadotropin data are presented in 75 IU equivalents and are aggregated at the market level by month from January 2017 to February 2022. CDC National Summaries from 2017-2020 were used to report number of ART cycles initiated per year. Percent increases in gonadotropin utilization and ART cycle starts were depicted relative to 2017.

RESULTS: Trends in increased gonadotropin utilization reflect available CDC data on ART cycles starts. Though CDC data are not yet available for 2021, we continue to observe increased gonadotropin utilization.

CONCLUSIONS: 2018 growth in cycles and utilization was modest relative to 2017. However, increased growth was observed in 2019 with a plateau noted in 2020 attributable to the pandemic. In 2021, dramatic acceleration was observed with gonadotropin utilization increasing 36.1% relative to 2017. Available 2022 data shows a similar trend. This durability is striking since pent-up demand resulting from the COVID-19 related treatment pause has presumably been relieved.

IMPACT STATEMENT: Gonadotropin utilization data could prove critical in ART resource planning as surging inflation and lingering pandemic impacts create continued volatility in the U.S. economy, both of which could impact treatment patterns. However, increased gonadotropin utilization could be linked to changes in clinical practice whereby higher gonadotropin doses are used to enable cryopreservation of more embryos. The 2021 and 2022 SART and CDC reports are necessary to confirm the stability of the relationship between the number of cycle starts and gonadotropin units.

<table>
<thead>
<tr>
<th>Year</th>
<th>% Increase Relative to 2017</th>
<th>Gonadotropin Utilization (75 IU equivalents)</th>
<th>ART Cycles (CDC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>+1.6%</td>
<td>+7.7%</td>
<td></td>
</tr>
<tr>
<td>2019</td>
<td>+8.3%</td>
<td>+16.3%</td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>+8.6%</td>
<td>+14.8%</td>
<td></td>
</tr>
<tr>
<td>2021</td>
<td>+36.1%</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>2022*</td>
<td>+36.8%</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

*January, February reporting


REFERENCES:

EFFECTIVENESS OF CONTINUOUS MONITORING TEMPERATURE OF EQUIPMENT IN FERTILITY LABORATORY: A TIME-SAVING QUALITY CONTROL SYSTEM. Wei-Hua Wang, PhD AspireHealth-Houston Laboratory, Houston, TX.

OBJECTIVE: Traditional laboratory equipment quality control (QC) is performed once a day, usually in the morning before starting procedures. It is a time-consuming procedure, especially in a large fertility laboratory. In this report, we aimed to assess the efficiency of an automatic and continuous monitoring system of the temperature of equipment in a fertility laboratory.

MATERIALS AND METHODS: A PharmaWatch monitoring system was installed to monitor the temperature changes of all equipment, including incubators, workstations, refrigerators, freezer, warming stages, liquid nitrogen storage tanks (inside and surface) and room temperature. A digital thermo probe was installed on each of the equipment, but two thermo probes were installed in a liquid nitrogen tank to measure both inside temperature and outside surface temperature. Temperature data were recorded and analyzed constantly on the data stream. Users are notified by any condition outside the control limits via email(s), text message and phone (voice) notification. The communication from the device to the servers is accomplished via cellular (CAT M1). The cloud-based server is fully accessible via web browser; no special software is required to access the data.

RESULTS: There are 24 incubators, 8 workstations, 4 warming stages, 3 refrigerators/freezers and about 100 liquid nitrogen storage tanks are monitored by this system. Digital temperature data was recorded every 5 minutes on the data stream. Technicians can log in the monitoring system any time and see all temperature data since the probe was installed. Any temperature fluctuations can be found during this checking. If a reading point is out of the range, an alert can be sent to receiver immediately for the corrective action. The time for checking the system can be reduced from up to hours with the traditional daily QC to a minute with this system. The PharmaWatch solution also offers a score associated with each zone (equipment). This score provides the end user information as to the hardware performance, the user interaction, and the device state. This feature allows one to assess the performance of each category to perform maintenance, assess product stress or determine the need for additional user training.

CONCLUSIONS: Our experience indicates that equipment’s temperature fluctuations can be monitored by this automatic and continuous monitoring system, and this is particularly important for incubators, refrigerators, and freezers as temperature changes may have negative effects on the culture media in the storage or embryos in the culture. Continuous monitoring is more important than the traditional one-time daily QC. The time for QC can be significantly reduced, especially if there are a lot of equipment in a large laboratory.

IMPACT STATEMENT: The automatic and continuous temperature monitoring system can reduce embryologists’ workloads and provide more data of each equipment’s performance, which should be a better QC system than the traditional QC.

SUPPORT: NA

E-POSTER ABSTRACT STATION: W9

REMOVING ASSESSMENT POINTS FOR TIME SAVINGS IN THE EMBRYOLOGY LABORATORY. R. Anthony,1,2 D. S. C. Anderson, M.S., M.Sc.,2 Selena Campbell Brewer, B.Sc.,1 Marie-Eve Ruest, M.Sc.1 Reproductive Medicine Associates of Texas, PA, Spring Branch, TX; 1EmbryoDirector IVF Academy, San Antonio, TX; 2The Fertility Center, Chattanooga, TN.

OBJECTIVE: Historically the timing if intracytoplasmic sperm injection (ICSI) has been required to be performed 4 to 6 hours post retrieval or 40
Employees were recruited to complete the survey in April 2022. The study was approved by the local ethics committee. Fifty-eight respondents were included after completing the survey. Participants were asked to rate their experience of laboratory staff and their perceptions of patient experience. The results were analyzed using descriptive statistics and Chi-square automatic interaction detection in SPSS.

RESULTS: A total of 58 responses were collected, with 79% from multi-center clinic groups (n=46) and an overall mean of 7.76 years of laboratory experience. Embryologists collectively made up the largest population of respondents (64%) with 21% being andrologists. Of the embryologists surveyed, 92% agreed that RI Witness was easy to use. Most respondents found the RI Witness system intuitive (90%), with 97% of embryologists finding that the system is intuitive. Job related stress was reduced in 72% of all respondents, with higher agreement among junior embryologists and embryologists (87%). RI Witness increased confidence in all junior embryologists and embryologists that they had not made any potential errors; this was slightly lower in the overall study population at 91%. The majority of all respondents agreed that patients were aware that their clinic was using RI Witness. Further evaluation of this subpopulation demonstrated that respondents believe patient experience was enhanced when using RI Witness. Patients were more likely to have treatment at their clinics (100%), patients were reassured the risk of mistakes were reduced (100%), and patients had greater confidence in the clinic due to the use of RI Witness (100%).

CONCLUSIONS: This research demonstrates that laboratory staff find RI Witness intuitive and easy to use. Use of RI Witness was shown to positively impact overall work experience, with embryologists collectively more strongly impacted than the laboratory technicians and andrologists. RI Witness has an important role to play in increasing confidence that procedures have been performed correctly, while reducing job-related stress. There was overwhelming agreement that when patients are aware RI Witness is being used, that the patient experience was positively impacted and that it plays a role in patient clinic selection.

IMPACT STATEMENT: RI Witness is intuitive and easy to use and has a positive impact on both staff and perceived patient experience.
RESULTS: Following CC and LTZ IUI, estimated cost per singleton live birth was $39,115 and per twin live birth was $153,448. Following GN IUI, estimated cost per singleton live birth was $41,429, per twin live birth was $155,762, and per HOM live birth (which only occurred in GN cohort) was $545,616.

CONCLUSIONS: This cost analysis using outcome data from the AMIGOS trial found that live birth for HOM, only seen in the GN IUI arm, is over 13 times more expensive than for singleton and 3.5 times more expensive than for twin live birth. GN IUI cycles do not increase the chance of singleton live birth compared CC or LTZ IUI but do increase the chance of multiple gestations which have higher complication rates and maternal/neonatal costs. Therefore, GN IUI is not an optimal treatment for unexplained infertility.

IMPACT STATEMENT: GN IUI is not an optimal treatment for unexplained infertility and clinicians should strongly consider CC/LTZ with IUI or IVF as safer and less costly alternatives.

**OOCYTES RETRIEVALS**

<table>
<thead>
<tr>
<th>Weekday (n=2563)</th>
<th>Weekend (n=634)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)*</td>
<td>36.0 (4.5)</td>
<td>36.5 (4.6)</td>
</tr>
<tr>
<td>AMH (ng/mL)*</td>
<td>2.1 (1.1-1.4)</td>
<td>2.1 (0.9-4.2)</td>
</tr>
<tr>
<td>Oocytes retrieved*</td>
<td>12 (7-18)</td>
<td>12 (7-19)</td>
</tr>
<tr>
<td>Mature oocytes*</td>
<td>9 (5-14)</td>
<td>9 (5-14)</td>
</tr>
<tr>
<td>Oocyte maturity rate (%)</td>
<td>80 (67-92)</td>
<td>82 (68-93)</td>
</tr>
<tr>
<td>2PN*</td>
<td>7 (4-11)</td>
<td>7 (3-12)</td>
</tr>
<tr>
<td>Fertilization rate (%)</td>
<td>83 (70-94)</td>
<td>80 (66-92)</td>
</tr>
<tr>
<td>ICSI</td>
<td>81 (70-92)</td>
<td>80 (66-91)</td>
</tr>
<tr>
<td>Conventional</td>
<td>83 (70-100)</td>
<td>83 (68-100)</td>
</tr>
</tbody>
</table>

**EMBRYO TRANSFERS**

<table>
<thead>
<tr>
<th>Weekday (n=1198)</th>
<th>Weekend (n=541)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)*</td>
<td>35.9 (4.1)</td>
<td>35.6 (4.2)</td>
</tr>
<tr>
<td>Age at Oocyte retrieval (FETs only) (y)*</td>
<td>34.7 (3.5)</td>
<td>35.7 (3.5)</td>
</tr>
<tr>
<td>Cycle type, n (%)</td>
<td>831 (69.4)</td>
<td>404 (74.7)</td>
</tr>
<tr>
<td>Fresh</td>
<td>367 (30.6)</td>
<td>137 (25.3)</td>
</tr>
<tr>
<td>FET</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embryos transferred (#)*</td>
<td>1 (1-2)</td>
<td>1 (1-2)</td>
</tr>
<tr>
<td>Implantation Rate (%)*</td>
<td>44.7 (48.6)</td>
<td>41.1 (48.0)</td>
</tr>
<tr>
<td>Fresh</td>
<td>39.0 (46.2)</td>
<td>37.7 (46.2)</td>
</tr>
<tr>
<td>FET</td>
<td>57.6 (51.5)</td>
<td>51.1 (52.0)</td>
</tr>
<tr>
<td>Clinical Pregnancy Rate (%)*</td>
<td>45.9 (49.9)</td>
<td>41.2 (49.2)</td>
</tr>
<tr>
<td>Fresh</td>
<td>41.8 (49.3)</td>
<td>39.6 (49.0)</td>
</tr>
<tr>
<td>FET</td>
<td>55.3 (49.8)</td>
<td>46.0 (50.0)</td>
</tr>
<tr>
<td>Miscarriage Rate (%)*</td>
<td>18.8 (39.1)</td>
<td>18.9 (39.3)</td>
</tr>
<tr>
<td>Fresh</td>
<td>21.4 (41.1)</td>
<td>17.9 (38.5)</td>
</tr>
<tr>
<td>FET</td>
<td>14.4 (35.1)</td>
<td>21.4 (41.3)</td>
</tr>
<tr>
<td>Live Birth Rate (%)*</td>
<td>39.6 (48.9)</td>
<td>36.0 (48.1)</td>
</tr>
<tr>
<td>Fresh</td>
<td>35.1 (47.8)</td>
<td>34.9 (47.7)</td>
</tr>
<tr>
<td>FET</td>
<td>49.6 (50.0)</td>
<td>39.4 (49.0)</td>
</tr>
</tbody>
</table>

*Mean(SD)
^Median(IQR)
GEE adjusted for age, AMH, +/- Insemination Method
GEE adjusted for age, day of embryo transfer, # embryos transferred,
+/- whether it was a biopsied embryo

P-524 6:45 AM Wednesday, October 26, 2022

MORE RISK THAN REWARD: A COST ANALYSIS OF THE AMIGOS TRIAL. Eden R. Cardozo, M.D.,1 Ruben J. Alvero, MD,2 Michael P. Diamond, MD,3 Nanette Santoro, MD,1 Brindha Bavan, MD1 Boston, MA; 2Stanford University School of Medicine, Stanford, CA, CA; 3Medical College of Georgia at Augusta University, Augusta, GA; 4University of Colorado School of Medicine, Aurora, CO; 5Stanford Medicine Fertility and Reproductive Health Services, Sunnyvale, CA.

OBJECTIVE: We conducted a cost analysis of clomiphene citrate (CC) versus letrozole (LTZ) versus gonadotropin (GN) with intrauterine insemination (IUI) for couples with unexplained infertility. Using pregnancy outcomes data from the AMIGOS trial, cost data from publicly available sources, and taking into account associated maternal and neonatal care and complications associated with singleton, twin (TIUP), and higher order multiple (HOM) gestations, the study assessed the relative costs of each strategy.

MATERIALS AND METHODS: A decision analytic model was created using the TreeAge Pro Healthcare 2021 software to compare the three groups (CC vs LTZ vs GN) and their respective probability and cost inputs for treatments and pregnancy outcomes. Probability data were directly calculated from reanalysis of the original AMIGOS trial data available through the Reproductive Medicine Network. Cost data were derived from published literature and adjusted for inflation to 2022 US$. These included costs for fertility treatment, pregnancy loss, HOM reduction, and live births (singleton, TIUP, and HOM) – including prenatal care, delivery, and NICU admission.

P-525 6:45 AM Wednesday, October 26, 2022

A SMALL DIGITAL FOOTPRINT OF PSYCHOLOGICAL SERVICES IN FERTILITY CLINICS: A WEBSITE CONTENT ANALYSIS. Georges Raad, Ph.D.1 Abdulla Almohammadi, M.Sc.,2 Okan Attilan, M.Sc.2 Nagham Younis, M.Sc.,3 Alia Al Hourani, M.Sc.,4 Fadi Choucair, Ph.D.5 1Middle East Fertility Society Embryology SIG; Al Hadi IVF Center, Beirut, Lebanon; 2Middle East Fertility Society Embryology SIG; Sidra Medicine, Doha, Qatar; 3Middle East Fertility Society Embryology SIG; University of Pittsburgh, PA, USA; 4Middle East Fertility Society Embryology SIG; International Hospital, Al Salmiya, Kuwait; 5Sidra Medicine, Doha, Qatar.
OBJECTIVE: The emotional turmoil endured by infertility patients can be overwhelming. There is mounting evidence that infertile couples are likely to experience depression, anxiety, and stress. As a supportive practice, infertility-related psychological distress management has recently emerged as a method of improving the overall quality of fertility care by alleviating the psychological underpinnings of infertility experience. However, it is not entirely clear how frequently psychological support services are integrated into the comprehensive treatment of infertility. Therefore, this study aims to evaluate the online presence of psychological services on fertility clinic websites.

MATERIALS AND METHODS: A list of websites of fertility clinics was retrieved from two public registries: The Society for Assisted Reproductive Technology (SART) and The Human Fertilization and Embryology Authority (HFEA). Each website of clinics located in the United States and the United Kingdom was individually queried for the presence of an on-site psychologist. Standard descriptive statistics were utilized.

RESULTS: The search scanned 447 fertility clinic websites. Of these, 83.42% were private clinics/centers, 10.88% hospital-based and 5.44% academic centers-based practices. Only 12% of clinic websites reported integrated mental health programs including on-site psychologists. For instance, most psychologists were identified as based out of group or solo private practice (9.39%), although the rest belongs to hospitals (2.01%) and academic centers-based (0.89%) practices.

CONCLUSIONS: Most fertility clinics in the United States and the United Kingdom had a very small digital footprint of psychological services. It may be beneficial to test whether scaling up psychosocial support interventions in fertility clinics leads to a pleasant treatment journey and higher patient retention.

IMPACT STATEMENT: Barriers to integrated mental health care in fertility clinics would seem to have been in part the lack of internet exposure to this service care.

P-526 6:45 AM Wednesday, October 26, 2022

AN ANALYSIS OF QUALITATIVE THEMES IN YELP REVIEWS OF ASSISTED REPRODUCTIVE TECHNOLOGY (ART) PRACTICES. Margot Gurganus, M.D., M.P.H,1 Olivia Chafitz, M.D.,2 Erica Mark, B.S.,3 Isabelle Gill, B.S.1 1University of Virginia, Charlottesville, VA; 2Hackensack Meridian Health, Hackensack, NJ.

OBJECTIVE: To identify qualitative themes distinguishing poorly-rated practices from highly-rated practices offering Assisted Reproductive Technology (ART) services.

MATERIALS AND METHODS: We conducted an IRB-exempt, qualitative review of the publically-accessible online review platform Yelp. ART practices were analyzed in over 30 highly-populated U.S. cities from each of the five geographic regions; reviews were only included on practices with 5+ total reviews. Reviews were coded for 14 qualitative themes grouped as a function of 1- to 5-star rating.

RESULTS: A total of 1232 reviews were analyzed, with nearly all being non-academic affiliated offices. The average star rating was 3.82 with 66.6% being 5-star practices and 23.5% being 1-star practices. 5-star practices were more likely to include positive physician-related themes (Table 1). Con- sumers leaving 5-star reviews mentioned providers by name in nine out of every ten reviews. The most common cited reasons for a 1-star rating included negative staff interactions, billing issues, and poor communication.

CONCLUSIONS: Online consumer platforms, such as Yelp, can provide important insight into the patient experience.

IMPACT STATEMENT: This study demonstrates the importance of understanding the consumer experience in the modern practice of Assisted Reproductive Technology. Online reviews can help target provider and practice-specific areas for improvement.

Table 1. Subdivision of theme categories.

<table>
<thead>
<tr>
<th>Theme Category</th>
<th>Positive variation % 1-star rating</th>
<th>Negative variation % 1-star rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician factors</td>
<td>(10.0, 82.8)</td>
<td>(18.6, 0.4)</td>
</tr>
<tr>
<td>Temperament</td>
<td>(2.1, 40.4)</td>
<td>(13.1, 0)</td>
</tr>
<tr>
<td>Competency/ knowledge base</td>
<td>(1.7, 61.9)</td>
<td>(38.6, 0.5)</td>
</tr>
<tr>
<td>Physician-patient communication</td>
<td>(0, 6.8)</td>
<td>(8.2, 0.2)</td>
</tr>
<tr>
<td>Support of patient autonomy</td>
<td>(0, 18.03)</td>
<td>(10.7, 0)</td>
</tr>
<tr>
<td>Thoroughness</td>
<td>(0.7, 11.8)</td>
<td>(11.7, 0)</td>
</tr>
<tr>
<td>Innovative use of technology</td>
<td>(0, 3.1)</td>
<td>(14.5, 0)</td>
</tr>
<tr>
<td>Cost consciousness</td>
<td>(0.3, 7.7)</td>
<td>(19.7, 2.4)</td>
</tr>
<tr>
<td>Practice factors</td>
<td>(0.3, 4.5)</td>
<td>(0.7, 0.1)</td>
</tr>
<tr>
<td>Wait times</td>
<td>(0, 4.5)</td>
<td>(2.8, 0.1)</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>(0, 10.4)</td>
<td>(50.3, 1.0)</td>
</tr>
<tr>
<td>Billing &amp; insurance</td>
<td>(0.7, 7.3)</td>
<td>(20.7, 0.5)</td>
</tr>
<tr>
<td>Scheduling</td>
<td>(0.3, 3.3)</td>
<td>(3.5, 0.4)</td>
</tr>
<tr>
<td>Interactions with staff</td>
<td>(6.6, 75.6)</td>
<td>(61.4, 0.9)</td>
</tr>
</tbody>
</table>

P-527 6:45 AM Wednesday, October 26, 2022

SARS-COV-2 VACCINATION HESITANCY IN WOMEN WHO DESIRE FUTURE FERTILITY/ PREGNANCY. Ariya Mobaraki, MD,1 Christina M. Stetter, B.S.,2 Allen R. Kuselman, M.A.,3 Stephanie J. Estes, MD,4 Hummelstown, PA; 3Pennsylvania State College of Medicine, Hershey, PA; 4Penn State Health, Hershey Medical Center, Hershey, PA.

OBJECTIVE: To evaluate the attitudes toward SARS-CoV-2 vaccination by partially or unvaccinated women who desire future fertility.

MATERIALS AND METHODS: An IRB approved electronic anonymous survey was sent to women ages 18-44 with a uterus seen at our institution between 2016 and 2021. We chose to exclude males, pregnant women, women without a uterus, fully vaccinated women, and partially vaccinated women who were unable to receive their second dose due to a medical reason or allergic reaction. To be deemed eligible, participants first answered a set of qualifier questions that determined vaccination status, pregnancy status, and whether the participant desired future fertility. Descriptive statistics were used to identify percentages of participants who chose a certain answer choice. Crosstabulations of data of particular interest were also performed.

RESULTS: 683 subjects were consented and met study criteria. 605 (88.6%) submitted the survey of which 214 (35.4%) were currently attempting or planning pregnancy within a year and 319 (52.7%) in the next 1-5 years. Of the 605 respondents, 452 (74.1%) worried the vaccine would decrease their chances of becoming pregnant. Of these participants, 249 (48.5%) stated they would reconsider their choice not to vaccinate if given information by a trusted source; the most common source being a healthcare provider. Women were not influenced by a family member or friend's decision to not vaccinate (496 (82.0%).

CONCLUSIONS: A majority of unvaccinated women were hesitant to receive the vaccine at least partially due to fear of harm to their baby or...
SUPPORT: Funding was obtained through our institution’s Obstetrics & Gynecology Departmental Research Committee.

Participants could select multiple sources.

Jennifer K. Blakemore, MD, MSc
NYU Langone Prelude Fertility Center, New York, NY.

#AMH levels on Instagram (IG) from 1/1/2019 to 12/31/2021. On IG, all sin-
the use of term ‘‘AMH level’’ on Google Trends (GO) and #AMHlevel/
objective was to understand the social media content surrounding the search
reserve is debated[1], patient interest in their own fertility is growing. Our
New York, NY.

P-528 6:45 AM Wednesday, October 26, 2022
A NEW ERA: HOW SOCIAL MEDIA CONTENT SUR-
ROUNDING “ANTI MULLERIAN HORMONE” HAS
CHANGED OVER TIME. Jenna Reich, MD; Nirali Jain, 
BA, MD; Jennifer K. Blakemore, MD, MSc
NYU Grossman School of Medicine, New York, NY; NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: Though the ability of an AMH result to predict ovarian
reserves is debated[1], patient interest in their own fertility is growing. Our
objective was to understand the social media content surrounding the search
term: AMH level.

MATERIALS AND METHODS: This is a retrospective cohort study of
the use of term “AMH level” on Google Trends (GO) and #AMHlevel/
#AMHlevels on Instagram (IG) from 1/1/2019 to 12/31/2021. On IG, all sin-
gle user posts in the “most recent” search function were included. Posts were
tegerized by author type (fertility clinic/ FC, influencer, provider, pa-
tient/parent), content, and tone (positive, negative, neutral). Likes per post
and total account followers were quantified to calculate percent of likes
(PL) and assess activity. Chi square and ANOVA was used with p-value <
0.05 considered significant.

RESULTS: On IG, the term “#AMHlevel” was mentioned in 196 posts
and #AMHlevels in 161 posts. Hashtag use increased over time, with
amounts of 19 (16.5%), 121 (33.9%) and 177 (49.6%) respectively by year
(Table 1). Mean number of likes, followers and PL was 93.7 ± 558.3,
2953.3 ± 12762.1 and 4.7 ± 6.3 respectively. PL was not associated with
author type (p-value=0.487). Positive and negative posts received a higher
PL compared to neutral (6.8 ± 6.4 v 3.8, p<0.00). Mean PL also varied by
content (Celebrity Story 10.0 ± 16.6, Patient Story 6.2 ± 6.2, Personal Story
5.6 ± 5.8, Support 4.5 ± 3.0, Literature 1.4 ± 1.4 p-value = 0.012)

On GO, “AMH level” was most searched in May – August 2021 and least
in April 2019 and 2020. Within the USA, it was most utilized in New York,
California, Texas, and Florida in descending order. Overall use has remained
consistent over time (m=0.009).

CONCLUSIONS: Use of #AMHlevel/s on Instagram, especially by FCs,
has grown. Activity on influencer and celebrity posts has also grown.
Comparatively, searches of “AMH Level” on GO has remained mostly un-
changed, possibly showing a shift away from search engines and towards so-
cial media for information.

IMPACT STATEMENT: This is the first study to characterize the use of
search terms related to AMH levels on social media. As access and attention
to AMH levels rises, it is important to understand where patients are
receiving their information.

REFERENCES:
1. Moolhuijsen LM, Visser JA. Anti-Müllerian hormone and ovarian
reserve: update on assessing ovarian function. The Journal of Clinical Endo-
crinology & Metabolism. 2020 Nov 1;105(11):3361-73.

TABLE 1. Comparing #AMHlevel/s use on IG over time

<table>
<thead>
<tr>
<th>Category</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>Total – N (%)</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>Author</td>
<td>23</td>
<td>41</td>
<td>111</td>
<td>175 (49.0)</td>
<td>0.00</td>
</tr>
<tr>
<td>FC</td>
<td>3</td>
<td>10</td>
<td>28</td>
<td>41 (11.5)</td>
<td></td>
</tr>
<tr>
<td>Provider</td>
<td>33</td>
<td>69</td>
<td>27</td>
<td>129 (36.1)</td>
<td></td>
</tr>
<tr>
<td>Patient/Parent</td>
<td>0</td>
<td>11</td>
<td>12</td>
<td>12 (3.4)</td>
<td></td>
</tr>
<tr>
<td>Influencer</td>
<td>7</td>
<td>9</td>
<td>9</td>
<td>25 (7.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Tone</td>
<td>41</td>
<td>71</td>
<td>128</td>
<td>242 (67.8)</td>
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<td>Neutral</td>
<td>9</td>
<td>41</td>
<td>40</td>
<td>90 (25.2)</td>
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<tr>
<td>Positive</td>
<td>10</td>
<td>22</td>
<td>75</td>
<td>107 (30.0)</td>
<td>0.00</td>
</tr>
<tr>
<td>Content</td>
<td>11</td>
<td>21</td>
<td>38</td>
<td>70 (19.6)</td>
<td></td>
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<tr>
<td>Informational</td>
<td>21</td>
<td>60</td>
<td>25</td>
<td>106 (29.7)</td>
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<td>Marketing</td>
<td>6</td>
<td>6</td>
<td>21</td>
<td>28 (7.8)</td>
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<tr>
<td>Personal Story</td>
<td>1</td>
<td>4</td>
<td>6</td>
<td>11 (3.1)</td>
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</tr>
<tr>
<td>Patient Story by provider</td>
<td>2</td>
<td>2</td>
<td>9</td>
<td>16 (4.5)</td>
<td></td>
</tr>
<tr>
<td>Emotional Support</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>3 (0.8)</td>
<td></td>
</tr>
</tbody>
</table>

* Participants could select multiple sources

SUPPORT: Funding was obtained through our institution’s Obstetrics & Gynecology Departmental Research Committee.

fertility, and a large subset responded that they would be willing to reconsider vaccination if given more information by a healthcare provider.

IMPACT STATEMENT: Future interventions aimed toward provider-driven vaccine promotion could potentially lower vaccine hesitancy rates in women desiring future fertility/pregnancy.

P-529 6:45 AM Wednesday, October 26, 2022
GLUTAMINE AND ACAI SUPPLEMENTATION IMPROVES OOCYTE YIELD IN AGED MICE. William Broussard, BS, MS; Didi Logsdon, B.A., M.SC; William B. Schoolcraft, MD, Mandy Katz-Jaffe, PhD, Ye Yuan, PhD Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Determine the effect of glutamine and acai supplementation on fertility outcomes in aged mice.

MATERIALS AND METHODS: At 57 weeks and 61 weeks, mice were supplemented with either water (C, n=20) or water containing 1:5 dilution of L-alanyl-glutamine (G, n=19) or acai + L-alanyl-glutamine (G+A, n=18). Before starting supplementation, mice were weighed and would be weighed at the end of supplementation. Bottles were weighed and replaced every three days to track water consumption. After 5 weeks of supplementation, each group was synchronized and superovulated with 5IU PMSG

<table>
<thead>
<tr>
<th>Source*</th>
<th>TV News</th>
<th>Social Media</th>
<th>Partner/Spouse</th>
<th>Family member other than spouse</th>
<th>Friend</th>
<th>Healthcare Provider</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA, MD</td>
<td>138 (30.5%)</td>
<td>205 (45.4%)</td>
<td>91 (20.1%)</td>
<td>161 (35.6%)</td>
<td>153 (33.9%)</td>
<td>118 (26.1%)</td>
</tr>
<tr>
<td>BA, MD</td>
<td>143 (45.3%)</td>
<td>70 (16.4%)</td>
<td>134 (31.3%)</td>
<td>141 (32.9%)</td>
<td>106 (24.8%)</td>
<td></td>
</tr>
<tr>
<td>BA, MD</td>
<td>75 (19.6%)</td>
<td>65 (16.4%)</td>
<td>82 (20.1%)</td>
<td>58 (14.5%)</td>
<td>43 (10.1%)</td>
<td></td>
</tr>
</tbody>
</table>

Vol. 118, No. 4, Supplement, October 2022
followed by 5IU hCG intraperitoneally 48 h later, and oocytes were collected, shielded, and oocytes were searched for. Following collection, the oocytes were incubated in maturation media for 18 hours at 37°C with a CO2 concentration of 7.5% and an O2 concentration of 6.5%. The number of oocytes, penetrated to MII were recorded.

RESULTS: There was a significant increase in water consumption in glutamine and glutamine+acai groups compared to the control after five weeks of supplementation (C=15.24, G=17.39, G+A=18.59, p<0.0001). There was no significant differences between the control group and glutamine group in oocyte production per mouse. However, there was a significant increase in oocyte yield in the glutamine + acai group compared to control (G=14.572, G+A=25.03, p<0.05). Additionally, both glutamine and glutamine + acai groups yielded significantly more good quality oocytes than the control group (C=1.25±0.1316, G=1.79±0.1153, G+A=2.12±0.1061; p<0.0001).

CONCLUSIONS: Supplementation of glutamine did not increase oocyte yield, but did increase the number of good quality oocytes retrieved per mouse. This suggests that glutamine supplementation may improve the number of good quality oocytes retrieved for advanced maternal age patients. Additional supplementation of acai improved both the number and the number of good quality oocytes from aged mice. Future studies with mice ages 12-13 months are being considered as this could show larger differences.

IMPACT STATEMENT: Glutamine in conjunction with acai may be used as a possible diet supplement to improve infertility in advanced maternal age patients.

FERTILITY & STERILITY®

E-PAPER ABSTRACT STATION: W10

P-531 6:45 AM Wednesday, October 26, 2022

TRANSCRIPTOMIC EVIDENCE OF AUTOPHagy IN CYCLOPHOSPHAMIDE-INDUCED PRIMORDIAL FOLLICLE DESTRUCTION. Xia Hao, PhD,1 Jian Zhao, PhD,2 Arturo Reyes Palomares, PhD, MSc,3 Kenny A. Rodriguez-Wallberg, M.D., PH.D, Professor;4 Laboratory of Translational Fertility Preservation, Karolinska Institutet, Stockholm, Sweden; 2Karolinska Institutet, Stockholm, Sweden; 3Karolinska University Hospital, Stockholm, Sweden.

OBJECTIVE: To investigate autophagy in cyclophosphamide (CPA)-treated newborn mouse ovaries as an explanatory mechanism of CPA-induced primordial follicle depletion.

MATERIALS AND METHODS: Randomised controlled study using 4-day old B6CBA/F1 mice. Ovaries were collected and randomly assigned to either medium with hydroperoxycyclophosphamide (4-HC, 5 µM) or control medium and subsequently cultured for up to 36 hours in 24-well plates with inserts. At 8, 12, 24 and 36 h after treatment, five ovaries from each group were collected for RNA sequencing. Analysis of differentially expressed genes and gene set enrichment analysis (GSEA) were carried out for interpreting biological means between the CPA-treated group and control group. Additionally, at 8 and 24 h after treatment, one ovary from each group were processed for transmission electron microscopy (TEM) analysis.

RESULTS: A significant proportion of differentially expressed genes were related to autophagy at 24 and 36 h in CPA-treated group compared to control group. At 24 h, significantly up-regulated expression of Autophagy-associated gene 9b (Atg9b) (Log2FC=1.40), Lysosomal membrane-associated protein 2 (Lamp2) (Log2FC=0.38), autophagy associated transmembrane protein (Eil24) (Log2FC=0.68), Voltage-dependent anion channels (Vdac1) (Log2FC=0.21), Pyruvate dehydrogenase kinase 4 (Pdk4) (Log2FC=0.82), Mitogen-activated protein kinase (Mapk11) (Log2FC=0.52) were found in CPA-treated ovaries. At 36 h, significantly up-regulated expression of Lamp2 (Log2FC=0.54), Eil24 (Log2FC=0.69), Vdac1 (Log2FC=0.29), Pdk4 (Log2FC=1.42), Mapk12 (Log2FC=0.36), FUN14 domain containing 2 (Fundc2) (Log2FC=0.35), Tropomyosin alpha-1 chain (Tpm1) (Log2FC=0.55) were found in CPA-treated ovaries.

Additionally, comparing to control group, CPA-treated ovaries showed after GSEA analysis an enrichment of Gene Ontology (GO) terms related to cellular compartment lysosome. A total of 41 genes were identified to be significantly up-regulated at 36 h increasing up to 111 genes at 36 h. Representative genes in this period were: Bbc3, Ape1, Vps36, Calcr1, Cldn4, Dna2a, Aga, Pdrfbr, Gnu, Fnbp1, Arl8a, Ctsj, Tmem44, Sid2, et al.

In TEM analysis at 24 h, primordial follicles showed an evident increase in the presence of vacuoles within cytoplasm of oocytes.

CONCLUSIONS: Key genes related to canonical autophagy were up-regulated in CPA-treated new born mouse ovaries in vitro. Our results indicate that autophagy could be induced as consequence of CPA exposure and be responsible of primordial follicle depletion. TEM ultrastructure observation of oocytes showed some changes in cytoplasm potentially linked to autophagy. Our results point out to autophagy as a different cell death pattern, other than apoptosis, which might have been involved in CPA-induced primordial follicle depletion.

IMPACT STATEMENT: This study provided a deeper insight into the mechanisms of CPA-induced follicle depletion through autophagy using data from gene expression and ultrastructure observation by TEM, which adds new knowledge on the processes explaining CPA induced ovarian toxicity.

P-532 6:45 AM Wednesday, October 26, 2022

SEnescence DURING IN VITRO EMBRYO DEVELOPMENT IN A MURINE MODEL. Eva Schenkman, PhD;1 Helena I. Russell, MSc;2 Jason E. Swain, PhD, HCLD;3 Marlene Angle, PhD;3 Eastern Virginia Medical School; 2Eastern Virginia Medical School, Norfolk, VA; 3CCRM Fertility, Lone Tree, CO; 4Laurel Fertility, San Francisco, CA.

OBJECTIVE: To define the mechanisms of CPA-induced follicle destruction through autophagy from gene expression and ultrastructure observation by TEM, which adds new knowledge to the processes explaining CPA induced ovarian toxicity.

IN VITRO SENESCENCE DURING IN VITRO EMBRYO DEVELOPMENT IN A MURINE MODEL. Eva Schenkman, PhD;1 Helena I. Russell, MSc;2 Jason E. Swain, PhD, HCLD;3 Marlene Angle, PhD;3 Eastern Virginia Medical School; 2Eastern Virginia Medical School, Norfolk, VA; 3CCRM Fertility, Lone Tree, CO; 4Laurel Fertility, San Francisco, CA.
OBJECTIVE: The objective of this study seeks to examine markers of senescence and the effect of environmental stressors on murine preimplantation embryos to develop a model to determine whether environmental stress can induce biomarkers of cellular senescence in the developing cells.

MATERIALS AND METHODS: This experiment aimed to evaluate the effect of oxygen tension (5% O2 vs 20% O2) and mild levels of H2O2 on senescence biomarkers in preimplantation murine embryos. Low oxygen (5%) was used as a control environment, high oxygen (20%) was used for oxygen tension, mild levels of H2O2 was used to mimic oxidative stress and Doxorubicin, a known senescence inducer, was used as a positive control. 350 Two-cell mouse embryos (Embryotech, USA) were thawed were cultured for 72 hours in vitro. The markers of senescence that were examined include senescence-associated β-galactosidase (SA-β-Gal), the cytokine interleukin 6 (IL-6), and gene expression of p21. Since Reactive Oxygen Species (ROS) are also implicated in senescence, CellRox™ Deep Red was also used as a ROS indicator. Quantification of Fluorescence was performed using Confocal imaging with Z-stack scanning. RNA isolation and extraction was performed with the Cells-to-CT kit (Thermo Fisher) and qRT-PCR was performed using Taqman gene expression assay on a QuantStudio 3 (Thermo Fisher). Continuous data was analyzed using unpaired student’s t-test or One-way ANOVA. Categorical data was analyzed using a Pearson two-tailed correlation analysis with a p < 0.05 considered to be statistically significant.

RESULTS: Corrected Total Cell Fluorescence (CTCF) was analyzed using confocal microscopy with z stack scanning and calculated as a percentage of low oxygen control group for SA-β-Gal using a novel live cell assay, SPI-DER. All groups showed a statistical increase in CTCF when compared to the low oxygen control environment (145% for high oxygen (20% O2), 162% for 250mM H2O2, 193% for 12.5nM DOX and 196% for 500mM H2O2, p < 0.05). CTCF was also analyzed for CellRox™ Deep Red as Percentage of low oxygen control, again all groups showed a statistical increase (289% for 12.5nM DOX, 492% for 250mM H2O2, 763% 500mM H2O2 and 925% for High Oxygen (20% O2), p < 0.05). The relative expressions levels of IL-6 was also measured, all groups relative to the control group showed a significant increase fold change in IL-6 expression (2.2 fold for High Oxygen (20% O2), 2.5 fold for 500mM H2O2, 2.9 fold for 250mM H2O2 and 7.432 fold for 12.5nM DOX, p < 0.05). The relative expression levels of p21 was also increased in the following groups (3.0 fold for high oxygen (20%O2), 2.8 fold for 500mM H2O2, and 5.3 fold for 12.5nM DOX, p < 0.05).

CONCLUSIONS: The results of these studies support the hypothesis that environmental stressors can induce senescence biomarkers in preimplantation stage embryos and implicate their participation in the degeneration of previously viable embryos.

IMPACT STATEMENT: This study confirmed that embryos exposed to environmental stress and suboptimal culture conditions can express markers of cellular senescence during in vitro culture.

SUPPORT: none

P-534 6:45 AM Wednesday, October 26, 2022


OBJECTIVE: To generate offspring with identical paternal haplotypes from haploid male genome replicates initiated through the ooplasmic male can be helpful in managing germline heterozygosity and provide a study platform for heritable genomic editing of the male gamete.

SUPPORT: None

RESULTS: A total of 421 oocytes were enucleated with a survival rate of 98.6% and yielded 351 (84.6%) constructs with a male pronucleus 6 hours post-ICSI. A total of 208 (59.3%) constructs cleaved to the 8-cell stage. A total of 148 haploid androgenetic blastomeres with GFP expression were grafted onto complemented activated oocytes of which 145 fused. A total of 481 untreated oocytes were inseminated, yielding 437 control zygotes. Development of reconstructed embryos into the 2-cell (96.4%), 4-cell (94.3%), and 8-cell stage (91.4%) was comparable with controls (97.5%, 93.8%, and 92.7% respectively). Compaction (80.0%) and blastulation (60.7%) were lower (P < 0.001) than controls (89.2% and 80.8%, respectively), but retained similar embryo developmental morphokinetics. A total of 145 constructs were transferred into 5 surrogates; 8 blastocysts (17.8%) and yielded 5 live pups (11.1%) weighing 1.5g±0.2g. All live offspring expressed GFP and retained fertility once they reached adulthood.

CONCLUSIONS: Our results confirm the feasibility of generating functional haploid replicates of the male gamete from a single spermatozoon, supported by the achievement of healthy offspring displaying the GFP genotype. This technique requires further optimization to enhance overall efficiency in generating offspring, particularly from the same spermatozoon.

IMPACT STATEMENT: The proposed technique of replicating a haploid male can be helpful in managing germline heterozygosity and provide a study platform for heritable genomic editing of the male gamete.

P-534 6:45 AM Wednesday, October 26, 2022

WESTERN-STYLE DIET FEEDING IN A PRIMATE MODEL OF TESTOSTERONE INDUCED POLYCYSTIC OVARIAN SYNDROME IS ASSOCIATED WITH MENSTRUAL CYCLE SPECIFIC ALTERATIONS TO THE GUT, VAGINAL, AND CERVICAL MICROBIOME. Alexa M. Sassin, MD,1 Diana Takashashi, BS, MS,2 Christina Megli, MD, PhD,1 Michael Jochum, PhD,3 Cecily Vauna Bishop, PhD,4 Jon D Hennibold, PhD,5 Kjersti M. Aagaard, MD, PhD1 Baylor College of Medicine, Houston, TX; 2Oregon Health and Science University (OHSU), Beaverton, OR; 3University of Pittsburgh Medical Center (UPMC) Magee-Women’s Hospital; 4Oregon National Primate Research Center, Oregon Health & Sciences University, Beaverton, OR; 5Oregon National Primate Research Center, Division of Reproductive & Developmental Sciences, Beaverton, OR.

OBJECTIVE: Polycystic ovarian syndrome (PCOS) is a prevalent endocrine disorder affecting the reproductive health of women. While the underlying causal mechanisms in PCOS are not fully elucidated, elevated testosterone (T; hyperandrogenemia) and an obesogenic diet contributes to its development. Given the endogenous microbiome may modulate fertility, we hypothesized these same microbiome communities may distinctly vary in structure and function in association with different aspects of PCOS etiology. To test this hypothesis, we leveraged a nonhuman primate (NHP) model to assess the individual effects of elevated T (PCOS levels), a high-fat, Western-style diet (WSD), and the combination of T+WSD on the microbiome community structure and function in these animals relative to controls (C).

MATERIALS AND METHODS: Rhesus macaque females (n=40) received subcutaneous implants of cholesterol (control; C) or T (serum T level ~1.4 ng/mL) and were fed either a low-fat control diet (CD; 14% fat) or a 36% fat WSD, resulting in four cohorts: 1) CD/C2) T+CD/3) C+WSD and 4) T+WSD (n=10/group). Oral, anal, rectal, cervical, and vaginal samples were collected at longitudinal time points to evaluate for changes during menses, follicular, and luteal phases of the menstrual cycle. Microbial DNA was extracted from all samples and rRNA amplicon sequencing of the V4 region of the bacteria-specific 16S RNA gene was sequenced on the Illumina platform. Customized bioinformatics pipelines were developed for longitudinal microbiome community and inferred functional analysis.

RESULTS: High quality microbial rRNA sequence datum (avg. 13,836 reads/sample) were obtained from each cohort. Permutational analysis of variance was computed. Analysis of the beta diversity of the microbial community revealed a significant difference in the anal (p=0.001) and combined vaginal and cervical microbiomes across each of the four cohorts (p=0.001). The C+CD (p=0.012) cohort was noted to have statistically distinct microbiomes.
at each phase of the menstrual cycle. However, microbiome differences amongst the three phases of the menstrual cycle were not significant in any of the treatment groups: T+CD (0.176), C+WSW (0.107) and T+WSW group (p = 0.278).

CONCLUSIONS: Treatment with chronic T, in both the absence and presence of WSD consumption, alters the community structure and function of the gut and lower reproductive tract microbiomes throughout the menstrual cycle. All variation between phases of the menstrual cycle was lost in each of the treatment cohorts (T+CD, C+WSW, and T+WSW), suggesting a potential interaction between the menstrual phase microbiome, hyperandrogenism, diet, and reproductive outcomes.

IMPACT STATEMENT: In primates, WSD feeding in combination with hyperandrogenemia is associated with menstrual cycle-specific alterations to the cervico-vaginal microbiome. These differences may directly contribute to the variation in fertility outcomes in PCOS patients. Given the independent involvement of WSD feeding, which is modifiable, there is the potential to modulate PCOS reproductive outcomes with beneficial dietary interventions.

SUPPORT: NIH/NICHD Women’s Reproductive Health Research program K12 HD103087, NICHD P50 HD071836 (NCTRI), P51OD011092 (ONPRC).

P-535 6:45 AM Wednesday, October 26, 2022

EVIDENCE FOR DIFFERENTIAL EFFECTS OF Δ9-THC (Δ9-TETRAHYDROCANNABINOL) ON PRE-VERSUS POST-IMPLANTATION EMBRYONIC STEM CELLS. Abigail D. Armstrong, M.D.; Gurugowtham Ulaganathan, B.S.; Roxane Verdikt, PhD; Patrick Allard, PhD; University of California, Los Angeles; University of California at Los Angeles.

OBJECTIVE: Recreational marijuana use is becoming increasingly widespread. With potential implications for fertility and embryonic development, we set out to evaluate the impact of THC exposure on the pre- and post-implantation embryo through embryonic stem cell proliferation, mitochondrial function and metabolism.

MATERIALS AND METHODS: Mouse embryonic stem cells (ESCs) can be differentiated into epiblast-like cells (EpiLCs) using known in vitro methods via growth factors and cytokines. ESCs recapitulate important features of pre-implantation stem cells; EpiLCs model post-implantation features of pre-implantation stem cells, mitochonndrial proliferation, mitochondrial function and metabolism.

RESULTS: In response to 10nM and 100nM Δ9-THC concentrations, ESCs demonstrated a biphasic dose-dependent proliferation response: low concentration THC increased proliferation, whereas high-dose THC increased apoptosis. These effects were not observed in EpiLCs. We demonstrated that these effects may be due in part to the differentiation of ESCs into EpiLCs, which are more susceptible to THC exposure.

CONCLUSIONS: Compared to untreated cells, Δ9-THC at low doses significantly increases proliferation in ESCs but not EpiLCs. We demonstrate evidence for metabolic differences underlying this unique proliferation response: ESCs represent pre-implantation cells, whereas EpiLCs model post-implantation cells, these data suggest an intriguing hypothesis that implantation may trigger a shift in endocannabinoid metabolism. Future work will be addressed toward clarifying these effects.

IMPACT STATEMENT: Although the impact of Δ9-THC on early developmental phenomena and programming is unknown, it is possible that Δ9-THC exposure may disrupt the metabolism and epigenetic machinery in germ cells. Given that cannabis is the most widely illicit drug used in the world, with increasing consumption in women of reproductive age, our work is relevant to understanding the basic action of cannabis on embryonic stem cells. Future research should investigate the transgenerational effect of marijuana use from in utero exposure.

SUPPORT: None

P-536 6:45 AM Wednesday, October 26, 2022

TESTOSTERONE TREATMENT NEGATIVELY IMPACTS THE REPRODUCTIVE POTENTIAL OF FIRST GENERATION FEMALE OFFSPRING CONCEIVED BY IN VITRO FERTILIZATION. Amanda R. Schwartz, MD; Min Xu, PhD; Cynthia Dela Cruz, PhD; Daniel Piau, PhD; Vasantha Padmanabhan, MS, PhD; Ariella Shikanov, PhD; Molly B. Moravek, MD; University of Michigan, Ann Arbor; University of Michigan, Ann Arbor, MI.

OBJECTIVE: The objective of this study was to examine in vitro fertilization (IVF) outcomes of first generation offspring conceived from oocytes with long-term testosterone (T) exposure versus control. We hypothesized that there would be no difference in outcomes.

MATERIALS AND METHODS: C57BL/6N female mice were implanted with silastic tubing with either 10 mg of T enanthate in ethanol (n = 9) or ethanol alone (n = 10) at 10 weeks. At 12-weeks post implantation, mice underwent ovarian stimulation with 0.2 ml intraperitoneal CARD HyperOva followed 48 hours later by 7.5 international units (IU) of intraperitoneal human chorionic gonadotropin (hCG) with collection of oocytes from vivids at 14 hours post hCG. Oocytes were fertilized and cultured to two-cell embryos, which were transferred into the oviducts of pseudopregnant recipient females to obtain first generation offspring. At 8 weeks, female offspring (n = 10) were stimulated by the same protocol with oocytes fertilized and cultured to blastocyst. Offspring were sacrificed for oocyte collection and terminal blood collected. For male offspring (n = 8), sperm was retrieved at 12-weeks and used to fertilize oocytes from 6-week female mice via a split fertilization method. Data were analyzed using Chi squared and unpaired t-tests with Prism 9.0.

RESULTS: Female offspring conceived with oocytes from T-treated mice had fewer oocytes retrieved (31.80 vs 63.00; p = 0.035), mature oocytes (22.80 vs 30.00; p = 0.050), 2 cell embryos (22.60 vs 30.00; p = 0.046), 4-8 cell embryos (22.40 vs 30.00; p = 0.043), morulas (22.20 vs 29.60; p = 0.036) and blastocysts (19.60 vs 27.00; p = 0.031) as compared to control offspring. There was no difference in individual ovarian weight (p = 0.061), maturity rate (p = 0.466), fertilization rate (p = 0.250) or hatching rate (p = 0.723). Female offspring from T-exposed oocytes had lower terminal anti-mullerian hormone (180.2 vs 236.6; p = 0.022) and progesterone (31.85 vs 56.05; p = 0.015) with no difference in terminal estradiol (54.4 vs 38.72; p = 0.110) or T levels (24.93 vs 32.06; p = 0.167). First generation male offspring from T-treated oocytes had no difference in fertilization rate (84.46 vs 87.55; p = 0.763), blastulation rate (71.71 vs 79.11; p = 0.558) or hatching rate (41.87 vs 46.15; p = 0.683) as compared to controls. Additionally, there was no difference in individual testis weight (p = 0.085), sperm concentration (p = 0.086) or sperm motility (p = 0.607) between male offspring from T-treated oocytes versus controls.

CONCLUSIONS: In a mouse model of gender-affirming hormone treatment, testosterone exposure had a detrimental impact on female offspring IVF outcomes with no change noted in male offspring.

IMPACT STATEMENT: Reproductive consequences of gender-affirming testosterone in transmasculine people are currently unknown with our mouse model suggesting a detrimental impact on female offspring. Further research is needed to determine whether these results are translatable to humans and whether effects are duration dependent or reversible with a period of testosterone cessation.

SUPPORT: This study was funded by National Institute of Health (NIH) R01HD098253-01.
decline remain unresolved. The ovary is a uniquely, heterogeneous organ comprised of many distinctive cell populations. The aim of this study was to spatially resolve the transcriptomic landscape of murine ovaries against the natural aging process.

**MATERIALS AND METHODS.** Ovaries were retrieved from Young (3-4 months; n=4) and Aged females (15-16 months; n=4) and fixed for HE&imaging and spatial transcriptomic analysis utilizing the 10X Genomics Visium Gene Expression Slide and transcriptome sequencing per manufacturer’s instructions. After sequencing, feature barcode matrices and tissue images were uploaded into R and processed using Seurat version 4.0.2. Cluster proportion differences were calculated using Fisher Exact Test followed by Benjamini-Hochberg p-value adjustment. Statistical significance for differential expression was defined by an adjusted p-value ≤ 0.05, a log fold change ≥1 or ≤-1, and ≥75% of spots in one group (pct.1 or pct.2) expressing the gene.

**RESULTS:** In total, we defined eight main ovarian cell populations, which were then further broken down into unique sub-clusters by gene expression. All clusters were characterized by significant changes to their transcriptomic landscape between young and aged samples, indicating that early onset aging affects all ovarian compartments. Differential analysis revealed that many pathways implicated in other age-related diseases, including Sirtuins Signaling and mTOR Signaling, are similarly dysregulated during ovarian aging. Further analysis of sub-cluster populations elucidated, for the first time, separate transcriptomes for distinctive granulosa cell sub-populations found in young and aged mice and morphologically identified them as the inner and outer granulosa cells based on their proximity to the oocyte. Cell-type specific spatial gene changes in granulosa cells associated with the disruption of inhibins, activins, and gap junction activity. Interestingly, four oocyte sub-cluster populations were uncovered, but only three were represented by aged ovaries.

**CONCLUSIONS:** Overall, this study provides analysis of mammalian ovarian aging using spatial transcriptomics to achieve deeper understanding of the localization and cell-population-specific mechanisms underlying age-related fertility decline. This is the first time spatial transcriptomic technology has been utilized to study mammalian ovarian biology, and the effect of aging on ovarian function and processes. Our study confirms that ovarian aging has widespread repercussions on gene expression and reveals age-related changes unique to various ovarian compartments in vivo.

**IMPACT STATEMENT:** This study provides novel insight to the relationship between distinct ovarian cell populations, ovarian aging; granulosa cells, and follicle development that may aid in the advancement of therapeutic intervention for advanced maternal age women.

**SUPPORT:** None

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**P-359**


**OBJECTIVE:** Ovarian aging associates with a decline in the number and quality of oocytes, which is related to mitochondrial dysfunction and decreased mitochondrial DNA (mtDNA) copies, playing oxidative stress a crucial role in age-related infertility. New therapies based on Platelet-rich plasma (PRP) and stem cell (SC) secreted factors have been employed to improve ovarian function in several animal models of ovarian damage. However, how these treatments regulate ovarian mitochondrial function and oocyte quality has not yet been assessed in age-related infertility models mimicking different stages of women’s reproductive life.

**MATERIALS AND METHODS:** Young (8-week-old, n=12), Advance Maternal Age (AMA, 28-week-old, n=12), and Old (36-week-old, n=12) NOD/SCID females were randomized to receive an intraovarian injection (10 μL/ovary) of saline (control group), activated PRP (PRPa), or activated plasma rich in BMDCS- and platelet-secreted factors (SC-PRPa). Seven days later, animals underwent ovarian hyperstimulation and sacrifice to collect metaphase-II (MII) oocytes and ovaries. Ovarian mtDNA copy number was assessed by qPCR, oxidative damage by immunohistochemistry for the lipid peroxidation product 4-hydroxynonenal (4-HNE), and oocyte quality was evaluated analyzing spindle formation and chromosome disposition.

**RESULTS:** Treated samples in the young mice did not show differences between groups, suggesting the absence of deleterious effects when treatments were administered.

In the AMA condition, SC-PRPa ovarian injection increased mtDNA copy number compared to control (mtDNA/nDNA ratio ND1: control 0.8±0.0, PRPa 1.0±0.2, SC-PRPa 1.3±0.4; p<0.05). Indeed, SC-PRPa also improved spindle assembly (Control 16%, PRPa 37%, SC-PRPa 44%), spindle angle (Control 109°±37° μm, PRPa 213°±38° μm, SC-PRPa 239°±36.9° μm, p=0.013) and reduced aneuploidy misalignment (Control 79%, SC-PRPa 58%, SC-PRPa 59%) in recovered MII oocytes.

In the old mice, the effects of SC-PRPa on mitochondria were even higher as the amount of mtDNA increased by up to 75% (ND1: control 0.9±0.0, PRPa 1.2±0.1, SC-PRPa 1.5±0.6; COX3: control 0.7±0.0, PRPa

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**P-358**

**6:45 AM Wednesday, October 26, 2022**

**MITOCHONDRIAL FUNCTION AND OOCYTE QUALITY IMPROVED IN AN AGING MODEL BY INTRAVARIAN ADMINISTRATION OF A COMBINATION OF STEM CELL-SECRETED- AND PLATELET-ENCLOSED GROWTH FACTORS.** Maria Marchante Cuevas, M.Sc.,1 Jessica Martinez Carmona, B. Sc.,2 Anna Buigues, PhD,1 Noelia Ramirez Martin, M.Sc.,4 Antonio Pellicer, M.D.,5 Sonia Herraiz, Ph.D.6 1Valencia, Valencia, Spain; 2IVI Foundation - University of Valencia, Valencia, Spain; 3IVI Foundation, Valencia, Valencia, Spain; 4IVI Foundation-IIS La Fe, Valencia, Spain; 5Instituto Valenciano Infertilidad (IVI), Rome, Italy; 6IVI Foundation - IIS La Fe, Valencia, Spain.

**OBJECTIVE:** Different approaches have been proposed to reactivate the ovarian function and increase the reproductive potential of patients with impaired ovarian reserves. However, a more efficient, feasible and non-invasive ovarian reactivation techniques without stem cell infusion.

**MATERIALS AND METHODS:** Young (3-4 months; n=12), Advanced pre-antral (Control: 25±2; SC-PRP: 56±21%; w/o THBS1: 25±3) when compared to controls (p<0.049 and p=0.049, respectively). These beneficial effects were not observed in POI mice treated with THBS1-depleted plasma, in which follicle counts were similar to controls and lower than in SC-PRP group (p=0.049 and p=0.046, respectively).

Indeed, the number of ovulated MI-oocytes (Control: 22±2; SC-PRP: 71±24%; w/o THBS1: 27±6) and folliculogenesis (Control: 25±2; SC-PRP: 56±21%; w/o THBS1: 25±3) when compared to controls (p<0.049, p=0.046, respectively), but did not after treatment with THBS1-depleted plasma, with a statistically significant reduction of both parameters compared to SC-PRP group (p=0.049 in both cases). However, blastocyst formation rates after in vitro culture were not different between groups (Control: 25±35%; SC-PRP: 30±21%; w/o THBS1: 21±36%).

**CONCLUSIONS:** THBS1 depletion from SC-PRP plasma suppressed its regenerative effects on chemotherapy-damaged mouse ovaries.

**IMPACT STATEMENT:** Our findings suggest that THBS1 has a crucial role in the regenerative effects of SC-PRP plasma, promoting follicle growth and stroma regeneration. To validate these findings by direct THBS1 administration in POI models would allow to develop more efficient and non-invasive ovarian reactivation techniques without stem cell infusion.
CHARACTERIZATION OF THE PROTEIN CONTENT OF PLATELET RICH PLASMA (PRP) AND A COMPARATIVE ANALYSIS OF DIFFERENCES AMONG TWO STRAINS OF MICE: IMPLICATIONS FOR REGENERATIVE MEDICINE. Yagmur Ergun, MSc,1 Cem Demirkiran, MD,1 Razye Melike Yildirim, MD,1 Murat Basar, Ph.D.,1 Emre Sel, MD1; 1Yale School of Medicine, New Haven; 2Yale School of Medicine. OBJECTIVE: Platelet Rich Plasma (PRP) is the plasma portion of the blood rich in platelets. Platelets produce a large number of clotting factors, cytokines, growth factors, and enzymes, which play key roles in the healing processes of the body. PRP has been utilized as a regenerative substance in orthopedics and plastic surgery. Injection of autologous PRP has been studied as a potential stimulating agent for follicular growth in women with poor ovarian response (POR) and primary ovarian insufficiency (POI), and to induce endometrial growth in women with endometrial hypoproliferation. Despite increasing utilization, the protein content of PRP preparations and differences between individuals remain poorly characterized. In this study, we aimed to determine the protein content of PRP prepared from two different strains of mice to characterize the protein landscape and to evaluate how genetic background may affect PRP content.

MATERIALS AND METHODS: Experiments were conducted in 2-month-old CD1 and C57BL/6 female mice (n=3 for each strain). Blood samples (1 ml) were collected under anesthesia by cardiac puncture into a syringe containing 0.5M EDTA to prevent coagulation. Blood was then centrifuged at 1500 rpm for 8 minutes. Plasma was isolated and transferred into another tube and centrifuged again at 2000 rpm for 15 minutes. One third of the plasma volume from the bottom containing the platelets was stored at -80°C. Samples were sent to Yale University Mass Spectroscopy & Proteomics Resource for protein profiling and quantitation. For statistical analysis, Student’s t-test was used.

RESULTS: Based on the absence/presence profile, 241 proteins were identified in both C57BL/6 and CD1 mice, while an additional 56 proteins were identified only in C57BL/6 and 26 proteins only in the CD1 strain. For most proteins found in both strains, expression levels were not different between CD1 and C57BL/6 mice: hepatocyte growth factor (HGF) (6.3±1.0 vs 5.0±0.76), vascular endothelial growth factor (VEGF) (2.1±0.2 vs 2.0±0.6, p=0.44), leukemia inhibitory factor (LIF) (30.0±2.0 vs 26.6±2.96, p=0.82), interleukin 1 receptor (IL1R) (6.3±0.3 vs 8.6±0.88, p=0.06). Quantitative analysis revealed that 21 proteins were higher in CD1 mice and 33 proteins were higher in C57BL/6 mice. Indeed, PRP from CD1 mice contained significantly a higher amount of insulin-like growth factor (IGF) compared to C57BL/6 (14.6±0.3 vs 11.3±0.6, p<0.01), while PRP from C57BL/6 mice had higher amount of EGF-containing fibulin like extracellular matrix protein (4.3±0.8 vs 3.0±0.5, p=0.05) and pregnancy zone protein (477±0.88 vs 398±9.71, p<0.05).

CONCLUSIONS: Our findings demonstrate that some of the growth factors and cytokines that play key roles in ovarian and endometrial biology are abundant in PRP. We also find that protein profile and quantity may differ between different mouse strains. IMPACT STATEMENT: PRP contains a large number of growth factors and cytokines that could affect follicle growth and endometrial proliferation. However, individual differences may exist and should be characterized when using autologous PRP injections.

E-POSTER ABSTRACT STATION: W11

P-541 6:45 AM Wednesday, October 26, 2022

MITOCHONDRIAL STRESS RESPONSE GENE CLPP IS REQUIRED FOR OOCYTE FUNCTION AND FEMALE FERTILITY. Yagmur Ergun, MSc, Aysegul Gizen Imamoglu, MD, Mauro Cozollolo, MD, Cem Demirkiran, MD,1 Murat Basar, Ph.D.,1 Emre Sel, MD1; 1Yale School of Medicine, New Haven; 2Yale School of Medicine, New Haven, CT; 3Yale Medical School; 4Yale School of Medicine.

OBJECTIVE: Caseinolytic Protease Prolyl cysteine Subunit (CLPP) is a protease responsible for the degradation of misfolded mitochondrial proteins. CLPP is activated at the time of cellular metabolic stress and helps maintain homeostasis. The aim of the study was to determine the role of CLPP in female reproductive competence and senescence using a mouse model with oocyte-specific Clpp deletion.

MATERIALS AND METHODS: Mice with oocyte-specific deletion of Clpp were generated by mating Clpp flox/flox female mice with Clpp flox/flox Zp3-Cre male mice. In all experiments, adult (2-, 6-, or 9-month-old) oocyte-specific Clpp knockout (Clpp KO) female mice were compared to wild-type (WT). To assess fertility, female mice from each group (n=5) were mated with adult WT males of proven fertility for 12 weeks. The ability to generate oocytes (germinal vesicle [GV]) was assessed 48 hours after injection with PMSG (10IU). Follicle development was assessed in ovaries from Clpp KO and WT mice after fixation, paraffin embedding, and sectioning, followed by hematoxylin and eosin (H&E) staining. ATP levels were determined by a Bioanalyzer ATP detection assay (Agilent, Waltham, MA). The expression of electron transport chain and mitochondrial unfolded protein response genes was evaluated with qRT-PCR. Student’s t-test was applied for comparison.

RESULTS: Clpp KO female mice had decreased fertility compared to WT (7.2±1.98 vs 14.40±1.66, p<0.05). 2-month-old and 6-month-old female Clpp KO had a similar number of primordial, primary, secondary, early antral and antral follicles compared to WT, and the number of GV stage oocytes they produced was not significantly different (44±2.8 vs 52.3±1.8 (p=0.05) and 28±5.0 vs 38.6±0.8 (p=0.1), respectively). However, at 9 months of age, the number of GV oocytes produced was significantly lower in Clpp KO female mice compared to WT (26±5.5 vs 44±1.2; p<0.05). In addition, targeted deletion of Clpp in oocytes caused several functional and metabolic abnormalities. Clpp KO oocytes showed significantly lower ATP production (0.52±0.41 vs 1.95±1.96, p<0.05); and decreased expression of electron transport chain genes Uqcr10, Ndufs5 and Atp6a1 (6.3±1.07 vs 1.03±2.06 (p<0.05), 5.9±1.18 vs 1.05±0.21 (p<0.001), and 6.0±1.18 vs 1.01±0.21 (p<0.05), respectively). Clpp KO oocytes also showed significantly lower expression of mitochondrial unfolded protein response genes DnaJA3, and Hspa1 (21.88±1.83 vs 1.01±0.15 (p<0.001); 7.4±1.14 vs 1.12±0.3 (p<0.001); respectively).

CONCLUSIONS: Our findings demonstrate that lack of Clpp causes metabolic and functional abnormalities in oocytes, and results in decreased female fertility. IMPACT STATEMENT: Mitochondrial stress response plays a key role in female fertility. Whether this pathway can be exploited as a diagnostic target or to improve human reproductive efficiency will need to be further investigated.

P-542 6:45 AM Wednesday, October 26, 2022

TOWARDS AN EXPLAINABLE ARTIFICIAL INTELLIGENCE TO PREDICT BLASTOCYST FORMATION POTENTIAL FROM SINGLE OOCYTE IMAGES. Roberto Valencia, MSc, PhD,1 Adolfo Flores Saifee Farias, MSc, Ph.D.,2 Gerardo Mendizabal, Ph.D.,3 Alejandro Chavez-Badiola, MD,4 Fatima Judith Acosta Gomez, Student1, IVF 2.0 LTD, Maghull, United Kingdom; 2IVF 2.0 Limited, London, London, United Kingdom; 3Universidad de Guadalajara.

OBJECTIVE: To assess the association between the size and shape of the oocyte cytoplasm and polar body with blastocyst formation using a machine learning-based automated feature extraction tool.

MATERIALS AND METHODS: For the training phase we used a database containing 500 images of oocytes and their corresponding segmentation of the cytoplasm and polar body identified by a gynaecologist. This database was used to train a deep learning model to automatically identify
both structures. The model was based on U-Net architectures using data augmentation, over 100 epochs and a learning rate of 0.001.

A test set with 100 images with known age group at the time of oocyte retrieval (group1: ≤ 37, group2: > 37) and its blastocyst formation result, uniformly distributed (i.e., half of each age group and half with blastocyst formation in each group). The blastocyst and PB of the test set were first identified by the previously trained model and rescaled to match 1 micrometer per pixel. Subsequently, with the Python skimage library, we compute the major and minor diameters, area, and eccentricity for both the blastocyst and the PB. The above features were pooled and differences between outcomes and age groups were tested using the Mann-Whitney U test.

RESULTS: Segmentation training obtained an accuracy of 0.98 and 0.99 for blastocyst and PB, respectively. We compared positive versus negative blastocyst formation in age group 1, in age group 2, and at all ages (Table 1). We can observe that there is a significant difference in the greatest diameter of the blastocyst, the area of the cytoplasm and the eccentricity of the PB in age group 1 but not in age group 2 or in all ages.

CONCLUSIONS: The presented tool is an automatic feature extraction for oocytes and is useful for future research. Our findings corroborate other investigations on the size and shape of both the blastocyst and the PB as a factor influencing blastocyst formation and which change according to the age of the oocyte.

IMPACT STATEMENT: Automatic feature extraction tools can standardize feature extraction methods, increase the explainability of machine learning models, and are a relevant tool for future research.

SUPPORT: IVF 2.0 Limited.
to EEC compared to BAP-ESC. Surprisingly, cells are more readily clustered by each model (BAP-ESC, TSC, and EEC) rather than the cell types (CTB, STB, and MTB/EVT), suggesting that neither BAP-ESC nor TSC can faithfully represent peri-implantation stage human trophoblast cells. Transcriptome analysis showed male and female trophoblast cells were observed, highlighting genetic background differences contributes to the placental trophoblast development. For example, several significantly down-regulated pathways in male STB from BAP-TSC are heavily implicated in trophoblast invasion including ECM-receptor interaction, regulation of actin skeleton, focal adhesion, cell adhesion molecules, and axon guidance.

CONCLUSIONS: This study is the first comprehensive characterization of the early placental transcriptome employing different cell types from three trophoblast models, highlighting similarities and differences between models and sexes. Therefore, the difficulty and inaccuracy of analyzing the existing dataset from different platforms was eliminated. Further detailed comparisons between cell models, cell types, and sex, will provide a more comprehensive understanding of early placentaation in human.

IMPACT STATEMENT: This study allows us to better understand how different trophoblast models can be utilized to answer important questions related to human implantation, providing possible solutions to address complications such as recurrent implantation failure, miscarriage, preeclampsia, and intrauterine growth restriction.

REFERENCES:

P-545 6:45 AM Wednesday, October 26, 2022
VITRIFICATION WITH DIMETHYL SULFOXIDE (DMSO) CRYOPROTECTANT ALTERS GENE AND TRANSPOSABLE ELEMENT (TE) EXPRESSION IN HUMAN OOCYTES. Ashley M. Wiltshire, MD,1 Renata Fioravanti Schaal, MD,1 Fang WANG, PhD,1 Tiffany Tsou, BS,1 Wilson McKerrow, PhD,1 David L. Keeve, MD1 New York University, New York, NY;2NYU Langone Health, New York, NY;3NYU Langone Medical Center, New York, NY.

OBJECTIVE: DMSO alters the epigenetic state of mouse oocytes and human cultured cells. The effect of vitrification with DMSO containing cryoprotectant on gene and TE expression in human oocytes is unknown.

MATERIALS AND METHODS: A prospective paired controlled cohort laboratory study was performed from February - June 2021. Twenty-four discordant oocytes in the germinal vesicle (GV) stage were donated from four patients. All oocytes were paired such that half of the oocytes from each patient were vitrified with DMSO-containing cryoprotectant, while the other half were frozen, unexposed to DMSO. All oocytes underwent RNA sequencing via Switching Mechanism At the end of the 5′-end of the RNA Transcript sequencing 2 (SMARTseq2). Reads containing adapters, bases that could not be determined >10% and low quality reads were excluded. Gene mapping to the human reference genome, followed by gene quantification, were performed. Next, differential gene expression analysis between the two cohorts was performed. Then functional enrichment analyses of dysregulated gene sets were performed with Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEOG), and Human Disease Ontology (DO). Raw data obtained from RNA sequencing was used to analyze TE transcript using the BonaFide-TEseq method, which were mapped to specific TE loci using Software for Quantifying Interspersed Repeat Expression (SQUIRE), to identify differentially expressed TEs. Real-time-qPCR validated results of selected genes and TEs.

RESULTS: Of the 27,837 genes identified by SMARTseq2, 7,331 (26.3%) were differentially expressed (p<0.05). Specifically, 3,987 genes were upregulated and 3,344 genes were downregulated in oocytes exposed to DMSO. Genes involved in chromatin and histone modification, and mitochondrial function, as well as WNT, insulin, MTOR, HIPPO and MAPK signaling pathways were affected by DMSO. There was no significant over expression of human disease ontology terms within our data set. Expression of a number of TEs was also affected by exposure to DMSO, including Alu, endogenous retrovirus family members 1 and K (ERV1, ERVK) and long interspersed nuclear elements 1 (LINE-1). Notably, the effects of DMSO on TE expression were most pronounced in the oldest patient. The expression of TEs was negatively correlated with age, and the expression of PIWI-like protein 2 (PIWIL2), DNA Methyltransferase (DNMT) 3A and 3B.

CONCLUSIONS: Vitrification with DMSO exposure leads to significant changes in gene and TE expression in human GV oocytes. Future experiments should determine whether MII oocytes respond similarly.

IMPACT STATEMENT: Oocyte vitrification with DMSO containing cryoprotectants induces significant transcriptome changes, including those involving TEs, in human GV oocytes. Further studies are needed to evaluate the clinical significance of these findings.

SUPPORT: This study was supported by the Stanley H Kaplan Fund.

P-546 6:45 AM Wednesday, October 26, 2022
ASSESSMENT OF TELOMERE PARAMETERS IN SHORT-TERM CULTURES OF GRANULOSA CELLS. Lucía Chico Sordo, MSc,1 Elena Martínez-Iglesias, BSc,1 Alba M. Polonio, M.Sc,2 Isabel Cordova-Oriz, MSc,1 Marta Medrano, BSc,1 Juan A. García-Velasco, MD, PhD,3 María Elisa Varela Sanz, PhD1 1IVI Foundation, IIS La Fe, Valencia, Spain;2Valencia, Valencia, Spain;3IVI Foundation, IIS La Fe, Rey Juan Carlos University, Madrid, Spain.

OBJECTIVE: The primordial follicles are formed by an oocyte arrested in meiosis surrounded by a layer of flattened cells called granulosa cells (GCs). During follicular development to preantral stage, GCs acquire a cuboidal shape and proliferate forming multiple layers, ensuring oocyte maturation, mediated by a cross-talk between the two cell types. Interestingly, these somatic cells have some common characteristics with stem cells, such as long telomeres and telomerase activity, which will ensure the potential for multiple divisions. The aim of this work is to evaluate telomere maintenance of GCs short-term culture in different media (A199 and DMEM), and the effects of follicular fluid (FF), which contains estrogens, known telomerase activators.

MATERIALS AND METHODS: During oocyte retrieval, GCs of seven healthy donors (25.14 years old) were separated from the FF. These cells were isolated using a Ficoll gradient, and cultured in the presence and absence of FF using two different culture medium: A199 and DMEM. All medium was supplemented with 15% fetal bovine serum, 25 nmol HEPES and 1% penicillin-streptomycin. Telomere length (TL) was measured by H-TqFISH, and TRF1 protein levels (to assess telomere protection) were measured by immunofluorescence.

RESULTS: A short-term culture protocol for GCs (for 4 days) in the absence and presence of FF has been established and tested to evaluate telomere parameters. Initially, GCs showed round morphology and during culture they adhered to the plate. In the absence of FF, GCs acquired fibroblast-like morphology and adhered strongly to the culture dish. However, in the presence of FF in the medium, GCs maintained their round morphology and were weakly attached to the culture dish. The short-term culture of GCs in the absence of FF maintained the TL of these cells for 4 days, with no statistically significant differences between the medium used. The addition of FF initially decreased the TL of GCs, for a subsequent increase on day 4 with respect to day 1 (p=0.0023 in A199 medium and p=0.0262 in DMEM). TRF1 levels were significantly higher in both A199 and DMEM culture medium supplemented with FF. This statistically significant difference was maintained for all four days of culture in A199 and DMEM medium.

CONCLUSIONS: There is no difference in the short-term culture of GCs between A199 and DMEM medium regarding morphology neither telomere parameters. The addition of FF to the culture medium caused a significant increase in TL on day 4 compared to day 1, and TRF1 levels of GCs were increased, which is also a shared characteristic with stem cells. Further studies are needed to evaluate the clinical significance of these findings.
THE IMPACT OF SODIUM BICARBONATE CONCENTRATION AND MEDIA pH ON MOUSE PREIMPLANTATION EMBRYO DEVELOPMENT. Heather Rogers, MSc,1 William B. Schoolcraft, MD,1 Ye Yuan, PhD,1 Jason E. Swain, PhD, HCLD2 1Colorado Center for Reproductive Medicine, Lone Tree, CO; 2CCRM Fertility, Lone Tree, CO.

OBJECTIVE: The pH of culture media is thought to impact embryo development. However, as pH is set via the equilibrium between CO2 and bicarbonate, isolating pH as the sole variable can be difficult. Improving preimplantation embryo development via optimizing bicarbonate concentration, bicarbonate concentration and pH of the culture media may help further improve culture conditions. To begin to investigate each variable’s individual impact on mouse embryo development, the impact of an increased sodium bicarbonate concentration in the culture medium on embryo development was explored. It is hypothesized that increased bicarbonate levels may improve embryo growth by meeting the increased metabolic demand during development when proper environment pH is maintained.

MATERIALS AND METHODS: Four replicates of in vivo matured oocytes were collected from CF-1 mice following PMSG and hCG stimulation and fertilized in vitro. Fertilization was confirmed by the presence of two pronuclei (2PN). 2PN selected embryos were divided into three treatments of in-house culture media with 20mM (N=96), 25mM-control (N=96), and 30mM (N=96) bicarbonate concentrations and cultured in an Embryoscope™ for 115 hours at 7.5% CO2 and 6.5% O2 (equivalent to 6% CO2 and 5.0% O2 at sea level). The pH of the culture media measured at 7.24, 7.34, and 7.54, respectively. The cleavage rates, Day 4 blastocyst rates, and Day 5 hatching blastocyst rates were recorded and analyzed using a chi-squared analysis. The morphokinetic timings of cleavage, start of compaction, blastocoe formation, blastocoeel reaches 50% of embryo, expansion, and hatching were recorded. All embryos that reached at least the full blastocyst stage were fixed and stained for SOX2 and CDX2 for cell counts. The morphokinetic and cell count data was tested for normality using the Shapiro-Wilk test. The data did not meet the assumption of normality; therefore, the Kruskal-Wallis non-parametric test was used to compare morphokinetic timings and ICM/TE ratios between treatment groups.

RESULTS: The Day 4 blastocyst rates and Day 5 hatching blastocyst rates between all treatments showed no significant difference (p>0.05). The morphokinetic timing for each development stage was not significant between treatments (p>0.05). Finally, the ICM/TE ratio of Day 5 blastocysts did not differ between the three treatments.

CONCLUSIONS: We demonstrated that differing bicarbonate concentrations and subsequent changes in pH of the culture media did not result in a significant difference in mouse preimplantation embryo development. Additional experiments will need to be conducted to demonstrate the individual impact of bicarbonate concentration and pH to determine if these two changes are acting as confounding variables and masking their true effect on embryo development.

IMPACT STATEMENT: Determining the ideal complement of bicarbonate concentration in culture media, CO2 incubator concentration, and culture media pH for preimplantation embryo development will improve clinical in vitro fertilization success rates.

THE IMPACT OF DEHYDROEPIANDROSTERONE SULFATE (DHEAS) ON THE TROPHOBLAST-DERIVED PRODUCTION OF STEROID HORMONE INFLUENCED METABOLITES AT THE SITE OF HUMAN IMPLANTATION. Arthi Taggar, M.D., M.PH.1 Maheshwor Thapa, Ph.D.2 Minghao Gong, Ph.D.3 Anahita Amiri, Ph.D.4 Daniel R. Grow, MD, MHCM, Shuzhao Li, Ph.D.2 Paul Robson, Ph.D.3 1The Jackson Laboratory for Genomic Medicine, University of Connecticut Health Center, Farmington, CT; 2The Jackson Laboratory for Genomic Medicine, Farmington, CT; 3University of Connecticut Health Center, Farmington, CT.

OBJECTIVE: The moments of human embryo implantation and the surrounding uterine environment have been often elusive to research methods but have significant implications for discovering possible early interventions and treatment opportunities. By deriving a trophoblast model from human induced pluripotent stem cells (hiPSCs) comparing a CYP19A1 gene knock-out (KO) cell line to a wild type (WT) cell line, we aim to use metabolomic technology to phenotype primitive syncytiotrophoblast cells (PSTd) under the influence of DHEAS with and without the aromatase enzyme.

MATERIALS AND METHODS: Undifferentiated KOL2F (WT) hiPSCs were maintained in culture on tissue culture treated plates in incubators at 37°C and 5.0% CO2. Differentiation of hiPSCs to trophoderm cells was begun one day after isolated single cell passages. The hiPSC culture medium was replaced with PrSynT differentiation medium. Complete differentiation was achieved on day 6, at which time the cells reached syncytialization. DHEAS was added to the experimental wells on day 6. The culture media and cells were collected 24 hours after being cultured in experimental versus control conditions. The supernatant media was flash frozen in nitrogen and stored at -80°C. The cells were washed, lifted, centrifuged and then were flash frozen in nitrogen and stored at -80°C. A metabolic analysis on the cell pellets was then performed. Metabolites were extracted using a biphasic extraction protocol. Methanol was used for polar molecules, and methyl tert-butyl ether was used for non-polar molecules with isotope labelled spike-in controls. Samples were analyzed by ultra-high performance liquid chromatography-mass spectrometry. Metabolite features were analyzed using Compound Discoverer v3.3 and in-house scripts.

RESULTS: 433 metabolites were significantly different across the two cell line groups in culture conditions with and without DHEAS treatments (one-way ANOVA; false discovery rate <0.05). These differences prominently featured estrogen metabolites. The most abundant differences were estrone glucuronide, estradiol-17beta, dihydroxy cortisol. The p-values on respective independent samples t-test for those metabolites were <0.01, <0.01, and 0.04, respectively. Pathway analysis indicates the CYP19A1 KO perturbs multiple metabolic pathways including androgen and estrogen biosynthesis and metabolism, C21-steroid hormone biosynthesis and metabolism, branched chain amino acid degradation, as well as fructose and mannose metabolism.

CONCLUSIONS: The level of metabolite and metabolomic pathway detail that we demonstrate in this context has not been explored before. Additionally, the findings emphasize the combined comprehensive phenotyping capabilities of metabolomic analysis with varying complex media supplementation for KO lines encompassing biological pathways active in the PrSynT.

IMPACT STATEMENT: The application of metabolomics shown here has exponential promise in uncovering previous inaccessible, and clinically applicable, answers about the impact of genetic and micro-environmental alterations on the implanting human embryo.
heteroplasmy transmission, the rate of de novo mutations, the role of mitochondrial dysfunction in infertility, and the technical challenges that exist towards better understanding mtDNA heteroplasmacy transmission to the preimplantation embryo.

RESULTS: Advancements in deep-sequencing technology have shed light on the nature of mtDNA heteroplasmacy. From large-scale studies in healthy humans, it has been found that 90% of healthy adults are heteroplasmic in at least one site, at allele frequency of >1%. It has also been shown, with maternal-offspring studies, that mothers transmit variable mutant loads to offspring due to a severe germline bottleneck that can be as low as 10 mtDNA segregating units. Furthermore, studies in the zebrafish female germline have shown that at least one de novo mutation (with heteroplasmacy >1.5%) was present in 20% of mature oocytes. A study in the human female germline found that 26.9% of tested oocytes carried de novo mutations. Both studies found the rate of de novo mutations to be similar to the error rate of PolG. To our knowledge, there are no studies that have looked at heteroplasmacy levels and de novo variation in preimplantation embryos. The technical challenges that whole genome amplification introduces (uneven coverage bias of Prostaglandin E1 Alcohol (Selective PTGER 4 receptor agonist), or of 17-phenyl trinor Prostaglandin E2 (Selective PTGER 1 receptor agonist)) remain a limiting factor. We hypothesize that it is through a direct effect of the agonist’s cAMP generation or other secondary intracellular messengers.

CONCLUSIONS: Similar to the PGE2-induced increased PAI-1 level in media of cultured endothelial cells, activation of PTGER1 and PTGER2 also increased PAI-1. Further studies are needed to assess whether this is through a direct effect of the agonist’s cAMP generation or other secondary intracellular messengers.

IMPACT STATEMENT: This is the first study to delineate how PGE2 stimulates the plasminogen activator inhibitor system, potentially affecting the clotting cascade in the menstrual cycle. Previous studies have shown a difference in PAI-1 levels between NMB, and heavy menstrual bleeding women exposed to PGE2. We hypothesize that it is through this pathway lies a difference in the pathophysiology of menstruation.

SUPPORT: This study was funded by the Jones Foundation grant.

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E-POSTER ABSTRACT: W12

P-551 6:45 AM Wednesday, October 26, 2022

VARIATION IN ENDOMETRIAL STROMAL STEM CELL NUMBER THROUGHOUT THE SECRETORY PHASE. Dimitar Parvanov, PhD, Rumiana Ganeva, MSc, Margarita Ruseva, MSc, Maria Handzhıyiska, MSc, Nina Vidolova, MSc, Dimitar Metodiev, M.D., Georgi Stameno, MD/PhD Nadezhda Women’s Health Hospital, Sofia, Bulgaria.

OBJECTIVE: It is well known that in human endometrial stroma the number of certain immune cell types and senescent cells fluctuates during the menstrual cycle. The observed change of the cellular profile is associated with the tissue remodeling during the window of implantation, occurring in the mid-secretory phase. This process is crucial for successful apposition, adhesion and invasion of the embryo. It has been suggested that the percentage of stem cell types, such as CD140b+CD146+ is constant at different menstrual cycle stages. However, the quantity of other stem cell types during the secretory phase has not yet been studied.

The purpose of this study was to analyse the variation of endometrial stem cells in human endometrial stroma throughout the secretory phase.

MATERIALS AND METHODS: This observational study was performed between July 2020 and January 2022. Endometrial samples of 181 women undergoing in-vitro fertilization were collected 3 days (LH+3) (n=17 patients), 4 days (LH+4) (n=16 patients), 5 days (LH+5) (n=20 patients), 6 days (LH+6) (n=19 patients), and 7 days (LH+7) (n=109 patients) after LH surge. The samples were subjected to immunohistochemical staining with antibodies against NOTCH1 (E-AB-12815, Elabscience) and CD117 (CD117/c-Kit/SCF-Receptor) (RB-9038-RQ, Epredia), to identify stem cells in the tissue sections was evaluated by Image-J software. Statistical analysis was performed by SPSS software (version 21). The normality of the variables was assessed using the Shapiro-Wilk test. The association between the stem cell percentages and the day of the menstrual cycle was analysed by Spearman correlation test.

RESULTS: Mean NOTCH1-positive cells percentage on days LH+3, LH+4, LH+5, LH+6 and LH+7 were 0.036±0.006%, 0.069±0.007%, 0.241±0.052%, 0.246±0.037% and 0.323±0.093%, respectively. Mean CD117-positive cells percentage on days LH+3, LH+4, LH+5, LH+6 and LH+7 were 0.036±0.006%, 0.069±0.007%, 0.241±0.052%, 0.246±0.037% and 0.323±0.093%, respectively.

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Table 1. Plasminogen Activator Inhibitor-1 (PAI-1) in response to of prostaglandin E2 and prostaglandin-E2 receptors (PTGER) 1 through 4 and in Human Endometrial Endothelial Cells from normal bleeding (NMB) (n=4)

<table>
<thead>
<tr>
<th>Control</th>
<th>PGE2</th>
<th>DMSO</th>
<th>PTGER1</th>
<th>PTGER2</th>
<th>PTGER3</th>
<th>PTGER4</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NMB (Mean ± SD)</td>
<td>81.09 ± 27</td>
<td>193.08 ± 60.7</td>
<td>74.99 ± 38.7</td>
<td>209.63 ± 57.9</td>
<td>187.43 ± 60.5</td>
<td>110.80 ± 43.2</td>
<td>111.87 ± 22</td>
</tr>
</tbody>
</table>

FERTILITY & STERILITY®
**P-552** 6:45 AM Wednesday, October 26, 2022

**ENDOMETRIAL ADHESION G-PROTEIN COUPLED RECEPTOR EXPRESSION IS ALTERED BY OVARIAN STIMULATION.** Nischelle R. Kalakota, MD, MS,1 Alexander Lemenche, PhD,1 Andy Babwah, B.A.A., PH.D.,2 Nataki C. Douglas, MD, PhD1 Rutgers New Jersey Medical School, Newark, NJ; 2Rutgers Robert Wood Johnson Medical School, New Brunswick.

**OBJECTIVE:** Ovarian stimulation (OS) is associated with altered endometrial histological development and gene expression which may impact receptivity in fresh embryo transfers. We sought to determine the effect of OS on the expression of endometrial genes encoding adhesion G protein-coupled receptors (ADGRs). While ADGRG2 has been identified as a regulator of human endometrial decidualization and receptivity, less is known regarding the roles of other ADGRs in the human endometrium. We hypothesized that in a natural cycle (NC) ADGRs are expressed in the secretory endometrium but following OS their expression is altered.

**MATERIALS AND METHODS:** Using the GEO dataset GDS2052 (endometrium throughout the menstrual cycle), an in silico analysis (n=21 women) was performed to identify differentially expressed (p<0.05) ADGR genes between the proliferative and secretory phases. Next, RNA sequencing (RNA Seq) was conducted to quantify the effect of OS on the expression of these differentially expressed genes (DEGs) in the secretory phase. Of the 20 women included, 11 were in NC and 9 were in OS cycles. Periovulatory endometrial biopsies were performed at LH+1 (n=6) in NC or after hCG trigger at hCG+2 (n=5) in OS cycles. Window of implantation (WOI) biopsies were performed at LH+8 (n=5) or at hCG+9 (n=4). RNA was isolated from each biopsy and RNA Seq and bioinformatics were conducted to identify DEGs between natural and OS cycles. Medians were compared using a Mann-Whitney U test (p<0.05 was significant).

**RESULTS:** In the in silico analysis, 12 ADGRs, representing 6 of the 9 ADGR subfamilies, were differentially expressed in the secretory vs proliferative phase of a NC. Of these genes, ADGRE5, ADGRL1 and ADGRL3 demonstrated significantly different expression, in our RNA seq analysis, across the secretory phase between periovulation and the WOI when comparing a NC to OS (Table 1). Additionally, ADGRL3 was also significantly decreased at periovulation in an OS cycle compared to NC (LH+1: 3307, hCG+2: 1089, p<0.01).

**CONCLUSIONS:** As hypothesized, this study revealed that members of the ADGR gene family are differentially expressed in the secretory phase of a NC and three of these members (ADGRE5, ADGRL1 and ADGRL3) are also altered by OS.

**IMPACT STATEMENT:** Our findings suggest that ADGRs are potentially involved in endometrial decidualization and their expression is dysregulated by OS. Further investigation of ADGRs in human reproduction may offer a plausible mechanism for the altered endometrial receptivity seen with fresh embryo transfers.

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**P-553** 6:45 AM Wednesday, October 26, 2022

**STEM CELL PROPORTIONS IN ADENOMYSIS LESIONS AND EUTOPIC FUNCTIONAL ENDOMETRIUM OF PATIENTS WITH ADENOMYSIS.** Georgi Stamensov, MD/PhD, Margarita Ruseva, MSc, Dimitar Parvanov, PhD, Rumiana Ganeva, MSc, Maria Handziyska, MSc, Nina Vidolova, MSc, Dimitar Metodiev, M.D., Nadezhda Women’s Health Hospital, Sofia, Bulgaria.

**OBJECTIVE:** Adenomyosis is a non-neoplastic gynaecological disorder characterized by the presence of endometrial glands and stroma within the myometrium. Its pathogenesis remains poorly understood, however, a common hypothesis implicates stem cells as its origin. The aim of this study was to quantify and compare the proportions of two stem cell types between adenomyosis lesions and eutopic functional endometrium of adenomyosis patients.

**MATERIALS AND METHODS:** Hysteroscopic endometrial and myometrial biopsies were obtained from 19 adenomyosis patients aged 26 to 54. Immunohistochemical staining of the tissue against stem cell markers NOTCH1 (E-AB-12815) and CD117 (RB-9038-RQ, Epredia) was performed to reveal and quantify these cells. Cells positive for these markers in eutopic functional endometrium and adenomyosis lesions as defined by experienced histopathologist were enumerated using ImageJ. Percentage stained cells was compared between the two tissue regions of each patient via a paired samples t-test (SPSS v21). Data are presented as mean ± standard error of the mean.

**RESULTS:** In the eutopic functional endometrium of the studied patients, the percentage of NOTCH1+ cells was 0.67±0.19%, and of CD117+ cells - 0.28±0.06%, whereas in the adenomyosis lesions NOTCH1+ cells percentage was 0.18±0.04%, and CD117+ cells were 0.23±0.04%. The percentage of cells positive for NOTCH1 was significantly larger in the eutopic endometrium compared to adenomyotic lesions (t(18)=2.48, p<0.004). In contrast, CD117+ cell percentage did not differ significantly between the studied biopsies from eutopic and ectopic endometrium (t(18)=1.37, p=0.18).

**CONCLUSIONS:** The current study revealed that the adenomyosis lesions and eutopic endometrium of adenomyosis patients contain different quantities of certain stem cell types (NOTCH1+) but not others (CD117+).

**IMPACT STATEMENT:** The findings of the present study do not seem to support the theory of stem cell aetiology of adenomyosis. Further insight into the underlying invasion mechanism of endometrial tissue into the myometrium might contribute to improved treatment strategies.

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**Table 1. Normalized mRNA expression counts in the secretory phase of NC and OS cycles.**

<table>
<thead>
<tr>
<th>Gene</th>
<th>LH+</th>
<th>LH+8</th>
<th>p-value</th>
<th>hCG+2</th>
<th>hCG+9</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADGRE5</td>
<td>1498</td>
<td>1998</td>
<td>0.02</td>
<td>1429</td>
<td>1969</td>
<td>0.19</td>
</tr>
<tr>
<td>ADGRL1</td>
<td>2598</td>
<td>1619</td>
<td>0.13</td>
<td>2589</td>
<td>1267</td>
<td>0.02</td>
</tr>
<tr>
<td>ADGRL3</td>
<td>3307</td>
<td>1707</td>
<td>0.02</td>
<td>1089</td>
<td>1711</td>
<td>0.06</td>
</tr>
</tbody>
</table>

**P-554** 6:45 AM Wednesday, October 26, 2022

**ASSOCIATION BETWEEN STEM CELLS AND SENESCENT CELLS IN HUMAN ENDOMETRIUM.** Dimitar Parvanov, PhD, Rumiana Ganeva, MSc, Margarita Ruseva, MSc, Maria Handziyska, MSc, Nina Vidolova, MSc, Dimitar Metodiev, M.D., Georgi Stamensov, MD/PhD Nadezhda Women’s Health Hospital, Sofia, Bulgaria.

**OBJECTIVE:** To analyse the relationship between stem cells and senescent cells in human endometrial stroma during the mid-luteal phase of the cycle in women with repeated implantation failure (RIF).

**MATERIALS AND METHODS:** This is an observational study of 45 women with RIF who had an endometrial biopsy during the mid-luteal phase (LH+7) in a natural cycle. We used immunohistochemical biomarkers NOTCH1 (E-12815, Elabscience), and CD117 (RB-9038-RQ, Epredia), to identify stem cells and p16 inks4a (MAD-000690QD-7, Master Diagnostics) to identify senescent cells in endometrial stroma. The percentages of positively stained cells in the endometrial stroma were calculated after enumeration by two independent investigators in multiple endometrial sections.
Spatial distribution analysis was performed on the cell segmentation data using multiple sections immunostained for the described markers for stem and senescent cells. The nearest-neighbor analysis function was used to compute the distance of each individual stem cell to the nearest senescent cell using Spatial Analysis module of HALO image analysis software (version 2.3, IndicaLabs). The random process of cell placement was analyzed by comparison of the theoretical Poisson curve with the empirical nearest neighbor cross-G-function. Statistical analysis was performed by Spearman’s correlation test and Paired t-test using SPSS v.21 (IBM Corp., Armonk, NY, USA).

RESULTS: The percentage of p16+ cells (0.71%±0.80%) was significantly higher compared to NOTCH1+ cells (0.12%±0.28%, p<0.001) and CD117+ cells (0.02%±0.03%, p<0.001) in the endometrial stroma.

We found a significant positive correlation between stromal NOTCH1+ cells and p16+ cells (r=0.39, p=0.008). Furthermore, NOTCH1/CD117 ratio also showed positive significant correlation with the percentage of p16+ cells (r=-0.42, p=0.006). However, there was no significant correlation between stromal CD117+ and p16+ cells (r=-0.05 p=0.741).

The mean distance from senescent cells to NOTCH1+ stem cells (131±53 µm) and to CD117+ stem cells (144±33 µm) were not significantly different, although the two stem cell types differ in quantity. However, only the distance between NOTCH1+ cells and p16+ cells was significantly larger than should be expected if they were independently distributed.

CONCLUSIONS: In conclusion, our results have shown that only certain types of stem cells have association with cellular senescence. A significant quantitative and spatial relationship was found between NOTCH1-positive stem cells and p16-positive-senescent cells in human endometrial stroma in RIF women during the mid-luteal phase.

IMPART STATEMENT: Our study revealed that the increased number of senescent cells in RIF patients is associated with increase in NOTCH1+ stem cells in endometrial stroma and a specific cell-to-cell orientation. Understanding the relationship and communication between these two essential cell types in the endometrium may lead to improvement of infertility management.

P-555 6:45 AM Wednesday, October 26, 2022
PRELIMINARY DATA ON THE SPATIAL DISTRIBUTION OF STEM CELLS IN THE MID-LUTEAL ENDOMETRIAL STRONG OF PATIENTS WITH RECURRENT IMPLANTATION FAILURE (RIF), Margarita Ruseva, MSc, Dimitar Parvanov, PhD, Rumiana Ganeva, MSc, Maria Handzhıyiska, MSc, Nina Vidolova, MSc, Dimitar Metodiev, M.D., Georgi Stamenov, MD/PhD Nadezhda Women’s Health Hospital, Sofia, Bulgaria.

OBJECTIVE: Endometrial stem cells have been proposed to play various roles in physiological processes like implantation as well as in pathologies. The aim of the present study was to describe the localization, density and distances between two stem cell types (NOTCH1+ and CD117+) in the human endometrium during the mid-luteal phase.

MATERIALS AND METHODS: Endometrial biopsies (n=15) were obtained during the mid-luteal phase from RIF patients who were undergoing assisted reproductive therapy. The tissue was stained with immunohistochemical markers for NOTCH1 (E-AB-12815, Elabscience) and CD117 (RB-9038-RQ, Epredia). Processed tissue sections were assessed microscopically and stromal stem cells were compared between the two markers were enumerated by two independent researchers. The association between stem cell percentages and age was assessed using Spearman correlation. The percentages of CD117+ and NOTCH1+ stem cells were also compared between age groups (<35 and ≥35) via Mann Whitney U-test.

RESULTS: The percentage of p16+ cells (0.71%±0.80%) was significantly higher compared to NOTCH1+ cells (0.12%±0.28%, p<0.001) and CD117+ cells (0.02%±0.03%, p<0.001) in the endometrial stroma.

CONCLUSIONS: In conclusion, our results have shown that only certain types of stem cells have association with cellular senescence. A significant quantitative and spatial relationship was found between NOTCH1-positive stem cells and p16-positive-senescent cells in human endometrial stroma in RIF women during the mid-luteal phase.

IMPACT STATEMENT: Our study revealed that the increased number of senescent cells in RIF patients is associated with increase in NOTCH1+ stem cells in endometrial stroma and a specific cell-to-cell orientation. Understanding the relationship and communication between these two essential cell types in the endometrium may lead to improvement of infertility management.

P-556 6:45 AM Wednesday, October 26, 2022
ENDOMETRIAL STROMAL STEM CELLS QUANTITIES SHOW NO ASSOCIATION WITH PATIENTS’ AGE, Margarita Ruseva, MSc, Dimitar Parvanov, PhD, Rumiana Ganeva, MSc, Maria Handzhıyiska, MSc, Nina Vidolova, MSc, Dimitar Metodiev, M.D., Georgi Stamenov, MD/PhD Nadezhda Women’s Health Hospital, Sofia, Bulgaria.

OBJECTIVE: The human endometrium contains various resident and hematopoietic stem cells which possibly underlie its highly regenerative nature. Its capacity for renewal is likely reduced by the process of aging. The aim of the present study was thus to investigate associations between female patients’ age and the quantities of two types of endometrial stem cells.

MATERIALS AND METHODS: Endometrial biopsies were obtained during the mid-luteal phase (LH+7) of a natural cycle from 109 female patients undergoing assisted reproductive therapy. The tissue was stained with immunohistochemical markers for NOTCH1 (E-AB-12815, Elabscience) and CD117 (RB-9038-RQ, Epredia). Processed tissue sections were assessed microscopically and stromal stem cells were compared between the two markers were enumerated by two independent researchers. The association between stem cell percentages and age was assessed using Spearman correlation. The percentages of CD117+ and NOTCH1+ stem cells were also compared between age groups (<35 and ≥35) via Mann Whitney U-test.

RESULTS: The mean age of the study population was 39.5 years (range: 26-56). The percentage of NOTCH1+ endometrial stromal cells in these patients varied between 0.003% and 2.11% (median 0.06%) and the CD117+ cells ranged from 0.00% to 0.21% (median 0.02%).

Neither of the stem cell markers revealed a significant correlation with patients’ age (p>0.05). This lack of association was confirmed by the comparison of stem cell percentages between the two age groups (<35 and ≥35 years old; p>0.05).

CONCLUSIONS: No link was found between CD117+ or NOTCH1+ endometrial stromal stem cells quantities and patients’ age.

IMPACT STATEMENT: While it stands to reason that the process of aging might affect the regenerative capacity of the endometrium, the present study demonstrates that the proportions of CD117+ and NOTCH1+ stem cells in the endometrial stroma are sustained regardless of age. It is possible that while the quantities of these stem cells remain unchanged, their role alters, potentially contributing to pathologies via abnormal endometrial proliferation.

P-557 6:45 AM Wednesday, October 26, 2022
VAPING LIQUID EXPOSURE INDUCES METABOLIC DISTURBANCE AND REDUCTED DECIDUALIZATION OF HUMAN INDUCED PLURIPOTENT STEM CELL DIFFERENTIATED ENDOMETRIAL STROMAL FIBROBLASTS, Mirabelle Ho, PhD,1 Miel Ho, PhD,2 Clifford Lawrence Librach, MD,1* Create Fertility Centre, Toronto, ON, Canada; 2Create Fertility Centre, Toronto, ON, Canada; 1Create Fertility Centre, Toronto, ON, Canada.

OBJECTIVE: The misconception of vaping as a healthier alternative to cigarettes has led to its increase usage amongst reproductive age women. To date, studies relating to vaping and fertility are largely based on rodent models, which are unable to undergo spontaneous endometrial decidualization. Our study employed endometrial stromal fibroblasts (EMFSs) differentiated from human induced pluripotent stem cells (hiPSCs), as a disease-modeling platform to gain mechanistic insights into the effect of vaping liquid (VL) exposure on the endometrium.

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RESULTS: Reduction (>85%) of hiPSC markers OCT4, SOX2 and increase (~90%) in mesodermal-specific T expression at D2, preceded an increase of intermediate mesoderm genes LHX1 and PAX2 by D4. Subsequent differentiation into ESps by D8 was evidenced by increased AMHR2 and endometrium-associated markers HOXA10, HOXA11 and vimentin expression. High K67 expression (>90%) reflected ESps’ proliferative nature. Increase expression of progesterone and estrogen receptors (p<0.05) signified successful maturation of ESps into iEMSFs at D12. Importantly, iEMSF decidualization was evidenced by a change from fibroblastic to compact, rounded morphology, along with elevated expression (p<0.05) of PRL, FOXO1 and IGFBP1. VLuc expression led to significant (p<0.05) decrease in K67+ cells and iEMSFs’ viability, corresponding to increased expression (p<0.05) of Annexin V/PI and cleaved Caspase 3 and 9. Concurrent decrease in ΔΨm but increase in ROS expression was further exacerbated by VL+nicotinamide. Importantly, VL exposure impaired iEMSF’s ability to decidualize as evident by reduced expression of PRL and IGFBP1.

CONCLUSIONS: Sequential differentiation of iEMSFs recapitulated in vivo developmental hierarchy. VL exposure adversely reduced iEMSFs’ viability and proliferation potential. Pertinently, disruption in iEMSFs’ metabolic profile, reduction in ΔΨm and elevated ROS, impaired their functional decidualization capacity.

FUNDAMENTALLY ACTIVE MICROBIOTA LANDSCAPE IN RECURRENT IMPLANTATION FAILURE. Alberto Solá-Levy, Ph.D., student, Laura Terrón-Camero, Ph.D., Nerea M. Molina, Ph.D., student, José Antonio Castilla, M.D., Juan Fontes, M.D., Luis Martinez, M.D., María José Sáez-Lara, Ph.D., Agne Velthut-Meikas, Ph.D., Andres Salumets, Ph.D., Eduardo Andrés-León, Ph.D., Signe Altmäe, Ph.D., 1Department of Biochemistry and Molecular Biology, Faculty of Sciences, University of Granada, Granada, Spain; 2Instituto de Parasitología y Biomedicina ‘López-Neyra’; CSIC (IPBIL-CNCSIC), Granada, Spain; 3University of Cincinnati, West Chester Township, OH; 4University of Cincinnati, Cincinnati, OH; 5University of Cincinnati Medical Center, West Chester, OH.

OBJECTIVE: To identify and map the functionally active microbial composition at the receptive phase endometria of women with recurrent implantation failure (RIF) vs. healthy controls.

RESULTS: A total of 4175 microorganisms in the human endometrial samples including different bacteria, fungi, viruses, and archaea were identified. At the taxonomic level, 180 microbes were differentially abundant between RIF patients and healthy controls (FDR<0.05). Streptomyces, Mycobacterium, and Fusarium showed the biggest differences and were significantly less detected in RIF. The metabolic functions analysis revealed significant differences between the groups, with a total of 93 different pathways, where fatty acid biosynthesis, retinol biosynthesis, folate pathway and serotonin pathways were influenced in RIF.

CONCLUSIONS: With this approach we were able to identify and map the metabolically active microorganisms in RIF patients and healthy control women. Particularly, we found that 180 microbes and 93 pathways were significantly different when compared the groups, which contribute to RIF development.

IMPACT STATEMENT: Our study findings are novel to demonstrate that viable microbes are involved in the uterine pathology as is RIF, where different metabolic pathways could be dysregulated. This knowledge could help to develop pre/probiotic strategies to modulate uterine environment for improving endometrial functions in RIF.
INHERITANCE OF A HETEROPLASMIC MTDNA MUTATION ASSOCIATED WITH LEIGH SYNDROME. Amy Koski, BA,1 Hong Ma, PhD,2 Ying Li, MS,1 Crystal Van Dyken, BS,1 Nuria Martí Gutierrez, PhD,1 Aleksie Mikhailchenko, PhD,1 Daniel Franà, BS,1 Paula Amato, MD,1 Shoukhrat Mitalipov, PhD3 Oregon Health and Science University, Portland, OR;4 OHSU, Portland, OR;5 Oregon Health & Science University, Portland, OR.

OBJECTIVE: Reproductive options to prevent maternal transmission of heteroplasmic mitochondrial (mtDNA) mutations to children are limited due to complex and often unpredictable inheritance patterns. We sought to evaluate transmission of pathogenic 13513G>A mtDNA associated with Leigh Syndrome from a heteroplasmic mother to her children with the intent to develop prenatal diagnostics.

MATERIALS AND METHODS: We evaluated 13513G>A mutation load (heteroplasy levels) using whole mtDNA sequencing (MiSeq) in peripheral tissues (skin, blood, urine) of a mother and her four children following natural conception. For two younger children, we also examined prenatal biotissues (skin, blood, urine) of a mother and her four children following natural conception. mtDNA heteroplasmy levels were assessed using whole mtDNA sequencing in peripheral blood, skin, and urine. Heteroplasmy levels of 33.0% in blood and 14.5% in skin at birth. 29.5% in amniotic fluid during fetal development but reduced to 0.07% in blood while in spleen, liver, large intestine, testis and lung heteroplasmy ranged between 1% and 3%. In child #2, heteroplasmy levels were at 27.5% in chorionic villi and 29.5% in amniotic fluid during fetal development but reduced to 0.07% in blood and 14.5% in skin at birth. In child #4, heteroplasmy for this mutation was 0.11% in chorionic villi, 1.4% in blood and 0% in skin.

CONCLUSIONS: Accurate prediction of mtDNA disease in children using prenatal samples is difficult due to complex nature of inheritance coupled with heteroplasmy changes in various tissues during development. Mitochondrial replication therapy (MRT) in oocytes may provide a strategy to reduce maternally transmitted mtDNA disease.
OBJECTIVE: Paternal aging is associated with increased prevalence of childhood neurodevelopmental diseases, including autism spectrum disorder (ASD) and schizophrenia. During spermatogenesis, chromatin becomes tightly packaged around protamines, with <15% histones remaining at loci of embryonic developmental importance. We hypothesize that this critical process of chromatin reorganization is susceptible to perturbations as men age, leading to changes in sperm chromatin accessibility and epigenetic dysregulation. The aim of this study was to investigate at a single sperm level the variability of human sperm chromatin accessibility within an ejaculate as well as in association with advanced paternal age (APA).

MATERIALS AND METHODS: Surplus sperm were donated with patient consent at the time of IVF cycle: APA (≥ 50 years, normozoospermia; n = 7) compared to young (≤ 30 years, normozoospermia; n = 7). Following density gradient centrifugation and swim-up purification methods, sperm underwent single cell ATAC-Seq (10X Genomics) with a capture target of 5,000 cells per sample. Libraries were sequenced (Illumina NovaSeq), processed (Cell Ranger ATAC v2.0) and analyzed (Seurat). Methyl-Seq (Zymo Research) generated significantly differentially methylated regions (DMRs) in R using DMRcate (v1.18.0). Peak- and DMR-associated genes were used for pathway analyses (IPA, Qiagen; p < 0.05). Gene enrichment analyses were performed in R using Fisher’s exact test (q < 0.05).

RESULTS: Single sperm ATAC-Seq revealed one large indistinct cluster of 1,456 genes. Conclusively, the presence of mcMTOCs in human oocytes and explore their possible roles in regulating spindle positioning.

OBJECTIVE: The asymmetric cell division during female meiosis requires the migration of meiotic spindle toward the peripheral position so that a tiny polar body can be extruded. Such asymmetrical division is essential for the egg to retain the maximum volume of the cytoplasm, necessary for supporting early embryo development. A recent study demonstrated the importance of metaphase cytoplasmic microtubule organizing centers (mcMTOCs) in regulating spindle positioning and faithful chromosome segregation to protect against aneuploidy in mouse oocytes. However, it is unclear whether the mcMTOCs are present and play similar roles in positioning spindles in human oocytes. The objective of this study is to examine the presence of mcMTOCs in human oocytes and explore their possible roles in regulating spindle positioning.

MATERIALS AND METHODS: Following routine ovarian stimulation and oocyte retrieval, immature oocytes at the germinal vesicle (GV) stage were vitrified and stored in liquid nitrogen and used for research with IRB approval. The oocytes were warmed and placed into in-house made Oocyte Handling Medium for Maturation for 27-30 h. Oocytes that reached metaphase II (MII) stage were fixed by 4% freshly prepared paraformaldehyde solution and co-immunostained against γ-tubulin (to visualize microtubule organizing centers, MTOCs) and α-tubulin (to visualize microtubules). Oocytes were then mounted on slides using VECTASHIELD mounting media with DAPI to stain DNA, and images were taken to span the entire oocyte at 3 to 4 μm Z-intervals using 3D confocal microscopy. A total of 17 MII human oocytes were used in this experiment.

RESULTS: Similar to mouse oocytes, we observed γ-tubulin enrichment at spindle poles. We also observed mcMTOCs formed at the periphery of the oocyte and did not contribute to spindle formation. These mcMTOCs localize asymmetrically in oocytes and seemed to anchor the spindle to the cortex.

CONCLUSIONS: Here, for the first time, we observed the presence of mcMTOCs that remain free in the cytoplasm during meiosis in human oocytes. Unlike the known function of MTOCs in spindle assembly, these mcMTOCs may play an important role in regulating spindle positioning and its timely migration to allow asymmetrical cell division of the human oocytes. The mcMTOCs may play crucial role in maintaining faithful chromosome segregation during oocyte meiosis, a process that is highly error prone in human oocytes.

IMPACT STATEMENT: Our findings provided the basis to further explore the role of mcMTOCs in regulating spindle positioning during human oocyte meiosis. Such work is important to elucidate how the fidelity of the asymmetric cell division and precise chromosome segregation in human oocytes are regulated, therefore, leading to possible solutions to address aneuploidy in human oocytes.

FULL TEXT AVAILABLE ONLINE
SUPPRESSION PATHWAY OF ANDROGEN PRODUCTION THROUGH SECRETED PROTEINS IN MSC-BASED PCOS TREATMENT.

Hanaa Mohammed, MD,6 Stephanie M. Cologna, PhD,3 Ayman Al-Hendy, MD, PhD,5 1The University of Chicago, Chicago, IL; 2University of Kansas Medical Center, Kansas City, KS; 3University of Illinois at Chicago; 4University of Chicago, Chicago, IL; 5Sohaq University, Egypt.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is the most common endocrine and metabolic disorder in reproductive-aged women, and it typically involves elevated androgen levels. Recently, it has been reported that human bone marrow mesenchymal stem cells (hBM-MSCs) can regulate androgen synthesis pathways. However, the details of the mechanism are still unclear. hBM-MSC-derived secreted factors are promising sources of cell-based therapy as they consist of various types of proteins. It is thus important to know which proteins interact with disease-implicated biomolecules. This work aimed to investigate which components are the key factor that inhibits androgen synthesis pathways. However, our study suggests that gene variants involved in folic acid availability seem to have no consequences for pregnancy establishment. The mean age of the patients included was 34.5 years and the mean AMH was 3.4 ng/ml. Indications for IVF varied among patients. On average, 2.3 GV oocytes were obtained and analyzed per patient. Using antibodies against human Nemp1, confocal microscopy revealed that Nemp1 localizes to the nuclear envelope in a similar pattern as previously observed in mouse oocytes. Variations in the staining patterns were seen among patients.

CONCLUSIONS: Nemp1 localizes to the nuclear envelope in human GV oocytes in abundant foci.

IMPACT STATEMENT: This novel oocyte nuclear envelope structure may reveal new and important function of the oocyte nuclear envelope in chromatin organization and developmental competence. The discovery that the Nemp1 protein family is important for fertility in flies, worms, fish, and mice shows its deep conservation. We hypothesize that variants in Nemp1 could be detected in patients with low ovarian reserve or poor oocyte developmental competence.

IMPACT STATEMENT: Folic acid supply could efficiently support initial steps of pregnancy establishment following IVF treatments in egg donor recipients, but its further availability in more advanced pregnancy stages could be differentially affected by genetic factors in the pregnant women.

SUPPORT: This study was financially supported by start-up funds from the University of Chicago (AA).

MATERIALS AND METHODS: Retrieved germinal vesicle-stage (GV) oocytes from female patients undergoing in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI) were used for the study. The GV oocytes were fixed in paraformaldehyde and incubated with primary and secondary antibody solutions. After immunostaining, the GV oocytes were analyzed under confocal microscopy for Nemp1 localization. The GV oocytes were concurrently stained with 4',6-diamidino-2-phenylindole (DAPI) which binds adenine-thymine-rich regions of DNA and antibodies of Lamin B1, a matrix protein in the nuclear membrane to determine nuclear envelope localization.

RESULTS: The preliminary results analyzed GV oocytes from 10 individuals. The mean age of the patients included was 34.5 years and the mean AMH was 3.4 ng/ml. Indications for IVF varied among patients. On average, 2.3 GV oocytes were obtained and analyzed per patient. Using antibodies against human Nemp1, confocal microscopy revealed that Nemp1 localizes to the nuclear envelope in a similar pattern as previously observed in mouse oocytes. Variations in the staining patterns were seen among patients.

CONCLUSIONS: Nemp1 localizes to the nuclear envelope in human GV oocytes in abundant foci.

IMPACT STATEMENT: This novel oocyte nuclear envelope structure may reveal new and important function of the oocyte nuclear envelope in chromatin organization and developmental competence. The discovery that the Nemp1 protein family is important for fertility in flies, worms, fish, and mice shows its deep conservation. We hypothesize that variants in Nemp1 could be detected in patients with low ovarian reserve or poor oocyte developmental competence.
OBJECTIVE: The intrauterine administration of autologous PBMC activated by human chorionic gonadotropin (hCG) is a widely used method for improvement of implantation by regulation of inflammatory and anti-inflammatory condition in the human endometrium. However, the relationship between PBMC cell content and its cytokine secretion is still scarcely studied. The aim of the present study was to investigate the effect of PBMC cell content on the secretion of pro- and anti-inflammatory cytokines (IL-6, TNFα, IL-4, and IL-10) of hCG-activated PBMC.

MATERIALS AND METHODS: Blood samples (8 ml) were collected from 20 healthy non-pregnant women during the mid-luteal phase. PBMC were isolated using Pansorbin (P04-60100, PanBiotech) gradient centrifugation for 25 min at 400G. PBMC cell content in terms of number and percentage of white blood cells, lymphocytes, monocytes, eosinophils, basophils, neutrophils, and platelets was determined by hematology cell counter analyzer BC-8000 (Mindray). PBMC were then cultured (1×10⁷ cells/well) in 1.5 ml RPMI-1640 medium (E15-842, APP) + 1% human serum albumin + 10IU/ml hCG (BT-HOR-250, Biotang) for 24h.

Interleukin-6 (IL-6), tumor necrosis factor alpha (TNFα), interleukin-4 (IL-4) and interleukin-10 (IL-10) in the cell culture media were then determined by sandwich enzyme-linked immunosorbent assay (CSB-E04638h, CSB-E04740h, CSB-E04633h and CSB-E04593h, Cusabio Technology, respectively). Statistical analysis was conducted using SPSS v.21. Spearman correlation test was used for correlation analysis.

RESULTS: The levels of secreted anti-inflammatory cytokines IL-4 (31.8±24.9 pg/ml) and IL-10 (22.8±18.1 pg/ml) correlated with the percentage of monocytes (r=0.52, p<0.01) and neutrophils (r=0.52, p<0.01), respectively) and eosinophils (r=0.77, p=0.01 and r=0.68, p=0.02, respectively).

The percentage of secreted proinflammatory cytokine IL-6 (897±4.69 pg/ml) showed significant positive correlation with the percentage of monocytes (r=0.72, p=0.01) and negative correlation with the percentage of eosinophils (r=0.60±0.48%) (r=0.73, p=0.01) and basophils (r=0.51±0.52%) (r=0.63, p=0.03). However, the concentration of TNFα (135.78±129.48 pg/ml) did not correlate significantly with any of the cell parameters (p>0.05).

CONCLUSIONS: The present study showed that the secretion of pro- and anti-inflammatory cytokines by hCG-activated PBMC is associated with the relative proportions of certain white blood cell types. The decreased percentage of monocytes and lymphocytes and increased percentage of neutrophils, eosinophils and basophils in PBMC might have a positive effect on its tolerogenic cytokine profile (low secretion of proinflammatory cytokines and elevated secretion of anti-inflammatory cytokines).

IMPACT STATEMENT: The obtained results demonstrate that hCG activation of PBMC could result in different cytokine secretion depending on the PBMC cell composition. The PBMC content might be optimized before its intra-uterine administration in order to achieve better IVF outcomes.
CONCLUSIONS: As more clinics begin regularly transferring embryos diagnosed as non-euploid, it is necessary to have a greater understanding of these “gray area” embryos to effectively manage treatment and expectations for both providers and patients during ART cycles. Additional research would help identify if the effects seen here are laboratory and technique specific or are generally observed.

IMPACT STATEMENT: This study presents data indicating that the probability of a partial chromosome mosaicism diagnosis decreases as patients age; however, the probability of a full chromosome mosaic diagnosis is unrelated to age.

REFERENCES:

P-573 6:45 AM Wednesday, October 26, 2022

PREIMPLANTATION GENETIC TESTING FOR ANEUPOIDY (PGT-A) FOR PATIENTS AGED ≤ 37 YEARS: EVIDENCE-BASED MEDICINE DOES NOT SUPPORT ITS USE A META-ANALYSIS. Felipe Deamant, M.D., Claudia G. Petersen, Ph.D., Fabiana C. Massaro, B.Sc., Bruna Petersen, B.Sc., Laura D. Vagnini, M.Sc., Andrea Nicoletti, R.N., Juliana Ricci, R.N., Camila Zamara, R.N., Antonio Helio Oliani, M.D., Ph.D., Joao B. A. Oliveira, M.D., M.Sc., Ph.D., Jose G. Franco, Jr., M.D., Ph.D. Center for Human Reproduction Prof. Franco Jr/ Paulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; Center for Human Reproduction Prof. Franco Jr, Ribeirao Preto, Brazil; Paulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; Sao Jose Do Rio Preto School of Medicine FAMERP, Sao Jose Do Rio Preto, Brazil.

OBJECTIVE: To evaluate if patients aged ≤37 years truly benefit from using PGT-A as an add-on to increase ongoing pregnancy rate (OPR)/live birth rate (LBR) in their first IVF/ICSI cycle?

MATERIALS AND METHODS: A systematic review based on electronic searches of databases up to March 2022 was conducted to identify randomised controlled trials (RCTs) comparing clinical outcomes of IVF/ICSI cycles with PGT-A versus Morphological embryonic selection. The primary outcomes were ongoing pregnancy and live birth rates. Seven RCTs were included as targets for data extraction and meta-analysis. Three studies were expressed as Relative Risk (RR) with a 95% confidence interval (CI). Study covariates.

RESULTS: Table 1 shows the data. -Ongoing pregnancy rates: PGT-A group: 67.4%; Morphological Embryo Selection Group: 63.2%. No statistically significant differences (P=0.35).
-Live birth rate: PGT-A group: 58.9%; Morphological Embryo Selection Group: 57.9%. No statistically significant differences (P=0.91).

Table 1. PGT-A vs. Morphology: Ongoing pregnancy rate and Live birth rate

<table>
<thead>
<tr>
<th>Study/OPR</th>
<th>PGT-A (n/N)</th>
<th>Morphology (n/N)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yang et al., 2012</td>
<td>69.1% (38/55)</td>
<td>41.7% (20/48)</td>
<td>1.66 (1.16-2.47)</td>
</tr>
<tr>
<td>Forman et al., 2013</td>
<td>60.7% (54/89)</td>
<td>65.1% (56/86)</td>
<td>0.93 (0.74-1.17)</td>
</tr>
<tr>
<td>Yan et al., 2021</td>
<td>68.2% (393/576)</td>
<td>64.6% (384/594)</td>
<td>1.06 (0.97-1.15)</td>
</tr>
<tr>
<td>Total</td>
<td>67.4% (485/720)</td>
<td>63.2% (460/728)</td>
<td>1.11 (0.89-1.39)</td>
</tr>
<tr>
<td>Chi² = 0.86; P=0.35</td>
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<tr>
<td>Cochran’s Q=6.65</td>
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<tr>
<td>I²=69.9%</td>
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<thead>
<tr>
<th>Study/LBR</th>
<th>PGT-A (n/N)</th>
<th>Morphology (n/N)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scott et al., 2013</td>
<td>84.7% (61/72)</td>
<td>67.5% (56/83)</td>
<td>1.26 (1.05-1.52)</td>
</tr>
<tr>
<td>Munne et al., 2019</td>
<td>41.9% (75/179)</td>
<td>50.3% (89/177)</td>
<td>0.83 (0.66-1.04)</td>
</tr>
<tr>
<td>Ozgur et al., 2019</td>
<td>41.3% (45/109)</td>
<td>58.6% (65/111)</td>
<td>0.71 (0.53-0.92)</td>
</tr>
<tr>
<td>Sui et al., 2020</td>
<td>33.3% (15/45)</td>
<td>13.3% (6/45)</td>
<td>2.50 (1.11-5.82)</td>
</tr>
<tr>
<td>Yan et al., 2021</td>
<td>66.3% (382/576)</td>
<td>62.1% (369/594)</td>
<td>1.07 (0.98-1.16)</td>
</tr>
<tr>
<td>Total</td>
<td>58.9% (578/981)</td>
<td>57.9% (585/1010)</td>
<td>1.01 (0.81-1.26)</td>
</tr>
<tr>
<td>Chi² = 0.01; P=0.91</td>
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<tr>
<td>Cochran’s Q=20.54</td>
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<tr>
<td>I² =80.5%</td>
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</table>

CONCLUSIONS: The use of PGT-A is not superior to classic morphological embryonic selection to increase OPR/LBR in patients aged ≤37 years in their first IVF/ICSI cycle.

IMPACT STATEMENT: This meta-analysis brings to light a fundamental discussion currently, in which physicians and embryologists employ add-ons to improve clinical outcomes even without adequate scientific support. Medical practices are based on scientific evidence and Reproductive Medicine is not different. Therefore, at the moment, PGT-A should not be indicated for patients aged ≤37 years.

P-574 6:45 AM Wednesday, October 26, 2022

TROPHOECTODERM BIOPSY AND IMPACT ON INCIDENCE OF ECTOPIC PREGNANCY. Meghan C. H. Ozcan, M.D., Alexis K. Gadson, M.D., Virginia Mensah, M.D., Christina Raker, ScD, Jennifer L. Eaton, MD, MSCI Warren Alpert Medical School of Brown University; Women & Infants Hospital of Rhode Island, Providence, RI; Warren Alpert Medical School of Brown University; Women & Infants Hospital, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Providence, RI; Warren Alpert Medical School of Brown University; Women & Infants Hospital, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Providence.

OBJECTIVE: Infertility is a known risk factor for ectopic pregnancy. Given that in vitro fertilization (IVF) bypasses the fallopian tubes, the underlying etiology of ectopic pregnancy among IVF patients is unclear. In particular, it is not known whether trophoderm biopsy for preimplantation genetic testing (PGT) increases the risk of ectopic pregnancy by interfering with normal implantation. Our primary objective was to assess the association between PGT and ectopic pregnancy among women undergoing frozen embryo transfer (FET). Our secondary objective was to compare ectopic pregnancy rates between PGT for aneuploidy (PGT-A) and PGT for other indications such as monogenic disorders and structural chromosomal rearrangements. We hypothesized that ectopic pregnancy rates would be increased with PGT, regardless of indication, after adjusting for covariates.

MATERIALS AND METHODS: Frozen single autologous blastocyst transfers with linked retrievals from January 1, 2014 to December 31, 2018 among women aged 18-42 years were obtained from the Society for Assisted Reproductive Technology Clinic Outcomes Reporting System (SART CORS). Cycles were classified according to the use of PGT and the indication for PGT. The primary outcome was ectopic pregnancy rate per embryo transfer. Generalized estimating equation (GEE) models for binary data with a logit link were used to test the effect of PGT on the primary outcome while adjusting for covariates and the correlation induced by repeated cycles within a patient. A sensitivity analysis of PGT-A compared with PGT for other indications was performed.

REFERENCES:
Lence of Reproductive Endocrinology and Infertility, Providence.

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RESULTS: Of the 105,863 included cycles, 65,832 (62%) were untested and 40,031 (38%) were biopsied for PGT. The ectopic pregnancy rate was 0.40% vs. 0.47%, P = 0.11. After adjusting for covariates, there was no significant association between the use of PGT and ectopic pregnancy (odds ratio [OR] 1.14, 95% confidence interval [CI] 0.80 – 1.43). Stratifying by PGT indication, the ectopic rate was 0.49% (N = 183/37,534) for PGT-A and 0.16% (N = 4/2,497) for PGT for other indications. This association persisted after covariate adjustment, although the confidence interval was wide due to the low number of outcomes in the group with PGT for other indications (OR 2.88 95% CI 1.07 – 7.78). The findings were similar in a sensitivity analysis of first transfers only.

CONCLUSIONS: The incidence of ectopic pregnancy is low and similar among patients who conceive with FET with or without PGT.

IMPACT STATEMENT: Patients undergoing frozen embryo transfer may be counseled that the use of PGT does not impact their risk of ectopic pregnancy.

SUPPORT: No financial support

P-575 6:45 AM Wednesday, October 26, 2022

RNA-SEQ ANALYSIS OF BLASTOCOELE FLUID-CONDITIONED UNCOVERS GENES INVOLVED IN CALCIUM SIGNALING AND EXTRACELLULAR MATRIX-RECEPTOR INTERACTION PATHWAYS IN EUPLOID EMBRYOS THAT SUCCESSFULLY IMPLANT.

Andrea Conry, B.S.,1 Eleanor Petyak, B.S.,2 William E. Rouddebush, Ph.D.,1 Richard J. Kordus, Ph.D.,1 Alyssa Clay-Gilmour, Ph.D.,1 Lisa Jeanette Green, MD, MPH, Renee J. Chosed, PhD,1 Angel Earle, MS3 Greenville, SC;3 University of South Carolina School of Medicine Greenville, Greenville, SC;4 Prisma Health, Greenville, SC;5 University of South Carolina School of Medicine Greenville, Greenville, SC;6 University of South Carolina Arnold School of Public Health, Greenville, SC;

OBJECTIVE: This retrospective study assessed global gene expression using RNA-Seq of blastocoele fluid-conditioned media from euploid ICSI-generated embryos to identify specific signaling pathway genes associated with positive implantation outcomes.

MATERIALS AND METHODS: Blastocoele fluid-conditioned media was obtained following biopsy (ploidy status via NextGen sequencing) of ICSI-generated day-5 blastocysts. Media samples selected for RNASeq were from 24 euploid blastocysts whereby half resulted in successful in implantation outcomes. RNA was extracted (Zymo Quick-RNA MicroPrep Kit) and libraries prepared (Takara Bio SMART-Seq Stranded Kit). Following Illumina NextSeq500 sequencing, sequences were aligned to the human genome, reads counted and gene expression determined (~30 million reads). After quality control (minimal pre-filtering to retain only rows with at least 10 reads total), the total gene count was 24,347. DESeq2 was used to test for differential gene expression. Raw read counts were normalized across all samples. Wald test statistic was used to compare successful versus unsuccessful implantation outcomes. Adjusted false-discovery rate (FDR) p-value < 0.05 were considered as statistically significant for the differential expressed genes. Normalized counts were further used in Gene set enrichment analysis (GSEA) and KEGG pathway analyses for functional annotation.

RESULTS: 29 genes associated with successful implantation outcomes that showed a statistically significant increase (p < 0.05) in expression compared to unsuccessful outcomes were identified in the analyzed blastocoele fluid-conditioned media samples from euploid embryos. Examples of the identified genes included cadherins encoding genes as well as genes encoding ion channels. The genes were predominately associated with Calcium Signaling and Extracellular Matrix-Receptor Interaction Pathways. A smaller set of genes were also found to have decreased expression (p < 0.05) in media from embryos associated with successful implantation outcomes compared to unsuccessful outcomes. The functions of some genes in this group included membrane-trafficking and protein scaffolding.

CONCLUSIONS: This study provides a unique snapshot of critical signaling events taking place during preimplantation development that differ between euploid embryos resulting in successful versus unsuccessful implantation. The presence of genes belonging to fundamental signaling pathways in the blastocoele fluid-conditioned media suggests that this media may serve as a representation for the overall viability of the preimplantation embryo. Future study is needed to determine how and why these specific genes contribute to a successful implantation.

IMPACT STATEMENT: Gene expression differences identified in blastocoele fluid-conditioned media from euploid embryos resulting in successful versus unsuccessful implantation outcomes reveal a potential embryo viability biomarker(s).

SUPPORT: Prisma Health Transformative Research Seed Grant

P-576 6:45 AM Wednesday, October 26, 2022

CONCORDANCE OF CHROMOSOMES WITHIN RE-BIOPSY SAMPLES OF EMBRYOS FOLLOWING INITIAl CHAOTIC RESULTS.

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OBJECTIVE: An embryo is labeled as chaotic when six or more aneuploidies are detected in a trophoectoderm biopsy sample. The presence of multiple chromosome abnormalities would be expected to result in failed implantation or miscarriage; therefore, embryos reported as chaotic are typically discarded. However, the positive predictive value of chaotic results from preimplantation genetic testing for aneuploidy (PGT-A) has not been investigated and is uncertain. We sought to gather additional information about chaotic results from PGT-A through re-biopsy of and re-testing embryos with chaotic results. The goal of this study is to evaluate the concordance rate between these results.

MATERIALS AND METHODS: We retrospectively reviewed re-biopsy results from 58 embryos originally reported as chaotic. Data included 10 in vitro fertilization (IVF) clinics with results reported from January 2018 to January 2022. PGT-A testing was performed by a single reference laboratory using next-generation sequencing (NGS). Samples from a re-biopsy of chaotic embryos were analyzed by PGT-A and compared to the embryo’s initial PGT-A result.

RESULTS: A total of 58 embryos, initially reported as chaotic, were re-biopsied and re-tested. The average maternal age within this group was 39.5 years. The results of re-biopsy testing reported 22 (38%) euploid, 7 (12%) chaotic, 24 (41%) single or complex aneuploid, 3 (5%) mosaic aneuploid, and 2 (3%) non-informative. All informative embryo-re-biopsy samples had sex chromosomes concordant with the initial result. All aneuploid, mosaic, and chaotic re-biopsies had at least one autosomal chromosome concordant with the initial chaotic result. Concordance with the initial chaotic result for all chromosomes showing copy number variations was found for 22 (88%) euploid (single or complex), 3 (100%) mosaic, and 2 (29%) chaotic re-biopsies.

CONCLUSIONS: Re-biopsy and repeat PGT-A testing of embryos initially reported as chaotic identified a spectrum of possible result categories, including euploid and repeat chaotic results. While potential results in the re-biopsy varied, sex chromosomes were concordant between the first and second biopsies in 100% of cases, and when aneuploidy was detected on the 2nd biopsy at least one chromosome was concordant. While the rate of chaotic results was 6 times higher than the expected ~2% rate for 1st biopsy results1, there was also a striking euploid rate of 38%. The 38% euploid rate suggests that chaotic results on PGT-A have reduced predictive value and may have reproductive potential. Research with clinical outcome data following transfer of embryos with euploid results on re-biopsy is needed to quantify their reproductive potential, and to help guide clinical recommendations for clients with chaotic PGT-A results on their initial embryo biopsy samples.

REFERENCES:
OBJECTIVE: Historically, PGT-A results were applied in a binary fashion: embryos categorized as normal were transferred, and those categorized as abnormal were not. While embryos with euploid results have consistent reproductive outcomes, it has now become evident that “abnormal” results can be subcategorized, depending on whether an intermediate copy number is observed (“mosaic”), range of intermediate copy number (estimated percentage of biopsied cells with the abnormality), and type of abnormality (segmental or full monosomy/trisomy).

MATERIALS AND METHODS: Frozen embryo transfers at our clinic in which PGT-A was performed by next-generation sequencing (NGS) were reviewed. Biopsies from embryos transferred were categorized as either euploid (<20% undetectable abnormal cells), low level segmental mosaic (LL-SM; 20-40% abnormal), high level whole chromosome mosaic (LL-WCM), high level whole chromosome mosaic (LL-WCM), or aneuploid (80-100% abnormal). Primary outcomes were implantation rate (IR; defined as presence of gestational sac), ongoing pregnancy rate at 7 weeks gestation (OPR), and spontaneous abortion rate (SABR; defined as loss of gestational sac). Contingency Chi-square (X²; 6x2) analysis with post hoc (2x2)’s were used for comparisons.

RESULTS: Table 1 lists the primary outcomes for each PGT-A category. For IR and OPR, euploid and LL-SM embryos were indistinguishable; however, HL-SM, LL-WCM, HL-WCM, and aneuploid embryos were significantly different (p<0.001). While the limited sample size of spontaneous abortions was too small to make accurate comparisons between all 6 groups, a significantly higher SABR was observed for non-euploid embryos (p<0.001). There were no cases in which a non-euploid PGT-A result was confirmed by amniocentesis or in the newborn.

CONCLUSIONS: Embryos with euploid and LL-SM results have the highest chance of producing a viable pregnancy. Those with other types of mosaic results can produce viable pregnancies, but at lower rates, and aneuploid embryos are least likely to be viable. Therefore, a spectrum of PGT-A results can help to predict reproductive potential. These data can be used to guide patient counseling about embryo transfer after PGT-A.

IMPACT STATEMENT: The amount and type of mosaicism in embryos correlates with OPR and SABR. Trophoderm biopsy with NGS is a powerful tool in predicting reproductive outcomes.

SUPPORT: None

P-579 6:45 AM Wednesday, October 26, 2022

ARE PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) OUTCOMES DIFFERENT IN INFERTILE (INF) AND FERTILE (FT) PATIENTS (PTS)?

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OBJECTIVE: Counseling patients regarding the use of PGT-A, it is unclear whether ploidy rates among INF pts who undergo PGT-A are comparable to FT pts. Our objective was to evaluate PGT-A outcomes in FT compared to INF pts.

MATERIALS AND METHODS: This is a retrospective cohort study of the first IVF cycle of all FT pts (pts without a diagnosis of infertility) who underwent PGT-A at one academic center from 2016-2021. Pts were 3-to-1 matched by age and # of oocytes retrieved to the first cycle of INF controls. Primary outcome was euploidy rate, defined as # euploids per # biopsied blastocysts. Secondary outcomes were # mature oocytes (M2), #2PN fertilization rate, blastocyst formation rate (BFR), and # of euploid, aneuploid, and mosaic embryos. BMI, AMH, day 2 FSH and E2, total gonadotropin (GND) dose, and stimulation days were compared. Subgroup analyses compared % mosaic, aneuploid, and no diagnosis embryos. Statistical analysis included Mann-Whitney U, Fisher’s exact, Chi squared tests, and multiple linear regression (p<0.05 significant).

RESULTS: 283 FT pts (reason for PGT-A: 64% embryo banking, 36% single gene disorders) were matched to 849 INF pts. Median age, AMH, and day 2 E2 were equivalent among groups (p>0.1). In FT pts, median day 2 FSH was higher (6.9 vs. 6.5, p<0.01) and median BMI was lower (22.1 vs. 22.5, p<0.05). FT pts received higher median doses of GNDs (3450 vs. 3150 IU, p<0.01), but had similar median stimulation days (p=0.19). Median number of oocytes retrieved, #2PN retrieved, and biopsied blastocysts did not differ among groups (p>0.29); nor did #M2s or BFR (p>0.29). #2PN fertilization was higher in FT pts (77.7 vs. 70.3%, p<0.05). See Table for PGT-A outcomes. Euploidy rate was higher in FT pts; among non-euploid embryos, INF pts had lower aneuploidy and higher mosaicism rates. The % of pts with ≥1 euploid embryo was similar in both groups. A multiple linear regression model continued to show the relationship between % euploid in FT vs. INF groups, while controlling for other significant covariates (BMI, total GNDs used, day 2 FSH, and #2PN fertilization rate).

CONCLUSIONS: FT pts had higher euploidy rates than INF pts, suggesting that infertility is associated with a lower euploidy rate. However, among non-euploid embryos, FT pts had higher aneuploidy and lower mosaicism rates compared to INF pts. An equivalent % of FT and INF pts yielded≥1 euploid embryo.

IMPACT STATEMENT: FT pts undergoing PGT-A can be counseled that they have a higher euploidy rate, but INF pts are just as likely to yield≥1 euploid embryo.
therefore, if successful, does not require an additional frozen cycle. In PGT-XS cycles, an egg transfer occurs within the first cycle and livebirth when compared to PGT-A without significant changes in pregnancy outcomes with no significant differences between groups. For subsequent FET (if embryos were available) was used. Table 1 displays pregnancy outcomes from 227 IVF cycles, 85 of which were frozen embryo transfer cycles. In the PGT-A and PGT-XS cycles had similar numbers of embryos adequate for biopsy (mean 3.54 and 3.68, respectively). For each patient, the first two cycles were used to compare pregnancy outcomes. In the PGT-A group, the pregnancy outcome of the first FET after embryos were created was used. For the PGT-A XS and NGT groups, the fresh transfer and subsequent FET (if embryos were available) was used. Table 1 displays pregnancy outcomes with no significant differences between groups. For patients who achieved LB, the median time from egg retrieval to LB for PGT-XS group was 259 days and 326 days for the PGT-A group (p=0.001, CI 58-106 days).

CONCLUSIONS: PGT-XS may decrease the time from egg retrieval to livebirth compared to PGT-A without significant changes in pregnancy outcomes. This is most likely because PGT-A requires a subsequent frozen cycle. In PGT-XS cycles, an egg transfer occurs within the first cycle and therefore, if successful, does not require an additional frozen cycle.

Table 1: Pregnancy outcomes for first cycle resulting in embryo transfer

<table>
<thead>
<tr>
<th>Patient Age</th>
<th>Sample Size</th>
<th>Non-PGT-A Implantation Rate</th>
<th>Idealized PGT-A Implantation Rate</th>
<th>Observed PGT-A Implantation Rate</th>
<th>Estimated PGT-A Efficiency</th>
<th>Estimated PGT-A Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;= 33</td>
<td>664</td>
<td>57%</td>
<td>67%</td>
<td>66%</td>
<td>99%</td>
<td>1%</td>
</tr>
<tr>
<td>34-36</td>
<td>388</td>
<td>52%</td>
<td>68%</td>
<td>68%</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>37-39</td>
<td>278</td>
<td>47%</td>
<td>71%</td>
<td>60%</td>
<td>84%</td>
<td>16%</td>
</tr>
<tr>
<td>&gt; = 40</td>
<td>119</td>
<td>30%</td>
<td>64%</td>
<td>62%</td>
<td>97%</td>
<td>3%</td>
</tr>
</tbody>
</table>

IMPACT STATEMENT: This study highlights the potential benefit for PGT-XS compared to PGT-A and underscores the need for further prospective research into the utility of PGT.
COMPARISON OF THE EPUOLOY RD AND CLINICAL PREGNANCY RATE OF PGTA TESTED EMBRYOS BETWEEN LONG GnRH AGONIST AND GnRH ANTAGONIST PROTOCOLS; A RETROSPECTIVE STUDY. Wenyao Yu M.M.,1 Junhao Yan, M.D., Ph.D.,1,2 Zi-Jiang Chen, M.D., Ph.D. 1,3 Shandong University, Jinan, China; 2Jinan, China; 3Center for Reproductive Medicine, Shandong University, Jinan City, China.

OBJECTIVE: Whether an association exists between the use of gonadotropin-releasing hormone (GnRH) analog and blastocyst euploidy rate as well as clinical pregnancy rate in preimplantation genetic testing for aneuploidy (PGTA-A) cycles.

MATERIALS AND METHODS: This is a retrospective study using anonymized data on PGTA-A cycles performed in China from 2017 to 2020. Data from 359 cycles and 1475 blastocysts were analyzed by 24-chromosome next-generation sequencing (NGS)-based PGTA-A with a diagnosis. Blastocyst euploidy rate was the primary outcome, and clinical pregnancy rate (CPR) was the secondary outcome.

RESULTS: No statistically significant differences were found in the good-quality blastocysts rate from MII oocytes (41.4% vs. 42.9%, P = 0.335), the euploid blastocyst rate (56.1% vs. 52.6%, P = 0.171) of biopsied blastocysts, and the clinical pregnancy rate (69.2% vs. 63.2%, P = 0.289) of the first frozen-thawed blastocyst transfer cycle. Following balancing several relative parameters (i.e., age, BMI, the number of MII oocytes, PCOS diagnosis, the dosage of gonadotropins and HCG), the selection of GnRH analog to achieve pituitary suppression did not affect the blastocyst euploidy rate or clinical pregnancy rate.

CONCLUSIONS: Stimulation with long GnRH agonist protocol and GnRH antagonist protocol resulted in a fairly similar euploidy rate and clinical pregnancy rate for young patients with ideal ovarian reserve. The finding supports the flexible use of GnRH analogs to optimize treatment for this group of patients.

IMPACT STATEMENT: Ovarian stimulation protocol plays an important role in assisted reproductive technology. The clinical outcomes, as well as biopsy results, can demonstrate the safety of antagonist protocol, remove the role in assisted reproductive technology. The clinical outcomes, as well as biopsy results, can demonstrate the safety of antagonist protocol, remove the role in assisted reproductive technology. The clinical outcomes, as well as biopsy results, can demonstrate the safety of antagonist protocol, remove the role in assisted reproductive technology.

The role of PGTA on OPR is controversial. After adjusting for age, PGTA increased OPR only for those diagnosed with DOR. PGTA was associated with 3.45 times higher OPR in patients with DOR regardless of age. While there was a trend towards increased OPR when PGTA was employed in patients with male factor infertility, this did not reach statistical significance. Despite limitations due to the sample size and the positively impacted by PGTA in our study, this is the first study, to our knowledge, to investigate usefulness of PGTA by infertility diagnosis.

IMPACT STATEMENT: By identifying a patient population that benefits the most from PGTA, this study provides novel information to tailor patient care and insight into the pathophysiology of DOR.

PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGTA) IMPROVES ONGOING PREGNANCY RATES IN DIMINISHED OVARIAN RESERVE REGARDLESS OF AGE. Audrey Garneau, M.D.,1 Anthony Bui, M.D., M.S.,1 Douglas Timmons, M.D., M.P.H.,1 Caitlin Boylan, M.Sc.,1 Steven L. Young, M.D., Ph.D.1 University of North Carolina, Chapel Hill, NC; 2University of North Carolina, Raleigh, NC; 3University of North Carolina School of Medicine, Chapel Hill, NC.

OBJECTIVE: To investigate the impact of PGTA on ongoing pregnancy rates based on infertility diagnosis.

MATERIALS AND METHODS: We conducted a retrospective cohort study of all patients who had a transfer of a frozen embryo that underwent PGTA or not (nonPGTA) between January 2018 and December 2021, excluding only those who utilized a gestational carrier or donor oocytes. Patients were stratified by infertility diagnosis. Baseline characteristics including age and BMI were compared. The primary outcome was ongoing pregnancy rate (OPR) and a secondary outcome was miscarriage. Data analysis was performed using Mann-Whitney U test and Chi-square (P < 0.05). A mixed-effects logistic regression was used to account for clustering of transfers associated with individual patients. Analyses were completed in R version 4.1.0 (Vienna, Austria).

RESULTS: A total of 1,574 transfers were identified; 484 transfers were of embryos who had PGTA, 1,090 were of embryos that did not. The PGTA and nonPGTA group were similar in BMI (mean 25.15 vs 25.40, P = 0.1482). The PGTA group was older, with median age 37 years compared to 33 years in the nonPGTA group (P < 0.001). The miscarriage rate was similar between the two groups (PGTA 5.8%, 32/550 vs nonPGTA 4%, 10/247; P = 0.30). When investigating by diagnosis, OPR was significantly higher in PGTA group only in the setting of diminished ovarian reserve (DOR) (58.5%, 24/41 vs 29.3%, 12/41; P = 0.0076). OPR was higher in the nonPGTA group with patients with absolute male factor such as same-sex couples or single females (63.6%, 14/22 vs 31.2%, 5/17; P = 0.0487). After adjusting for age and BMI, PGTA was associated with statistically significant increase in OPR only in those with DOR diagnosis (adjusted OR 3.41, CI 1.27–9.38; P = 0.014). There was a trend towards higher OPR with PGTA with male factor infertility, though this did not reach statistical significance (adjusted OR 1.53, CI 0.96–2.42; P = 0.172). There was no diagnosis for which PGTA was negatively impacted by PGTA.

CONCLUSIONS: The impact of PGTA on OPR is controversial. After adjusting for age, PGTA increased OPR only for those diagnosed with DOR. PGTA was associated with 3.45 times higher OPR in patients with DOR regardless of age. While there was a trend towards increased OPR when PGTA was employed in patients with male factor infertility, this did not reach statistical significance. Despite limitations due to the sample size and the positively impacted by PGTA in our study, this is the first study, to our knowledge, to investigate usefulness of PGTA by infertility diagnosis.

IMPACT STATEMENT: By identifying a patient population that benefits the most from PGTA, this study provides novel information to tailor patient care and insight into the pathophysiology of DOR.

PREIMPLANTATION GENETIC TESTING IN OPTIMIZING CLINICAL OUTCOMES IN INFERTILE COUPLES WITH ADVANCING MATERNAL AGE. Sydney Souness, B.S., Philip Xie, B.S., Stephanie Cheung, M.S., Olena M. Kocur, B.A., Zev Rosenwaks, M.D., Gianpiero Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To assess the role of preimplantation genetic testing for aneuploidy (PGTA) on ICSI frozen embryo transfer (FET) cycle outcomes.

MATERIALS AND METHODS: Over a ten-year period, we evaluated FET cycles of blastocysts generated through ICSI using ejaculated spermatozoa in two cycles, embryos were transferred with and without PGTA for aneuploidy. Clinical outcomes including implantation, clinical pregnancy, and delivery/ ongoing rates were assessed and compared between FET cycles of untested embryos and cycles with embryos tested by PGTA-A, stratified by maternal age, and grouped as Cohort 1 (≤31), Cohort 2 (32–35), Cohort 3 (36–42), and Cohort 4 (≥43). To minimize bias of morphological embryo selection, only first-time single embryo transfer cycles were included.

RESULTS: Of the total 2,371 first-time single embryo FET cycles, 408 transferred untested day-5 embryos and 1,963 transferred euploid blastocysts confirmed by PGTA-A.

In Cohort 1, the implantation rate of FET cycles performed with untested embryos was 65.6% (65/99), comparable to cycles using PGTA-A-tested embryos at 72.0% (154/214). Following a similar trend, cycles with untested embryos had a delivery/ongoing rate of 49.5% (49/99), and cycles with PGTA-A–screened embryos had a slightly higher rate of 59.3% (127/214).

In Cohort 2, FET cycles with untested embryos resulted in 60.3% (73/121) and 45.4% (55/121) for implantation and delivery/ongoing rates, respectively. PGTA-A–screened FET cycles yielded a 72.2% (333/461) implantation rate and a 59.4% (274/461) delivery/ongoing rate.

In Cohort 3, there was a significant difference in the implantation rates between untested (57.6%, 83/144) and PGTA-A embryos (68.9%, 804/1166) (P < 0.01). Similarly, the delivery/ongoing rates for cycles with embryos tested by PGTA-A (54.4%, 634/1,166, P < 0.01) were remarkably higher than for cycles utilizing their unscreened counterparts (36.1%, 52/144).

In Cohort 4, 54.5% (24/44) of untested embryos implanted, proceeding to a 31.8% (14/44) delivery/ongoing rate. Contrastingly, FET cycles with screened embryos observed resulted in an implantation rate of 70.5% (86/122, P < 0.05) and a delivery/ongoing rate of 55.7% (68/122, P < 0.01).

CONCLUSIONS: The implementation of testing embryo ploidy has shown its validity and usefulness in FET cycles with advanced maternal ages. The additional costs and presumed embryo distress involved with PGTA-A are justified beginning at age 36.
ENDOMETRIAL PREPARATION BY HORMONE REPLACEMENT AND DAY 6 BIOPSED EUPLOID BLASTOCYST TRANSFER (BT) INCREASES THE RISK OF MISCARRIAGE COMPARED WITH AN OVULATORY CYCLE AND DAY 5 BIOPSED EUPLOID BT. Takashi Horikawa, MD, Koji Nakagawa, M.D., Ph.D., Hideaki Watanebe, Ph.D., Keiji Kuroda, MD, PhD, Satoru Takamizawa, MD, PhD, Rikikazu Sugiyama, MD, PhD Sugiyama Clinic Shinjuku, Tokyo, Japan.

OBJECTIVE: Accepted theory posits that more than half of the causes of pregnancy loss involve aneuploidy of the transferred embryos or blastocysts. This explanation has recently come into question, however, due to the clinical application of preimplantation genetic testing for aneuploidy (PGT-A). In an effort to further elucidate the risk factors for miscarriage, we retrospectively evaluated the clinical data between ongoing pregnancies and cases of miscarriage following euploid blastocyst transfer.

MATERIALS AND METHODS: Between January 2020 and April 2021 we evaluated 389 pregnant women who had received euploid blastocyst transfer. Written informed consent was obtained from each participant. All blastocysts underwent a TE biopsy on either Day 5 (D5) or Day 6 (D6) for PGT-A, and those were cryopreserved. The extracted TE cells were analyzed via NGS. The endometrial preparation for thawed euploid blastocyst transfer was accomplished either by hormone replacement cycle (HRC) or natural ovulatory cycle (NOC). Clinical pregnancy was defined as the existence of a gestational sac via transvaginal ultrasound. The miscarriage rate was evaluated according to the clinical background. A p-value of <0.01 was considered statistically significant. All statistical analyses were performed with EZR.

RESULTS: Among 389 pregnant women, 42 miscarried for a miscarriage rate (MR) of 10.8%. According to the endometrial preparation, HRC showed a higher MR (16.0%) than NOC (7.5%, p<0.01). D6 biopsy and repeated implantation failure (RIF) cases also showed a higher MR than that shown by D5 biopsy (17.3% vs. 9.1%, p<0.05) and non-RIF cases (18.5% vs. 6.7%, p<0.01). However, there was no difference between the MR in the cases of repeated pregnancy loss (PRL) (9.2%) and that in the non-PRL cases (11.6%, p=0.487).

CONCLUSIONS: From this evaluation using euploid blastocyst transfer, HRC showed an MR that was higher than that for NOC. It seemed that no formation of corpus luteum in the HRC could lower the MR. Moreover, the extended culture needed for TE biopsy could cause the cytoplasm of embryos to age, and this could be a reason for the lower MR of the D6 blastocysts. IMPACT STATEMENT: This study suggests that practitioners should either use a method to select the best blastocyst from among euploid blastocysts or use an endometrial preparation method.

SUPPORT: None

P-586 6:45 AM Wednesday, October 26, 2022

COMPARISON OF CLINICAL OUTCOMES IN THE SLOW-DEVELOPING BLASTOCYSTS WITH OR WITHOUT PREIMPLANTATION GENETIC TESTING-ANEUPOLOIDY (PGT-A) IN THE FROZEN-THAWED CYCLE. Jihye Jeong, M.S., Juhee Lee, M.S., S. O. L. A. Yoon, B.S., Jisoo Han, PhD, Tae Hyung Kim, B.S., Jin Hee Eum, Ph.D., Ji Eun Park, M.D., Haengjun Jeon, M.D., Jin Yeong Kim, M.D. Ph.D., Woo Sik Lee, M.D. Ph.D. CHA Gangnam Medical Center, CHA University, Seoul, Korea, Republic of (South).

OBJECTIVE: Preimplantation genetic testing (PGT) is used for selecting euploid embryos to improve pregnancy outcomes after embryo transfer. Several research studies have suggested that slow-developing blastocysts on day6 show lower implantation rates (IR) compared to normal developing embryos on day5. However, some of researchers focus on that slow developing embryos are highly derived from women with diminished ovarian reserve. Therefore, this study was performed to investigate the potential of the slow-developing blastocysts with PGT-A in patients with recurrent spontaneous abortion (RSA) and/or recurrent implantation failure (RIF) undergoing FET.

MATERIALS AND METHODS: A total of 127 FET cycles with single embryo transfer (SET) were evaluated. This study evaluated the slow-developing blastocysts with or without PGT-A in couples with RSA and/or RIF undergoing FET from January 2020 to January 2022. 90 patients underwent freeze on day6, and 37 patients underwent freeze after embryo biopsy on day 6, respectively.

RESULTS: Female age was not different (36.1±3.5 yr vs. 36.7±3.6 yr, p=0.19) in the two groups. The clinical pregnancy rate and miscarriage rate were analyzed in these two groups. The clinical pregnancy rate (CPR, detectable gestational sac in 6th week of gestation) in the biopsy group was higher than that in the non-biopsy group, but there was no statistical significance (56.8% vs 52.2%, p=0.64). Otherwise, the miscarriage rate in the non-biopsy group (31.9%) was significantly higher than that in the biopsy group on day6 (4.8%, p=0.051).

CONCLUSIONS: The present study demonstrate that the biopsy group on day 6 showed higher clinical pregnancy rate and lower miscarriage rate than those in the non-biopsy group on day 6. IMPACT STATEMENT: Our data support that the selecting day6 blastocysts using PGT-A for transfer may reduce the risk of miscarriage and maintain pregnancy in women with RSA and/or RIF.

SUPPORT: This research was supported by a grant from Republic of Korea, NRF-2018R1D1A1B07043250.
IVF cycles that have a high percentage of embryos classified as mosaic. Further research into the mechanism behind post-fertilization mitotic errors and predisposing risk factors is needed.

**IMPACT STATEMENT:** Patients can be assured that there is no individual and/or cycle-specific characteristic found to be associated with experiencing >20% embryos diagnosed as mosaic in a single IVF with PGT-A cycle.

**SUPPORT:** None

**REFERENCES:**


**P-588 6:45 AM Wednesday, October 26, 2022**

**ASSESSING PATIENT COMPLIANCE WITH RECOMMENDED PRENATAL TESTING AND IDENTIFYING PREGNANCY AND NEONATAL OUTCOMES AFTER MOSAIC EMBRYO TRANSFER.** Stephanie M. Hallisey, MD,1 Katherine Koniaris, MD,1 Arti Taggar, M.D., M.P.H,1 Prachi N. Godiwala, MD,2 Daniel R. Grow, MD, MHCM 1University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT; 2Center for Advanced Reproductive Services, Farmington, CT.

**OBJECTIVE:** Preimplantation genetic testing for aneuploidy (PGT-A) is used to aid in selecting optimal embryos for transfer after in vitro fertilization (IVF) cycles. There is building evidence that transferring mosaic embryos can lead to live births clinically unaffected by chromosomal abnormalities. Prenatal testing with an amniocentesis is recommended after mosaic embryo transfer due to the possibility of placental mosaicism. Though this recommendation exists, no studies have evaluated patient compliance. Likewise, limited studies have evaluated the effect on mosaicism may have on pregnancy outcomes and neonatal/infant syndrome after transfer. Therefore, our objective was to assess patient compliance with recommended prenatal aneuploidy testing following mosaic embryo transfer and to investigate the effect of mosaic embryo transfer on pregnancy and neonatal outcomes.

**MATERIALS AND METHODS:** This case series included 21 mosaic embryo transfers from 19 women aged ≤45 years who underwent IVF with PGT-A. Single mosaic frozen embryo transfers performed between 5/2017 and 3/2021 at a single academic fertility center were included. Data collection was performed via chart review and telephone interview of patients. The primary outcome was performance of prenatal amniocentesis. Secondary outcomes included alternative prenatal genetic testing, pregnancy or delivery complications and diagnosed neonatal/infantile medical conditions.

**RESULTS:** Of the 21 mosaic embryo transfers included in the study, 14 were low-level mosaic (67%) and 7 were high-level mosaic (33%). Four transfers did not result in pregnancy (19%), four resulted in biochemical pregnancy (19%), one resulted in miscarriage (5%), one resulted in an ongoing pregnancy (5%), and eleven resulted in live births (52%). Of the 12 ongoing pregnancies/live births, only 2 prenatal amniocenteses were performed (16.7%). Both amniocenteses were negative for all conditions tested. Chorionic villus sampling was not performed after any transfer. Non-invasive prenatal testing with cell-free DNA was performed in 6 cases and was negative for all conditions tested. A postnatal karyotype was performed in one case with findings of a balanced translocation consistent with the paternal karyotype. There were no pregnancy or delivery complications. There was one case of Tetralogy of Fallot identified prenatally with an underlying chromosome abnormality. There were no other neonatal/infantile medical conditions identified.

**CONCLUSIONS:** Most patients achieving pregnancy after a mosaic embryo transfer did not undergo recommended prenatal aneuploidy testing. Of those who did, the results were negative for all tested conditions. There were no pregnancy or delivery complications, or neonatal/infantile medical conditions identified after transfer.

**IMPACT STATEMENT:** Patient compliance with prenatal aneuploidy testing following mosaic embryo transfer is low. To address this, we recommend initiating the use of clinical educational protocols and specific consent forms for mosaic embryo transfer to emphasize the recommendations for genetic testing.

**P-589 6:45 AM Wednesday, October 26, 2022**

**THE PERFORMANCE AND IMPACT OF TWO WHOLE GENOME AMPLIFICATION APPROACHES FOR NON-INVASIVE GENETIC TESTING.** Zhixin Hu, B.S.,1 Yonggang Li, M.S.,2 Lifeng Xiang, Ph.D,2 Kexin Chen, B.S.,1 Mei Tian, M.D.,2 Mingying Li, M.SC,1 Yunxiu Li, M.D.,2 Xi Luo, M.D.,2 Xiaorang Wu, M.D.,2 Ze Wu, Ph.D,1 Jiayong Yan, Ph.D 1Kuming University of Science and Technology School of Medicine, Kunming, China; 2Department of Reproductive Medicine, First People’s Hospital of Yunnan Province, Kunming, China.

**OBJECTIVE:** To investigate the performance and differences of two whole-genome amplification (WGA) methods of Malbac and PicoPLEX in non-invasive preimplantation genetic testing(niPGT) based on spent media (SCM) in in vitro cycle.

**MATERIALS AND METHODS:** From 2020~2022, 122 embryos from PGT-SR patients and 61 embryos from PGT-A patients were tested with invasive biopsy based NGS as golden standard. All embryos underwent laser-assisted hatching incubation on Day4. Trophoectoderms(TE) cells were collected from each embryo on day 5-6 and detected by MALBAC-NGS. SCM samples(30µl) were collected at Days5/6, and a single SCM sample was divided into two aliquots using two WGA methods, noninvasive genetic testing(MALBAC,Yikon) or DOP-PCR(PicoPLEX.Agene). All SCM samples were from fresh embryos. For TE biopsy, >4Mb copy number variation(CNV) and 30~80% mosaic ratio is considered. For SCM, >10Mb CNV and 30~80% mosaic ratio is considered.

**RESULTS:** In the whole PGT, SCM-DOP-PCR and SCM-MALBAC had a higher karyotype concordance rate of 79.03%(49/62) and 82.1%(55/67) for apparently abnormal (abnormal fragments >20M) TE biopsy. However, for PGT-SR, SCM-DOP-PCR and SCM-MALBAC showed 66.7%(60/90) and 69.3%(61/88) clinical concordance with the corresponding TE biopsy samples. For PGT-A, SCM-DOP-PCR and SCM-MALBAC samples showed 51.2%(21/41) and 53%(25/46) clinical concordance with the corresponding TE biopsy samples. Additionally, no statistically significant differences were detected in the aforementioned values of the SCM-DOP-PCR and SCM-MALBAC in either clinical concordance rate or apparent abnormal concordance rate (P > 0.05). In addition, the amplification rates of DOP-PCR and MALBAC were 77.6%(142/183) and 77.05%(141/183), respectively. Though both methods show higher abnormal chromosome rate with differences region, no significant hotspot observed. In general, there are some differences between SCM and biopsy, for which we focused on follow-up. The current 4 follow-up results showed that the prenatal diagnosis was consistent with the TE biopsy, even in the miscarriage samples.

**CONCLUSIONS:** Our result suggest that there seems no significant difference(including amplification success rate, clinical consistency and many more) between DOP-PCR and MALBAC in niPGT studies. However, the high karyotype concordance rate of niPGT and biopsy in clearly abnormal fragments will have certain application prospects.

**IMPACT STATEMENT:** Two different detection approach with different bias suggest the technic details of non-invasive testing requires improvement currently. More basic and clinic research are required to promote the application of this technology. Combining biopsy based approach and non-invasive approach may be considered as a comprehensive tools for embryo implantation prediction. At the same time, the current research results can prove that niPGT is a good choice in excluding obviously abnormal embryos for people who do not meet the subclinical criteria for PGT application.

**SUPPORT:** Natural Science Foundation of China: 31700798, 82060282, 82160294

High level Project of Yunnan Province: YNOQ-QNRC-2018-126, H-2017024, 2017HC009;

**P-590 6:45 AM Wednesday, October 26, 2022**

**IMPACT OF DISCREPANT VARIANT CLASSIFICATION ON PREIMPLANTATION GENETIC TESTING FOR MONOGENIC CONDITIONS (PGT-M).** Rawan I. Awwad, MS, CGC,1 Andria G. Besser, MS, CGC,1 James A. Grifo, MD, PhD,1 Gina M. Davis, MS, CGC1 Certified Genetic Counselor, Birmingham, MI; 2NYU Langone Fertility Center, New York, NY; 3NYU Langone Prelude Fertility Center, New York, NY; 4Advocate Genetics, Elk Grove, CA.
OBJECTIVE: The use of sequencing-based genetic testing has resulted in increasingly complex results interpretation. In contrast to diagnostic testing, only variants believed to be pathogenic or likely pathogenic (LP) are reported in carrier screening, while variants believed to be benign, likely benign (LB), or of unknown clinical significance (VUS) are not typically reported by the testing laboratory. However, laboratories frequently disagree on variant classification, and classifications may also change over time, as more data is compiled. Therefore, the same patient may have different results depending on the laboratory used and time of results reporting. The objective of this study was to assess the impact of discrepant variant classifications on use of PGT-M.

MATERIALS AND METHODS: Known cases in which discrepant variant classification complicated PGT-M decision-making. Nine cases were identified through carrier screening, and one involved both carrier screening and diagnostic testing. The condition involved was X-linked in six cases, and autosomal recessive in four cases. The variant in question was initially reported as LP in 6/10 cases, and as pathogenic in 4/10 cases by the carrier screening laboratory. In 8/10 cases, at least one other laboratory disagreed with the initial classification and instead classified the variant as VUS, LB, or benign. In one case, the laboratory informed about a reclassification of an LP variant to VUS upon further inquiry, and in the last case, the laboratory reported a variant as pathogenic while omitting essential details about recessive and variable expressivity. In the majority of cases (6/10), learning about discrepant variant information altered patient decision making regarding use of PGT-M; however, only one patient elected not to continue with PGT-M. Four other patients continued with PGT-M but planned to consider variant-positive embryos for transfer if needed, and in the last case, the patient was undecided between PGT-M or selecting a new gamete donor.

CONCLUSIONS: Discrepancies in variant classification between testing laboratories can pose challenges for decision-making about the use of PGT-M, and may lead to unnecessary use of this technology. Genetic counseling and thorough variant review is essential prior to PGT-M initiation, to ensure that both patients and clinicians have all necessary and current data to make informed reproductive decisions. The need for carrier screening laboratories to contribute variant-specific information to publically available databases and include thorough variant-specific annotations on test reports is paramount to improving patient care and reducing both emotional and financial burdens of this costly and complex treatment.

IMPACT STATEMENT: This study is the first to demonstrate the impact of discrepant variant classification between carrier screening laboratories on PGT-M use.

E-POSTER ABSTRACT STATION: W16

P-591 6:45 AM Wednesday, October 26, 2022

CONFLICT RESOLUTION: DISCORDANT REPORTING OF CANCER GENE VARIANTS: VUS VS PATHOGENIC: Alexandra Peyser, M.D.,1 Kenan Onel, M.D., Ph.D.,2 Avner Hershlag, MD3 Northwell Health Fertility, Zuckier School of Medicine at Hofstra Northwell, Manhasset, NY, 2Sema4, New York, CT, 3Island Fertility, Stony Brook University, Commack, NY.

OBJECTIVE: Identifying correctly germline pathogenic variants in hereditary cancer genes has enormous consequences for individuals and families potentially at high risk for cancer due to genetics. Because each testing laboratory uses its own algorithms to determine pathogenicity, there can be conflicts whereby one lab classifies a variant as pathogenic (P) or likely pathogenic (LP) and therefore actionable, whereas another classifies the same variant as a Variant of Uncertain significance (VUS) and therefore not actionable. Here, using a core panel of 21 cancer genes, we investigated the occurrence of conflicted classification among testing labs over time.

MATERIALS AND METHODS: For the National Comprehensive Cancer Network recommended 21 gene cancer screening panel, we analyzed the number of variants in conflict per gene (P/LP vs. VUS) over time using ClinVar Miner1 to assess conflicts in the ClinVar database2 (a public archive of human genetic variants) in 2019, 2021, 2022 (Note: no data reported for 2020). The number of conflicted variants per gene over time was compared using ANOVA.

RESULTS: We found a 65% increase in the total number of VUS identified over time (2019: 25,492, 2021: 22,434, 2022: 42,166), and a 157% increase in the total number of conflicted variants (2019: 313, 2021: 506, 2022: 806; 2019: 1.2% vs. 2022: 1.9%, p = .12). ATM and BRCA1 were among the top 3 genes with the highest percentage of VUS in conflict (2019: 50%, 2021: 59%, 2022: 61%). Dominant genes consistently had more VUS’s than recessive genes (2019: 69% vs. 50%; 2021: 67% vs. 32%, 2022: 67% vs. 32%) as well as a higher percentage of VUS’s in conflict (2019: 89% vs. 11%, 2021: 80% vs. 20%, 2022:83% vs. 16%).

CONCLUSIONS: 1. The rate of conflicting reports of variants (VUS vs. Pathogenic or Likely Pathogenic) has increased in 3 years by 157%, while the overall percentage of VUS’s in conflict has remained below 2%.

2. These data indicate that many more cases reported initially as VUS’s may be reclassified as pathogenic and therefore become actionable.

3. Dominant cancer genes have a statistically significant higher rate of VUS’s in conflict.

4. This finding is of especially relevant in reproductive genetics since dominant cancer gene mutations are more actionable than recessive variants.

5. Upgrading of VUS’s for cancer genes has dual clinical significance: Cancer prevention measures in the patient carrying the mutation, coupled with PGT-M to prevent increased transmission to the offspring.

6. As the genomic basis of malignancy continues to unravel, we should be aware that variants reported as VUS’s could potentially be upgraded and therefore demand appropriate counseling and action. ART holds the only powerful tool to date to alter the burden of cancer each year. The gene with the higher percent in conflict varied each year. (2019: BRCA1 3.3%, 2021: TP53 3.3%, 2022: BRCA1 4.9%).

IMPACT STATEMENT: Variants of unknown significance (VUS’s) for hereditary cancer genes are increasingly reported, with more variants in conflict between different labs, presenting a dilemma for REI physicians as to whether PGT-M should be recommended.

REFERENCES:
1. https://clinvarminer.genetics.utah.edu

P-592 6:45 AM Wednesday, October 26, 2022

KARYOMAPPING AS A UNIVERSAL APPROACH FOR PGT-M: OVER 14, 6 THOUSAND CYCLES, 8 6 THOUSAND CASES, 4000 MUTATIONS AND 900 DISEASES: Alessia Schadwell, MSc,1 Olivia Whiting, BS MSc,1 Pere Colls, Ph.D,2 Elizabeth Cameron, M.S.,2 Thomas McWilliams, BS,3 N-neka Goodall, NYS CLT, BA,4 Leoni Xanthopoulou, Ph.D,5 Evangelia Bakosi, M.S.C,5 Tony Gordon, PHD,5 Darren K. Griffin, DSc1 1University of Kent, Canterbury, United Kingdom, 2University of London, Kent, Canterbury, United Kingdom; 3CooperSurgical, Trumbull, CT; 4CooperSurgical; 5CooperSurgical, Livingston, NJ; 5COOPERGENOMICS, London, United Kingdom.

OBJECTIVE: To demonstrate the universality of Karyomapping, through a large series of preimplantation genetic testing for monogenic diseases (PGT-M) cases.

MATERIALS AND METHODS: Cases with known monogenic disease status were prepared and processed for PGT-M by three CooperSurgical laboratories between 2014 and 2021, using Karyomapping with concurrent direct mutation analysis by Sanger sequencing. All patients were counselled at enrolment regarding specific genes, mutations and inheritance patterns associated with certain hereditary monogenic disorders. Confirmation through an external mutation report was a requirement for inclusion and 23 functional groups were created to categorize each disease for downstream analysis.

RESULTS: A total of 14,606 PGT-M cycles from 8,615 cases were performed using Karyomapping, with 4,082 pathogenic gene mutations identified and additionally confirmed in cycle by Sanger sequencing. We identified 912 individual monogenic disorders, of which cystic fibrosis was the most common (n=789 cases), followed by hereditary breast and ovarian cancer 1 and 2 (n=673 cases), then Fragile X Syndrome (n=654 cases). Classification of all disorders into functional groups showed that metabolic disorders were the most frequent type (n=1,121), followed by diseases of the musculoskeletal system (n=1,10), then multisystemic conditions (n=76).

CONCLUSIONS: Karyomapping is a highly versatile and accurate technology that facilitates PGT-M. With over 900 different disorders identified, this is the largest case series of individual PGT-M disorders, in which we demonstrate that it provides a reliable and adaptable methodology to discover novel pathogenic mutations, avoid at risk haplotypes and hence prevent the implantation of affected embryos for IVF patients.
OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) is widely used in IVF and aims to improve outcomes by avoiding aneuploid embryo transfers. Unlike other PGT-A methods, PGT-A analyzed using next generation sequencing (NGS) make it possible to identify mixes of aneuploid and euploid cells in trophoderm biopsies. In such instances the source embryos are classified as mosaic. Also, some IVF clinics are routinely transferring embryos diagnosed through PGT-A as mosaic aneuploid with greater frequency to patients who lack available euploid embryos. However, there is little data concerning the impact of mosaicism on viability, and the optimal clinical pathway for such embryos is unclear. This study aimed to report on our clinic’s clinical outcomes associated with mosaic embryo transfer, and to find out whether it should be considered for transfer when no euploid embryos are available.

MATERIALS AND METHODS: This is a retrospective cohort study that reviewed 70 mosaic embryo transfers from February 2020 to August 2021. Mosaic embryo transfer was offered to 58 women who only had mosaic embryos. Mosaic embryos were labeled by utilizing next generation sequencing (NGS) based PGT-A for day 5/6 trophoderm (TE) biopsies.

RESULTS: Mosaic embryo transfer occurred in 58 cycles (mean age = 38.0) with 70 embryos. Of the 58 mosaic embryo transfer cycles, 32 (55.2%) established a chemical pregnancy, 30 (51.7%) developed an embryonic sac (implantation), and 26 (44.8%) developed a fetal heartbeat (FHB). Of those 30, 23 (47.9%) established a chemical pregnancy, 30 (51.7%) developed an embryonic sac, and 26 (44.8%) developed a fetal heartbeat. Of those 26, 14 (50.0%) whole chromosome mosaic embryos implanted. The ongoing pregnancy rate was significantly higher in segmental mosaic embryos (14/24; 58.3%) compared to IF/SAB (8% vs. 59%, p = 0.041). Similar proportions of low vs. high mosaicism (OP/LB: 80% low vs. IF/SAB: 76% low, p = 0.41). Similar proportions of low vs. high mosaicism (OP/LB: 80% low vs. IF/SAB: 76% low, p = 0.99) were seen.

CONCLUSIONS: This study demonstrates that mosaic embryos can have high implantation potential according to embryo grading systems established for euploid embryos. Only 25% of Day 7 embryos resulted in OP/LB, indicating that, similar to euploid embryos, mosaic day 7s may have lower success rates but can still be worth transferring. Our findings suggest that embryos reported as mosaic which result in OP/LB are likely to have normal preimplantation genetic testing.

IMPACT STATEMENT: It is imperative that the modern fertility center contribute to collaborative efforts required for accurate data modeling. Detailed analysis of embryo composition, prenatal testing, and pregnancy outcomes enables evidence-based support to increase clinical adoption of mosaic embryo transfer in routine care.

OBJECTIVE: Transfer of mosaic embryos has been demonstrated to result in healthy live births. Acceptance for mosaic embryo transfer has grown among many reproductive clinics, yet additional data is needed to establish mosaic embryo transfer as standard of care. This study aims to assess embryo characteristics, prenatal genetic testing, and pregnancy outcomes following transfer of embryos reported as mosaic at a single academic center.

MATERIALS AND METHODS: The study included all patients who had mosaic results after preimplantation genetic testing for aneuploidy using Next Generation Sequencing and planned a single, frozen-thawed mosaic embryo transfer from July 2020-March 2022. Embryo grade, day of biopsy, prenatal genetic testing, and transfer outcomes were assessed. Types of chromosomal anomalies and low vs. high mosaicism were compared among transfers resulting in ongoing pregnancy/live birth (OP/LB) vs. implantation failure or loss (IF/SAB) using chi square and Fischer’s exact tests.

RESULTS: A total of 28 patients with a planned single, frozen-thawed mosaic embryo transfer were identified. One embryo did not survive thaw, and a total of 27 transfers were performed. Pregnancy occurred in 15 patients (55%), and 10 transfers resulted in OP/LB (37%). 5 pregnancies ended in spontaneous abortion (SAB) (33%). 4 of 8 eligible patients underwent diagnostic prenatal genetic testing via amniocentesis, all with normal results. Microarray was performed in one 11 week SAB and was normal; the other pregnancy losses could not be tested. All 5 live births resulted in healthy neonates. Trends were observed in embryo quality, day of biopsy, and types of chromosomal anomalies when comparing embryos resulting in OP/LB to those resulting in IF/SAB. A higher proportion of high quality embryos (≥4BB) was seen among those transferred in OP/LB (80% vs. 59%, p = 0.41), and higher proportions of Day 5 embryos vs. Day 7 embryos resulted in OP/LB (OP/LB: 60% vs. 59% Day 5 vs. 10% vs. Day 7; IF/SAB: 24% Day 5 vs. 18% Day 7, p = 0.17). Compared to transfers resulting in IF/SAB, successful transfers involved a higher proportion of single segmental anomalies and a lower proportion of single whole chromosome anomalies (OP/LB: 40% segmental vs. 20% whole; IF/SAB: 2% segmental vs. 65% whole, p = 0.15). Similar proportions of low vs. high mosaicism (OP/LB: 80% low vs. IF/SAB: 76% low, p = 0.99) were seen.

CONCLUSIONS: Transfer of mosaic embryos has been demonstrated to result in healthy live births. Acceptance for mosaic embryo transfer has grown among many reproductive clinics, yet additional data is needed to establish mosaic embryo transfer as standard of care. This study aims to assess embryo characteristics, prenatal genetic testing, and pregnancy outcomes following transfer of embryos reported as mosaic at a single academic center.

MATERIALS AND METHODS: The study included all patients who had mosaic results after preimplantation genetic testing for aneuploidy using Next Generation Sequencing and planned a single, frozen-thawed mosaic embryo transfer from January 2020 to February 2022. Our primary outcome was embryo mosaicism status; secondary outcome was the level of mosaicism. Embryos were classified as euploid if the trophoderm (TE) biopsy result contained <20% mosaicism; low level mosaic with 20–40%; high level mosaic with 41–80%; and aneuploid with >80%. Baseline demographics including age, BMI, AMH, baseline FSH, baseline antral...
follicle count, infertility diagnosis and gravity, cycle characteristics and embryologic data were collected. ANOVA, Kruskal-Wallis, chi-square, and multivariate logistic regression were used for statistical analysis.

RESULTS: A total of 1583 women that underwent an IVF cycle with ICSI/PGT-A had mosaic embryos: Of these women, 786 self-reported as White (49.6%), 92 as Black (5.8%), 389 as Asian (24.5%), 185 as Hispanic (11.6%), 47 as other (2.9%), and 84 (5.3%) did not specify their race. Black women were significantly older (38.0 ± 3.1 years, p = 0.006), had a higher BMI (28.1 kg/m², p = 0.001) and a higher prevalence of uterine factor infertility (14.5%, p < 0.0001; 9.4%, p = 0.0001 respectively). Asian women had the highest fertilization rate (79.7 ± 16.3%; p<0.0001), however, Black women had the highest rate of biopsied blastocyst (70.6%; p = 0.0001) compared to other groups. All other cycle characteristics were similar among groups. A total of 10650 embryos were analyzed, 5052 were reported as euploid (47.5%), 2256 as mosaic (21.1%) and 302 as indeterminate (2.9%). After re-biopsing the indeterminate embryos, a total of 2362 mosaic embryos were included in the analysis. The rate of embryonic mosaicism was similar among all groups (22.3%; p = 0.6), however, Black women had on average more high-level mosaic embryos (68.5%) when compared to their counterparts (White 48.1%, Asian 49.4%, Hispanic 52.3%, other 50.1%, non-specified 53.5%, p = 0.02). After adjusting for age, BMI, infertility etiology, fertilization rate and number of biopsied embryos there was no association between race and higher odds of mosaicism (aOR 0.96, 95% CI 0.6-1.3, p = 0.85) nor higher odds of high-level mosaic embryos (aOR = 1.01, 95% CI 0.9-1.08, p = 0.51).

CONCLUSIONS: The rate of embryos identified as mosaic was comparable among women of different racial backgrounds. These results suggest that the occurrence of mitotic errors involved in mosaicism is neither influenced by self-reported race nor ethnicity.

IMPACT STATEMENT: With the increasing availability of large-scale multi-ethnic disease modeling, we are able to provide a better insight to biological processes of embryonic mosaicism.

P-596 6:45 AM Wednesday, October 26, 2022

MOASIC DEVELOPMENT IS MORE STRONGLY INFLUENCED BY THE FREEZE/THAW PROCESS RATHER THAN BY THE NUMBERS OF CELLS COLLECTED AND LASER IRRADIATIONS

Yamato Mizobe, Ph.D.1, Yukari Kuwatsuru, Bachelor,1 Yuko Kuroki, Bachelor,1 Yumiko Fukumoto, Registered Nurse,1 Mari Tokudome, Bachelor,1 Harue Moewaki, Master,1 Marina Tabira, Medical Doctor,1 Tokiko Iwakawa, Medical Doctor,1 Kazuhiro Takeuchi, Ph.D.1 1Takeuchi Ladies Clinic, Aira-shi- Kagoshima, Japan; 2Takeuchi Ladies Clinic/Clinic for Reproductive Medicine 502-2 Higashimochida- Aira-shi- Kagoshima, Japan 899-5421, Japan; 3Takeuchi Ladies Clinic/Center for Reproductive Medicine 502-2 Higashimochida- Aira-shi- Kagoshima, Japan.

OBJECTIVE: Frozen blastocysts are occasionally used for biopsy after thawing. It has been reported that this procedure increases the incidence of mosaic development. However, studies have reported that the incidence of mosaic development differs between institutions, raising the possibility that the varying biopsy procedures may be responsible for this difference. In this study, we focused on the number of cells collected and the number of laser irradiations as distinguishing factors of the different biopsy procedures, and retrospectively investigated whether the difference in these numbers as well as the freeze-thaw of blastocysts influence the incidence of mosaic development.

MATERIALS AND METHODS: We performed an NGS-based diagnosis on blastocysts collected from 2020 to 2021 from females who provided consent to discard them at the end of the culture. Thaw-biopsy was designated as Group A and normal biopsy as Group B. The blastocysts were classified into three categories: euploid, mosaic, and aneuploid. These were also not differentiated based on the results of the NGS diagnosis. Pulling method with laser irradiation was employed for biopsy. We comparatively examined the effects of differing numbers of cells collected and laser irradiations on the determination of blastocyst categorization (euploidy: 23.2-31.5%, mosaic: 14.2-16.1%, aneuploidy: 22.3-62.6%). The results were further analyzed for mosaicism ratio (20%-25% and 30%-40%) mosaic embryos. Neither the mosaicism ratio, nor number of laser irradiations was large. These results suggest the number of cells collected and laser irradiations do not influence mosaic development. The freeze-thaw increased incidence of mosaic development.

IMPACT STATEMENT: Neither the number of cells collected nor the number of laser irradiations influenced mosaic development. However, the freeze-thaw increases the incidence of mosaic development.

P-597 6:45 AM Wednesday, October 26, 2022

PREGNANCY OUTCOMES OF EUPOID EMBRYOS ARE COMPARABLE TO LOW-RATE MOSAIC EMBRYOS: RESULTS OF 403 EMBRYOS FROM A SINGLE ART CENTER.

Mehmet Ali Tufekci, PhD, Beril Yuksel, Assoc. Prof. MD, Gulcin Ozkara, PhD, Hakan Kadir Yelke, M.SC, Cigdem Cinar Yapan, MsC, Semra Kahraman, Prof. MD Istanbul Memorial Sisli Hospital, Istanbul, Turkey.

OBJECTIVE: To compare the pregnancy outcomes of euploid and low-rate mosaic embryos transferred between April 2021 and February 2022, in a single ART center.

MATERIALS AND METHODS: As of April 2021, we started to report embryos with 30% or less mosaicity detected by next generation sequencing (NGS) as euploid embryos. Although the genetic laboratory knew the exact result, the clinicians and the patients were blind to the NGS results at time of embryo transfer. In order to see if this decision was the right one, we aimed to evaluate whether the outcome of euploid embryos and these low-rate mosaic embryo transfers were different or not, during the same time period. Low-rate mosaicism was defined as mosaicism affecting between 20% and 30% (30%) included). The implantation rate (IR), total pregnancy loss rate (TPL) and ongoing pregnancy rates (OPR) were compared.

The results were further analyzed for mosaicism ratio (20%-25% and 30%) and mosaicism type (segmental mosaicism, single chromosome mosaicism, double chromosome mosaicism and complex mosaic which was defined as mosaicism affecting more than two chromosomes).

RESULTS: Out of 3151 trophoectoderm biopsied embryos from 905 PGT cycle, 1112 were reported as euploid. A total of 403 embryo transfers were done within the specified time. Of these, 299 were diagnosed as euploid and 104 as low-rate mosaic.

When pregnancy outcomes were compared between euploid and low-rate mosaic embryos, there were no statistical difference in terms of IR, TPL rate or OPRs (Table 1). The mosaicism ratio did not change the results. However, the IR and OPR showed a decreasing trend as the number of chromosomes involved in mosaicism increased, although the difference was not statistically significant (p<0.05). There were no difference in terms of morp-kokinetic parameters in time lapse imaging system and top-good quality (TG-QG) blastocyst ratios between euploid and low-rate mosaic embryos (p>0.05).

CONCLUSIONS: Pregnancy results were comparable between euploid and low-rate (≤30%) mosaic embryos. Neither the mosaicism ratio, nor the mosaicism type affected the results.

IMPACT STATEMENT: With NGS technique becoming more applicable for PGT-A instead of a-CGH, the rate of reporting mosaic embryos has also
increased. However, despite the large number of studies published, many couples still refrain from mosaic embryo transfers, which have the potential to achieve a live birth. Our data has shown that low-rate mosaic embryos (≤30%), behave like euploid embryos. Therefore, reporting low-rate mosaicism (≤30%) as euploid, will prevent unnecessary discard of potentially viable embryos.

OBJECTIVE: With increasing use of NGS as the platform of PGT-A, more embryos were categorized as mosaic, which led to many challenging clinical questions for both clinicians and patients, not only regarding the causes of mosaicism but also its clinical outcomes. The aim of this study was to assess which blastocyst characteristics were the most correlated with the outcomes of single mosaic embryo transfers (METs).

MATERIALS AND METHODS: Data was collected retrospectively from January 2018 to December 2021. A total of 596 cycles of single blastocyst transfer after PGT-A. There were 565 single euploid blastocyst transfers. Single mosaic/aneuploid embryo transfer was offered to 31 women who did not have euploid embryos (25 mosaic and 06 fully abnormal blastocyst cycles). Embryos were categorized as mosaic when abnormal cells were identified within the 20–80% range of aneuploid embryo biopsy, and we used 50% as a cutoff to classified mosaic level into low or high. Mosaic type referred to whole chromosome or segmental mosaicism. The blastocysts were graded at the time of biopsy based on the Gardner and Schoolcraft scoring system. The pregnancies after mosaic/aneuploid embryo transfer were performed amniocentesis and diagnosed by SNP array.

RESULTS: METs showed a significant lower live birth rate (LBR) and higher spontaneous abortion rate (SAR) when compared with control group (LBR: 32.0% vs 52.2%; SAR: 16.1% vs 6.8%, p<0.05, respectively). There was one live birth after six cases of abnormal embryo transfer, accounting for 16.7%. There was no correlation between low or high level of mosaic and unfavorable outcomes (LBR: 28.6% vs 36.4%, SAR: 14.3% vs 18.2%, respectively). Segmental mosaicism tended to have better clinical outcomes than the whole-chromosomal mosaic group, but the difference was not significant (LBR: 33.3% vs 25%; SAR: 20.0% vs 12.5%, p<0.05). Embryo morphology showed a strong correlation between mosaicism and potential of getting pregnancy. Grade 1 embryo transfers resulted in significantly higher live birth rate than grade 2/3 group (66.7% vs 14.3% and 13.6%, p<0.05). Amniocentesis results of all 09 pregnancies were euploid karyotype and gave birth to healthy babies.

CONCLUSIONS: Mosaic embryos have lower pregnancy rates while increase the risks of miscarriage. There is no correlation between mosaic type and mosaic level with the success rate. The quality of embryo transfer is the most important factor influencing pregnancy outcomes. Further studies with a larger sample size are essential to confirm these findings.

IMPACT STATEMENT: In patients with no euploid embryos after PGT-A, mosaic embryos with a good quality could be the choice for transfer because they still have the potential to implant and develop into normal healthy babies.

P-600 6:45 AM Wednesday, October 26, 2022
ARE THE MORPHOKINETIC PARAMETERS OF MOSAIC EMBRYOS DIFFERENT FROM EUPOID EMBRYOS? RESULTS OF 1167 EMBRYOS DIAGNOSED BY NEXT GENERATION SEQUENCING (NGS) FROM A SINGLE CENTER. Beril Yuksel, MD, Assoc. Prof.,1 Gülcin Ozkara, PhD,2 Mehmet Ali Tufekiçi, PhD,3 Gonul Ozer, MD,4 Melih Aygun, M.D.,4 Senem Kahraman, MD Prof.4 1Istanbul Memorial Sisi Hospital, Istanbul, Turkey; 2Senior Embryologist, Istanbul, Turkey; 3Infertility specialist, Istanbul, Turkey.

OBJECTIVE: To compare the morphokinetic parameters of mosaic and euploid embryos in time lapse imaging system (TLI) and to analyze the relation between these parameters and clinical outcomes of mosaic embryo transfers.

MATERIALS AND METHODS: TLI parameters of euploid and mosaic embryos tested with next generation sequencing (NGS) in Istanbul Memorial Hospital between March 2017 and March 2022 were retrospectively compared. TLI parameters of mosaic embryos were also analyzed within themselves according to their mosaicism type (segmental, single chromosome, double chromosome and complex mosaic (mosaicism affecting more than two chromosomes)) and mosaicism rate (<40% vs ≥40%).

The pregnancy outcomes after transfer of all single mosaic embryos and their relation between TLI parameters were also analyzed.

RESULTS: TLI parameters, except for time to reach morula (tM) and blastulation (tB), were comparable between euploid and mosaic embryos (Table). Mosaicism rate did not affect TLI parameters (p>0.05). However, time of pronuclei appearance (DNAs) was longer in double compared to single chromosome mosaics (p=0.01). The interval between tM and tB was longer in double chromosome vs segmental mosaics (p=0.04).

A total of 245 mosaic embryos were transferred within the specified time. The overall implantation rate was 71%, biochemical and clinical pregnancy loss rates were 17.8% and 11.9%, and ongoing pregnancy rate (OPR) was 51.4%. The evaluation of both mosaicism type and ratio revealed a highest OPR with <40% segmental mosaic embryos (65.0%).
TLI data were available for 74 of the transferred mosaic embryos and these parameters did not reveal any significant differences according to implantation and ongoing pregnancy rates.

CONCLUSIONS: The morphokinetic behavior of mosaic embryos is similar to euploid embryos except that they reach the morula and blastulation faster.

IMPACT STATEMENT: Mosaic embryo transfers have introduced a relatively new concept in the field of ART and researchers keep investigating the parameters that affect pregnancy outcomes after mosaic embryo transfers. Our data has shown that mosaic embryos have similar morphokinetic features compared to euploid embryos and these parameters have no effect on pregnancy outcomes.

<table>
<thead>
<tr>
<th>Euploid Embryo (n=864)</th>
<th>Mosaic Embryo (n=303)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>tPNa</td>
<td>8.44±2.43</td>
<td>.73</td>
</tr>
<tr>
<td>tPNF</td>
<td>23.48±4.27</td>
<td>.55</td>
</tr>
<tr>
<td>t2</td>
<td>26.00±3.14</td>
<td>.88</td>
</tr>
<tr>
<td>t3</td>
<td>36.86±4.36</td>
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<td>t4</td>
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<td>.75</td>
</tr>
<tr>
<td>t6</td>
<td>52.12±6.17</td>
<td>.26</td>
</tr>
<tr>
<td>t7</td>
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</tr>
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<td>t8</td>
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<td>.24</td>
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<td>t9</td>
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<td>tSC</td>
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<td>.51</td>
</tr>
<tr>
<td>tM</td>
<td>86.17±8.88</td>
<td>.04</td>
</tr>
<tr>
<td>tSB</td>
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<td>.09</td>
</tr>
<tr>
<td>tB</td>
<td>105.03±7.10</td>
<td>.01</td>
</tr>
<tr>
<td>tEB</td>
<td>111.08±7.00</td>
<td>.37</td>
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</tbody>
</table>

SUPPORT: None

E-PERSON ABSTRACT STATION: W17

P-601 6:45 AM Wednesday, October 26, 2022

SEGMENTAL ANEUPLOID HOTSPOTS IDENTIFIED ACROSS THE GENOME WERE highly concordant with trophectoderm (TE) biopsies.

MATERIALS AND METHODS: Segmental aneuploidies were identified at hotspots across the genome and were highly concordant in blinded re-analysis. The most frequent coordinate was observed at chr1q21.2 (n=378). Blinded re-analysis of 162 blastocysts validated the original TE diagnosis in 20 of 21 euploid blastocysts, 85 of 87 aneuploid blastocysts and 51 of 54 segmental deletion embryos for overall concordance of 96.3%. All remaining blastocysts were identified with a mosaic configuration (n=6; 3.7%).

CONCLUSIONS: Hotspots for segmental imbalances, which predominantly included distal ends of chromosomes, were identified in this large cohort of embryonic sub-aneuploidy variants. Concordance rates across blastocyst re-analysis segments showed high uniform consistencies with the initial TE biopsy and the entire embryo, including for segmental aneuploidies. Nevertheless, future studies assessing their reproductive potential are critical to rule out any potential gestational risks.

IMPACT STATEMENT: Segmental aneuploidies were identified at hotspots across the genome and were highly concordant in blinded re-analysis.

SUPPORT: None

P-602 6:45 AM Wednesday, October 26, 2022

UNBALANCED TRANSLLOCATION RATES IN PREIMPLANTATION EMBRYOS FROM COUPLES WITH COMPLEX CHROMOSOMAL REARRANGEMENT.

UNBALANCED TRANSLLOCATION RATES IN PREIMPLANTATION EMBRYOS FROM COUPLES WITH COMPLEX CHROMOSOMAL REARRANGEMENT. Eun Jeong Yu, M.D.,1 Min Jee Kim, M.S.,2 Sun Ok Park, M.S.,2 Ye Seul Hong, M.S.,2 Gaeul Han, M.S.,2 Eun A Park, M.S.,4 Kyong Hui Choi, Ph.D.,5 Hye Ok Kim, M.D.,6 Inn Soo Kang, M.D., Ph.D.6 Department of OB/GY CHA Fertility Center Seoul Station, CHA University, Seoul, Korea, Republic of (South); Labor-atory of Medical Genetics, CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South);1 Labor-atory of Medical Genetics, CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South);2 Labor-atory of Medical Genetics, CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South);3 Labor-atory of Medical Genetics, CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South);4 Labor-atory of Medical Genetics, CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South);5 Labor-atory of Medical Genetics, CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South);7 Labor-atory of Medical Genetics, CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South).

OBJECTIVE: Complex chromosomal rearrangements (CCRs) are constitutional structural rearrangements that involve three or more chromosomes with more than two breakpoints. CCR carriers have a high risk of recurrent spontaneous abortion and birth of offspring with abnormal phenotype. The Preimplantation genetic testing for structural rearrangement (PGT-SR) can reduce the miscarriage rate and improve clinical outcomes. However, the odds of normal or balanced embryo for CCR carriers is not clear. There are scanty data on the effect of different types of CCR on abnormal embryo rate. Herein, we evaluated the difference in the unbalanced translocation rate in a series of preimplantation embryos from couples with CCR.

MATERIALS AND METHODS: This retrospective study included 17 couples who underwent assisted reproduction and PGT-SR at the CHA Seoul Fertility Center, Seoul Station from July 2015 to January 2022. The trophectoderm (TE) biopsies on day 5 and 6 were analyzed by NGS. All the patients have been informed by a written informed consent. A total of 260 embryos were transferred from 17 couples who underwent the PGT-SR cycle by NGS. Results were classified as ‘euploid’ for normal or balanced, ‘unbalanced’ if segmental aneuploidy is detected for chromosomes involved in the parental CCR, or ‘sporadic aneuploidy’ if other chromosomes were among among CCR carriers.

RESULTS: Overall mean maternal age was 33.4 years (range 29–42). PGT-SR results were obtained from 250 (96.2%) samples. Overall rates are euploid, 13.5%; unbalanced, 29.3%; unbalanced plus sporadic aneuploidy, 16.1%; sporadic aneuploidy, 37.3%. For three-way CCR type (mean maternal age 33.5 years), 20 cycles with 163 samples were tested with the following rates: euploid, 11.6%; unbalanced, 28.8%; unbalanced plus sporadic aneuploidy, 17.2%; sporadic aneuploidy, 39.3%. For exceptional CCR type (mean maternal age 33.7 years), 10 cycles with 80 embryos were tested with the following rates: euploid, 17.5%, unbalanced, 30%, unbalanced plus sporadic aneuploidy, 12.5%; sporadic aneuploidy, 36.3%. For double two-way CCR type (mean maternal age 32.2 years), 4 cycles with 17 samples were tested with the following rates: euploid, 11.8%; unbalanced, 29.4%; unbalanced plus sporadic aneuploidy, 23.5%; sporadic aneuploidy, 23.5%.

CONCLUSIONS: There was no significant difference in the unbalanced rates among CCR carriers. Different types of CCR may have little effect on the abnormal embryo rate.

SUPPORT: None

e360 ASRM Abstracts Vol. 118, No. 4, Supplement, October 2022
IDENTIFICATION OF MATERNAL CELL CONTAMINATION IN EMBRYO CULTURE MEDIA USING PARENTAL BuccAL SWABS AND NON-INVASIVE PGT-A. Bryan Nikolai, PH.D.,1 Alexander Griffith, B.S.,2 Christopher Wejer, Ph.D.3 Mike Large, Ph.D.,1 Joshua Blazeck, Ph.D.3 Houston, TX; 3Coopersurgical, Houston, TX; 4CooperSurgical, Houston, TX.

OBJECTIVE: This study sought to sensitively detect maternal cell contamination and describe the biochemical nature of DNA in embryo culture media for the purpose of non-invasive PGT-A.

MATERIALS AND METHODS: Research participants were identified with collaborating assisted reproductive technology centers and consented under IRB supervision. Intent to treat for PGT-A was a requirement of the study, there were no other exclusion criteria. Buccal Swab Kits (BSK) were requested of both parents to sequence in parallel. A total of 160 patients, 151 of which provided pairs of BSKs, resulted in 626 informative outcomes.

The primary outcome tested was ploidy concordance between culture media and trophoderm biopsy (TE), with secondary outcomes being maternal cell/DNA contamination (MCC) and parental dosage. Alternative whole genome amplification techniques allowed resolution of DNA molecular length. Antibodies against histone H3 were used to immunoprecipitate cfDNA from embryo culture media.

RESULTS: Consistent with previous reports suggesting a model where cfDNA accumulates with time the embryo is in culture, pre-amp and post-amp concentrations of DNA were elevated when media was harvested on Day 6 or Day 7 versus those collected on Day 5. Average DNA concentrations of embryo culture media was estimated to be ~1pg/μL, using at least two different methods of quantification. This extrapolates to about 3-4 cell-genome equivalents being present in a 20μL culture droplet.

A major advance of this study is the use of parental genetics to perform trio analyses and obtain parental dosage scores for each media sample. The sophisticated data analysis platform for PGTai uses artificial intelligence to reliably predict karyotype from trophoderm biopsy NGS results. This platform was retrained with data from noninvasive PGT-A results to incorporate the unique nature of cfDNA in embryo culture media. Concordance rates between TE and embryo culture media improved with time in culture. Remarkably, less than half of 46,XX samples were concordant with TE biopsy including 20% of media samples identified as euploid female actually being euploid male or mosaic in the TE biopsy. The new analysis pipeline can identify MCC and apply a parental dose score for each parent, whereby a threshold can then be set to flag or gate samples with contamination.

CONCLUSIONS: This study was performed to test PGT-A concordance rates between DNA amplified from TE biopsy and embryo culture media. Results indicate that concordance between embryo culture media and TE biopsy is generally about 80% and is affected by the amount of time the embryo spends in the culture media. Parental buccal swabs allow detection of MCC and identification of unreliable non-invasive PGT-A results for 46;XX embryos. Finally, the existence of chromatinized DNA in embryo culture media may give clues to the cellular origin and mechanism of egress of cfDNA in the media.

IMPACT STATEMENT: This study demonstrates the utility of parental genetics for detection of maternal cell contamination during non-invasive PGT-A testing and advances understanding of the nature of cfDNA in embryo culture media.

EVALUATION OF CELL-FREE NUCLEIC ACIDS IN BASTOCOEEL FLUID CONDITIONED MEDIA AND ITS POTENTIAL FOR NON-INVASIVE EMBRYO ASSESSMENT. Jacob Meyers, PhD.1 Linbo Zhao, PhD.1 Nao Yasayuma, MS.1 Jay Kim, PhD.1 Karthik Padmanabhan, PhD.1 Nathan R. Trefl, PhD.1 HCLD.1 Diego Marin, PhD.2 Licrciott, NJ.1 Genomic Prediction, Inc., North Brunswick, NJ; 2University of South Carolina School of Medicine Greenville, Greenville, SC.

OBJECTIVE: The goal of this project is to evaluate cell-free nucleic acids released into blastocoel fluid-conditioned media (BFCM) by a mature blastocyst as a sample type for non-invasive embryo assessment.

MATERIALS AND METHODS: To generate BFCM samples, embryos were washed and moved into individual biopsy media droplets for trophectoderm (TE) biopsy. TE biopsy was performed and blastocysts were collapsed, releasing blastocoele fluid into the media droplet. The entire BFCM droplet was collected for downstream cfDNA and cfRNA analysis. Sample processing for cfDNA was done using Embgenix™ ESM Screen.

To quantify the cfDNA/cfRNA, we evaluated the quantity and level of fragmentation of cfDNA/cfRNA in the BFCM. Libraries were constructed for sequencing on an Illumina MiSeq and analyzed using Embgenix™ Analysis Software. BFCM results were also compared to previously generated spent media results from a separate cohort of embryos. Both cfDNA/cfRNA concentration and fragmentation was analyzed for each sample and compared by using generalized linear mixed models.

RESULTS: BFCM samples contained a similar cfDNA quantity and fragmentation score compared to embryo spent media from embryos. WGA yields correlated with cfDNA input quantity, but not cfDNA fragmentation grade. Informative sequencing reads and calculated copy number noise (measured by DLRS) also correlated with cfDNA input, with stable performance down to approximately 2pg of cfDNA input. Detectable cfDNA was observed in BFCM and was described to generate a cfDNA library for sequencing. Compared to the cfDNA, the quality and quantity of RNA in BFCM samples was found to vary considerably.
CONCLUSIONS: The cfDNA released into BFCM following TE biopsy is similar to the quantity and quality (fragmentation) of cfDNA passively released into spent culture media by a developing embryo. WGA yield, informative reads and DLRS of BFCM samples were also similar to data previously generated with spent media samples, suggesting that BFCM has potential as a non-invasive assessment of embryo ploidy status. In the case of cfRNA, the intrinsic instability of RNA remains a challenge for employing RNA to investigate embryo health.

IMPACT STATEMENT: The BFCM samples are often discarded in general PGT-A practices. Our results suggest that these typically discarded BFCM samples contain significant amounts of cf-nucleic acids that pose diagnostic potential with spent media samples. Analysis of these BFCM samples could be used in parallel with conventional PGT-A to select and/or rank embryos for implantation.

P-606 6:45 AM Wednesday, October 26, 2022

SHOULD SLOW DEVELOPING BLASTOCYSTS THAT DO NOT REACH THE FULLY EXPANDED STAGE ON DAY 5 BE BIOPSIED ON DAY 6? Eun A. Park, MS, Jung Hyun Lee, MS, Gayun Song, MS, Juyeong Lee, MS, Hyunsoo Kim, MS, Min Jee Kim, MS, Yun Jung Hur, M.D., Eun Jeong Yu, M.D., You Shin Kim, M.D, Ph.D., Myung Joo Kim, M.D.1 CHA Seoul Fertility Center, Seoul, Korea, Republic of (South); 2CHA Seoul Fertility Center Seoul Station, Seoul, Seoul, Republic of (South); 3CHA Fertility Center Seoul Station; 4CHA Fertility Center-Seoul Station, Seoul, Korea, Republic of (South); 5Laboratory of Medical Genetics, CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South); 6CHA Fertility Center Seoul Station; 7CHA Fertility Center-Seoul Station, Seoul, Korea, Republic of (South); 8CHA Fertility Center Seoul Station; Obstetrics and Gynecology, Seoul, Korea, Republic of (South); 9CHA University, Seoul, Korea, Republic of (South).

OBJECTIVE: Not all blastocyst reach the fully expanded stage by day 5; those are the slow developing blastocysts. There is a lack of evidence regarding the implantation potential of slow developing blastocysts that determines the day of TE biopsy. To evaluate the clinical outcomes of not fully expanded blastocysts biopsied on day 5 and fully expanded blastocysts biopsied on day 6.

MATERIALS AND METHODS: This retrospective cohort study included 572 FETs of slow developing euploid blastocysts frozen on day 5 or 6, belonging to patients undergoing preimplantation genetic testing A (PGT-A) between January 2019 and October 2021, in a single fertility center. Laser assisted hitching (Hamiliton Thorne Bioscience, USA) was not performed on day 3-4. Blastocysts were analysed either with comparative genomic hybridization or next generation sequencing. All euploid blastocysts were transferred 18-24h after thawing. We compared clinical outcomes of slow developing euploid blastocysts on day 5 versus (n = 372) and day 6 (n = 200). Among these groups, good-quality (grade: ≥BB) blastocysts on day 5 versus (n = 247) day 6 (n =103) were compared outcomes. Slow developing euploid blastocysts group consisted in graded 1,2(blastocyst stage) on day 5 and 3,4,5(blastocyst stage) on day 6 according to the Gardner’s system. Differences in pregnancy rates between study groups were compared using a Chi2 test. A p-value <0.05 was considered statistically significant.

RESULTS: The clinical pregnancy outcomes were significantly higher when FET slow developing day 5 euploid blastocysts compared to day 6 for all the pregnancy outcomes analyzed: biochemical pregnancy rate was 75.0% vs 60.5%, p < 0.05; clinical pregnancy rate was 67.5% vs 47.0%, p < 0.001); ongoing pregnancy rate was: 62.9% vs 40.0% (p < 0.05). Also, slow day 5 blastocyst of good-quality (grade: ≥BB) had a significantly higher than those day 6 in pregnancy rates (CPR: 74.1% vs. 57.3% P<0.001; OPR: 68.0% vs. 49.5%, P<0.001) The biochemical loss rates were significantly lower in slow day 5 blastocysts(7.5% vs 13.5%, p < 0.05). Similarly, slow day 5 blastocyst of good-quality (grade: ≥BB) had a significantly lower than those day 6 in biochemical loss rates (5.3% vs 12.3%, p < 0.001).

CONCLUSIONS: Slow developing blastocysts that is not fully expanded on day 5 should be biopsied on day 5.

IMPACT STATEMENT: These results suggest that when blastocysts exhibit a slow speed of development behavior(not reaching full blastocysts at day 5), waiting until day 6 for expansion does not improve clinical outcomes. Such data not only can help to determines biopsy dates in slow developing blastocysts, but also it may be an additional selection criterion for transfer in patients with multiple euploid blastocysts.

Table 1. PGT-A utilization in 2010 compared to 2020.

<table>
<thead>
<tr>
<th># of pts (% total)</th>
<th>n=49 (2.3)</th>
<th>n=2448 (49.7)</th>
</tr>
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<tr>
<td>Diagnosis: Mean (SD)</td>
<td>8.2 (318)</td>
<td>13.0 (13.0)</td>
</tr>
<tr>
<td>DOR</td>
<td>1 (2.0)</td>
<td>71 (2.9)</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>0</td>
<td>21 (0.9)</td>
</tr>
<tr>
<td>Hydroalpinx, in place</td>
<td>0</td>
<td>144 (5.8)</td>
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<tr>
<td>Other tubal disease</td>
<td>5 (10.2)</td>
<td>439 (17.9)</td>
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<tr>
<td>Male infertility</td>
<td>4 (8.2)</td>
<td>286 (11.7)</td>
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<tr>
<td>Ovulation disorder</td>
<td>0</td>
<td>51 (2.1)</td>
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<tr>
<td>Uterine factor</td>
<td>5 (10.2)</td>
<td>464 (19.0)</td>
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<td>Unexplained</td>
<td>3 (6.1)</td>
<td>76 (4.9)</td>
</tr>
<tr>
<td>RPL</td>
<td>30 (61.2)</td>
<td>654 (26.7)</td>
</tr>
</tbody>
</table>

Table 1. PGT-A utilization in 2010 compared to 2020.

2010 2020 p-value

| Age at Retrieval | 36.10 (4.74) | 36.06 (3.87) | 0.55 |
| Gs | 4.00 (2.14) | 1.69 (1.53) | <0.001 |
| Ps | 0.96 (0.76) | 0.31 (0.64) | <0.001 |
| Prior Miscarriage | 39 (79.6) | 825 (33.7) | <0.001 |

SUPPORT: None

REFERENCES:
GROWTH HORMONE SUPPLEMENTATION AMELIORATES BLASTOCYST EUPLOIDY RATES AND PREGNANCY OUTCOMES IN PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY CYCLES. Qingqing Gao M.M.,1 Junhao Yan, M.D., Ph.D.,2 Zi-Jiang Chen, M.D., Ph.D.3 Center for Reproductive Medicine, Shandong University, Jinan, China; 2Center for Reproductive Medicine, Shandong University, Jinan, China; 3Center for Reproductive Medicine, Shandong University, Jinan City, China.

OBJECTIVE: To investigate whether growth hormone (GH) improves blastocyst euploidy in women undergoing preimplantation genetic testing for aneuploidy (PGT-A) cycles.

MATERIALS AND METHODS: This was a prospective cohort study conducted from January 2018 to September 2020 among women whose previous PGT-A cycle ended up with no transferrable blastocysts, or the aneuploidy rate was above 50% and no live birth was acquired. The participants were divided into two groups according to whether GH co-treatment was implemented, which was initiated at the dosage of 2 IU/d on day 1–5 of the previous menstrual cycle until the trigger day of ovarian stimulation. Frozen single euploid blastocyst transfer was performed. The frequency of euploidy and the live birth rate of the two groups were compared.

RESULTS: A total of 208 women were recruited for the study: the GH group, including 96 women, the control group, including 112 women. Women’s demographic and cycle characteristics did not differ significantly between the two groups. Compared to the control group, the number of euploid blastocysts was greater (0.67±0.97 vs. 0.36±0.66, p=0.020) and the aneuploidy rate was lower (32.00% vs. 21.05%, P=0.015) in the GH group. The rate of women who had euploid blastocysts was also higher in the GH group (40.63% vs. 27.68%, P=0.049). In the frozen-embryo transfer cycles, women in the GH group demonstrated a higher implantation rate (72.09% vs. 42.11%, P<0.001) and clinical pregnancy rate (72.09% vs. 43.24%, P=0.009). Live births occurred in 27 women (28.13%) in the GH group and in 12 (10.71%) in the control group (P=0.001).

CONCLUSIONS: Our study presented preliminary evidence that GH supplementation could ameliorate blastocyst aneuploidy and pregnancy outcomes for women with previous PGT-A cycle failure. The application of growth hormone for women who experienced a failed PGT-A cycle might be considered and further studied.

IMPACT STATEMENT: The GH adjuvant in assisted reproductive technology has been in the spotlight of scientific concern in recent years. The beneficial effect of GH on embryo euploidy indicates that GH may process the potential of improving oocyte quality. This emphasizes the possibility of GH clinical application, especially among women who are in urgent need to enhance the oocyte quality such as those with advanced age, recurrent pregnancy loss, et al. This study also figures out the necessity of further scientific research of the underlying mechanism as well as clinical trials with larger sample size to confirm the conclusion.

P-600 6:45 AM Wednesday, October 26, 2022

INNER CELL MASS AND TROPHOECTODERM MORPHOLOGY PATTERN IN LOW AND HIGH-LEVEL MOSAIC EMBRYOS: WHERE ARE THEY IN THE EUPLOID-ANEUPLOID LINE? Renata Erberelli, BSc, Catherine K. Jacobs, MSc, Mariana Barreto, BSc, Jose Roberto Alegretti, MSc, Aline R. Lorenzon, PhD Huntington Medicina Reprodutiva - Eugin Group, Sao Paulo, Brazil.

OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) by next generation sequencing (NGS) has improved sensibility for the embryo’s ploidy report, however provides some diagnostic of uncertain clinical significance, such as mosaicism. Clinical management and ranking of mosaic embryos remain a challenge for providers. There is still lack of knowledge if other parameters could help to identify and better classify mosaic embryos. Since embryo morphology grade is routinely used for embryo selection, the aim of this study was to assess if there are differences in the morphology grade of inner cell mass (ICM) and trophoectoderm (TE) in blastocysts reported as low or high mosaics, comparing to the grading of euploid and aneuploid embryos.

MATERIALS AND METHODS: Retrospective cohort study with patients undergoing PGT-A-IVF cycles, according to medical referral, between Jan/ 2018 and Dec/2021, in a private ART center. All embryos were cultured in a time-lapse system incubator (Embryoscope) until blastocyst stage when a TE biopsy was performed. A total of 3278 biopsied embryos from 890 patients were included in this cohort. Blastocysts were graded morphologically according to Gardner’s criteria (9 groups, from AA to CC) and reported by PGT-A as euploid, aneuploid, low or high level mosaic. Mann-Whitney, Fisher and Chi-square tests were used for statistical analysis, p<0.05 was considered significant.

RESULTS: Most of embryos were reported as aneuploid (n=1753, 53.5%), followed by euploid (n=1472, 44.9%) and mosaic (n=53, 1.6%); high-level n=19, 0.6% and low-level n=34, 1.0%. Maternal age was similar between mosaic and euploid embryos (37.61±3.88 vs. 37.62±4.24, p=0.64, respectively); aneuploid embryos presented higher maternal age (39.42±3.33, p<0.0001). No difference in maternal age was observed between low and high level mosaicism (37.97±3.96 vs. 37.43±3.86, p=0.34, respectively). The incidence of mosaic embryos were similar across Gardner groups (lower incidence of 0.5% in BA to higher incidence of 2.4% in AB, p=0.072), as well in high and low levels of mosaicism (lower of 0.3% in BB to higher of 2.1% in CB, p=0.783). As expected, the highest euploid rate was found in top quality grade (AA, 66.3%) and the lowest in poorest quality embryo (CC, 21.0%). The opposite was observed for aneuploid embryos (CC, 77.5% and AA, 32.3%). Moreover, the presence of an A grade in TE increased the rate of euploidy in our cohort (p=0.00045). Patients under 38 years old showed a higher frequency of A grade in ICM and TE when compared to patients ≥38 years old in euploid embryos (p=0.015 and 0.0018, respectively). In mosaic embryos there was no difference of frequency in morphology grades according to subgroup of maternal age (<38 and ≥ 38 years old).

CONCLUSIONS: The ICM and TE morphology grades in mosaic embryos, independently of maternal age and the subclassification in low or high levels of mosaicism does not show a pattern of morphology frequency distribution, which is seen between euploid and aneuploid embryos.

IMPACT STATEMENT: Blastocyst ICM and TE morphology grades do not seem a good parameter to sub classify low and high level mosaicism.
OBJECTIVE: Perform a systematic review of cost-effectiveness studies of pre-implantation genetic testing and assess overall quality based on criteria proposed by the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.

MATERIALS AND METHODS: We performed a systematic review to identify all published studies performing cost-effectiveness analyses of pre-implantation genetic testing (PGT).PubMed, Embase, and Cochrane libraries were used to identify publications from inception to December 1, 2020 without date or language limits. Two independent researchers searched: “cost effectiveness analysis” and “preimplantation genetic screening”, “preimplantation genetic diagnosis”, “preimplantation genetic testing”, MeSH analysis: “cost-benefit analysis”, “costs and cost analysis” and “preimplantation diagnosis”, EMBASE: “preimplantation genetic testing” and “cost effectiveness analysis”, “preimplantation genetic screening” and “cost effectiveness analysis”. Studies in English were included if a cost-effective analysis was performed assessing PGT for aneuploidy (PGT-A) or single-gene disorders (PGT-M), with a comparator and cost data. Animal studies, abstracts, or secondary research were excluded. Reviewers scored articles based on criteria of the CHEERS checklist and extracted analysis type, costs, outcome, horizon, and willingness to pay threshold. A discussion and consensus process occurred to settle disagreements.

RESULTS: A total of 227 records were identified from the databases. One additional study was found through reference review. Of the 227 records, 81 were duplicates. Of the remaining studies, 37 were only abstracts and 95 full text articles were excluded (review n=24, editorial=13, no cost comparison = 47, technology other than PGT = 10). Ultimately 15 studies were included, published between 2008 to 2020. The number of analyses performed annually increased over time, with 5 published in 2020. Analyses were performed in many countries though the majority, 46% (n=7), were in the United States. Only 2 studies met all recommended criteria proposed by the CHEERS checklist. Studies met an average of 83% of the required and relevant components. Willingness-to-pay thresholds were reported in 13% (n=2) and time horizons in 60% (n=9) of the studies. All studies assessing monogenic disorders (n=5) were cost-effective, compared to only 60% (n=6) of those assessing PGT-A.

CONCLUSIONS: Cost-effectiveness analyses assessing the quality of PGT is a growing heterogeneous body of literature not uniformly adhering to recommended reporting guidelines to ensure reproducible and reliable results. PGT-M was consistently found to be cost-effective compared to PGT-A, which was cost-effective in only 60% of studies.

IMPACT STATEMENT: Despite widespread use of PGT-A, a systematic review of cost-effectiveness analyses rarely demonstrated reliable reporting of all key criteria and only 60% of PGT-A studies, compared to 100% of PGT-M studies, demonstrated higher quality, cost-effective care.
CONCLUSIONS: PGT-M has grown significantly over the past decade and is available for common and rare single gene conditions. This data shows that most patients who undergo PGT-M/IA will have at least one unaffected/uniparental embryo for transfer.

IMPACT STATEMENT: The availability of PGT-M as a reproductive option has increased significantly over the past decade and should be discussed in the setting of common and rare genetic conditions.

P-614 6:45 AM Wednesday, October 26, 2022
DEVELOPMENT AND VALIDATION OF A PRE-PLACEMENT GENOMIC TEST FOR MONOGENIC DISORDERS USING TARGETED NEXT-GENERATION SEQUENCING (PGTMxNGS). Christopher Weener, Ph.D.,1 Kedrick McKinsson, BS,1 Kavitha Mani, MS,1 Alexander Griffith, B.S.,2 Mike Large, Ph.D.,1 Joshua Blazeck, Ph.D.1 1CooperSurgical, Houston, TX; 2Spring, TX; 3CooperSurgical, Houston, TX.

OBJECTIVE: PGT-M is a molecular test that leverages SNV data to identify embryos that carry heritable genetic disorders. Array-based platforms have traditionally been utilized to obtain these data. The aim of this study was to evaluate the accuracy of a new NGS-based PGT-M karyomapping platform, encompassing workflow and bioinformatics pipelines. Concordance with the validated platform is the principal objective, followed by a test of the NGS platform’s ability to resolve challenging sample types, gene targets, and reference relationships with high confidence.

MATERIALS AND METHODS: Forty PGT-M cases (100 embryos) were used for method comparison. These cases represent the breadth of gene targets, inheritance patterns and reference relationships commonly observed in the clinic. Cases consisted of genomic DNA from maternal, paternal and reference buccal swabs, and amplified trophectoderm biopsies. Reference relationships ranged across siblings, grandparents and more distant relatives. Samples were processed in parallel using a commercial array-based platform and the newly developed capture sequencing approach. To resolve the mutation status of each embryo, SNV data was processed using a commercial software package or custom bioinformatics pipeline developed for the NGS platform.

RESULTS: PGTMxNGS showed 100% concordance with the array-based platform on calling the mutational status (100/100), agnostic of amplification type, gene target, and reference relationship. The density of SNV data was nearly equivalent between the array and NGS platforms (~10 SNV/Mb) with consistency, a measure of confidence in SNV data across the region, showing a high value for both (~.98 out of 1.0). Considering the entire diploid genome, approximately 96% of the total length was phased concordantly between both systems. Discordant regions are the combined result of a phased algorithm that considers individual SNV confidence and the dynamic nature of sequencing data that permits greater resolution of recombinant and repetitive regions.

CONCLUSIONS: This study aimed to show clinical equivalence between a commercially available array-based PGTM assay and one developed internally using a targeted NGS system. The outcome data shows 100% concordance between the platforms and strongly supports the overall accuracy and utility of PGTMxNGS. The mutational status of each embryo was derived from data that showed SNV quality, consistency, and distribution was similar across the platforms. Importantly, PGTMxNGS displayed a robust handling of challenging cases including distant relative references, consanguineous pedigrees, and de novo mutations as well as difficult centromeric and telomeric targets, and genes located in SNV-deserts.

IMPACT STATEMENT: PGTMxNGS represents a streamlined platform capable of efficiently generating large SNV datasets. Combined with an advanced phasing algorithm, the system produces accurate, highly resolved karyomap data and robustly identifies the mutational status of each embryo. The dynamic nature of the method suggests that even greater improvements are possible with future development.

P-615 6:45 AM Wednesday, October 26, 2022
LEVERAGING THE POWER OF THE TRIO IN PGT-A TO ASSESS FOR EXPECTED PARENTAL INHERITANCE IN A TROPHECTODERM BIOPSY. Alexander Griffeth, B.S.;1 Michael Large, Ph.D.2 Joshua Blazeck, Ph.D.1 1Coopersurgical, Houston, TX; 2Spring, TX; 3CooperSurgical, Houston, TX.

OBJECTIVE: The purpose of this experimental study was to develop an assay and bioinformatics algorithm to interrogate parental genome inheritance in an embryo trophectoderm biopsy during routine pre-implantation genetic testing for aneuploidy.

MATERIALS AND METHODS: 189 Trios (maternal DNA + paternal DNA + embryo biopsy) from 42 families with expected inheritance patterns as determined by PGT-M analysis that utilized the gold standard genome-wide SNP analysis (Karyomapping) were de-identified and utilized for this study. As part of Trio selection, both families with and without known sanguinity were included in the development process to ensure the algorithm’s robustness in various clinical scenarios.

Parental genomic DNA (gDNA) obtained from buccal swabs and DNA from embryo biopsies were processed through our standard PGT-A workflow and analyzed for CNV by the PGTAi2.0 algorithm. Embryo biopsies, regardless of ploidy status, were analyzed alongside the confirmed correct parents to establish reference ranges for expected inheritance. Each embryo biopsy was then tested against at least 3 different incorrect parental samples for each potential mismatch scenario to ensure robustness in the resulting PGT-complete platform.

RESULTS: In total 189 correct Trios, 887 Trios with unrelated maternal sample, 899 Trios with unrelated paternal sample, and 837 Trios with both parental samples unrelated were analyzed to assess the performance of the PGTAi2.0 plus parental QC algorithm. Total accuracy of the Parental QC algorithm was determined to be 99.85% (2808/2812) with a sensitivity of 99.96% (95CI: 99.79 – 100) and a specificity of 98.43% (95CI: 95.48 – 99.67).

CONCLUSIONS: This study demonstrates the ability to interrogate expected parental inheritance in a trophectoderm biopsy leveraging our standard PGT-A workflow and novel bioinformatics pipeline. Interrogation of inheritance patterns in embryo biopsies provides an additional level of confidence that would have been undetected. Further studies will be conducted to understand the frequency of unexpected inheritance patterns in trophectoderm biopsies.

IMPACT STATEMENT: This study demonstrates the ability to interrogate expected inheritance patterns in trophectoderm biopsies during routine PGT-A providing clinicians and patients alike additional confidence in both routine and custom bioinformatics pipelines developed for the NGS platform.

P-616 6:45 AM Wednesday, October 26, 2022
SINGLE-CELL MULTIOMIC ANALYSIS REVEALS DEFECTIVE GENE EXPRESSION AND DNA METHYLATION TOGETHER WITH CELL ANELOIDY ASSOCIATED WITH CLEAVAGE-STAGE EMBRYO ARREST. Marcos Meseguer, Ph.D.,1 Lorena Bori Arnal, PhD, Student,2 Jose Ramon Hernandez Mora, PhD,3 Claudia Buhiagas, PhD, Stephen Clark, Ph.D.,1 David Monk, Ph.D.1 JIVI Foundation Innovation - Reproductive Medicine IIS; 1La Fe, Valencia, Spain; 2IVIRMA Global, Valencia, Spain; 3University of East Anglia, Norwich, United Kingdom.

OBJECTIVE: The dynamic nature of the method suggests that even greater improvements are possible with future development.
OBJECTIVE: To characterize embryonic genome activation (EGA) and epigenetic reprogramming events in developmentally high-quality cleavage stage embryos and compare the resulting signatures with embryos that have undergone spontaneous cleavage-stage arrest, as determined by time-lapse imaging.

MATERIALS AND METHODS: High quality Day 3 embryos (CL3) em-

bryos were obtained following informed consent from couples who had delivered a healthy baby who wished to donate their remaining frozen em-

bryos for scientific research. In addition, cleavage embryos that had arrested at 4-16 cell stages were collected at day 5 having deemed to have undergone spontaneous cleavage arrest. These possessed good morphology with minimal fragmentation. Following laser incision-mediated blastomere biopsy to analyze the resulting single cells were subject to single-cell methylome and transcriptome sequencing (scM&T-seq) that allows for the physical separation of mRNA and genomic DNA. Single-cell bisulfite libraries (scMethyl-seq) were then prepared on purified DNA and RNA sequencing libraries were prepared using SMART-seq2 protocols.

RESULTS: Initial unsupervised clustering revealed that 40% of cells from arrested embryos (CL3a) clustered autonomously with the CL3 reference samples (CL3r), indicating they had activated their genomes appropriately, while the remaining CL3b clustered away from CL3r. Next, we focused on determining the differential expression profile of individual transcripts that had been previously identified as either specifically activated or expressed in CL3r datasets. DNA methylation analysis in arrested embryos revealed 8/13 embryos had significantly increased global methylation levels when compared with the CL3r dataset, indicative of a failure in epigenetic reprogramming. The 5/13 embryos that had largely normal methylomes possessed the aberrant CL3b expression signature. By utilizing the sequence coverage information from the scMethyl-seq datasets we determined chromosome complements. CL3r embryos had significantly less aneuploidy events compared to the arrested cohort (CL3a/CL3b). While the analysis was performed at single-cell rather than at embryo resolution, cell-specific aberrations were detected consist-

ent with mosaicism.

CONCLUSIONS: We identify embryos that fail to appropriately activate their genomes or undergo epigenetic reprogramming. Our results indicate that a failure to successfully accomplish these essential milestones impedes the developmental potential of pre-implantation embryos and is likely to have important implications, similar to aneuploidy, for the success of assisted reproductive cycles.

IMPACT STATEMENT: Our datasets will be useful in developing bio-
markers to improve our capacity to select the most competent embryos for transfer or cryopreservation.

SUPPORT: Monk lab: Spanish Ministry of Economy and Competitiveness (MINECO; BFU2017-85571-R), co-funded with the European Union Regional Development Fund (FEDER), the H2020 HUTER project from the European Union’s Horizon 2020 research and innovation program under grant agreement No 874867 and the BBSRC (BB/V016156/1). Meseguer lab: received funding from the Spanish Ministry of Economy and Competitiveness (CDTI; IDI-20180248), co-funded with the European Union Regional Development Fund (FEDER).

P-617 6:45 AM Wednesday, October 26, 2022

A QUALITY IMPROVEMENT PATHWAY (QIP) FOR FERTILITY CARE (FC) IN GENERAL OBSTETRICS AND GYNECOLOGY (GYN) CLINIC AT NEW YORK CITY (NYC)’S LARGEST PUBLIC HOSPITAL. Carlos M. Parra, MD; Jacqueline Shaw, MD; Sarah D. Cascante, MD; Shannon DeVore, MD; Jennifer K. Blakemore, MD, MSc; NYU Grossman School of Medicine, New York, NY; NYU Langone Fertility Center, New York, NY; NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: Infertility affects >100 million people worldwide; improving FC access is essential, especially for low socioeconomic and minority groups. In NYC’s public hospital system, patients (pts) are referred to a fellow-led reproductive endocrinology and infertility (REI) clinic that provides consults, work-ups and ultrasound-monitored controlled ovarian hyperstimulation and ovulation induction (OI). REI referrals (REF) are in high demand limiting appointment (appt) availability1 with new pts waiting 3-6 months. We executed a QIP to identify pts for OI counseling and initiation in GYN clinic.

MATERIALS AND METHODS: REI fellows screened all REFs, and scheduled eligible pts in GYN. QIP criteria: age <38 years (y); anti-Mullerian hormone (AMH) ≥2ng/mL; normal prolactin, thyroid function and hemoglo-

bin A1C; no known reproductive issues/comorbidities requiring high risk obst-

etrics; <3 prior OI cycles. Eligible pts received early follicular lutetrazone 2.5mg for 5 days (d) in GYN and were then followed in REI’s OI program. Non-eligible pts were scheduled in REI. To assess effectiveness, we retrospectively compared all REF-OUTcomes from PRE-(3/1/21-5/31/21) to POST-(9/1-

21-11/30/21) QIP as of 2/14/22. A transition period (6/1/21-8/31/21) was excluded. Primary outcome was time from REF to scheduled appt. Secondary outcomes included time from REF to OI prescription/cycle start. Statistics included Mann-Whitney, Chi-square, Fischer’s exact and Two-sample t tests (p<0.05 significant).

RESULTS: PRE (n=121) and POST (n=102) REFs had similar median ages [36 (interquartile range (IQR): 32-39) PRE vs 35y (IQR: 31-40) POST, p=0.73], ethnic/racial identity [56.2% (68/121) PRE vs 53.9% (55/ 102) POST Hispanic (p=0.79); 34.7% (42/121) PRE vs 30.4% (31/102) POST Black (p=0.59), and rates of no prior FC [88.4% (107/121) PRE vs 93.1% (95/102) POST, p=0.15]. QIP identified pts for GYN who were younger [median age 29 (IQR: 27-33) vs 38y (IQR: 33-41), p<0.01], had higher AMHs [median 3.065 (IQR: 2.315-4.883) vs 1.230 ng/mL (IQR: 0.513-3.630), p<0.01], and had fewer comorbidities [100% (19/19) vs 72.5% (50/69), p<0.01] compared to PRE. After QIP implementation, me-

dian time from REF to scheduled appt decreased from PRE 151 (IQR: 125-173) to POST 98d (IQR: 73-137) (p<0.01). For pts seen in clinic thus far, median time from REF to OI prescription decreased from 150 (IQR: 122-173) to 82d (IQR: 63-119) (p<0.01) and to 1st follicle check from 202 (IQR: 159-221) to 107d (IQR: 98-115) (p<0.04). In the POST cohort, 86.3% (88/102) of REFs had OI scheduled, with 21.6% (19/88) in GYN and 78.4% (69/88) in REI. OI was started at initial visit for 61.5% (8/13) of GYN pts vs 25.8% (8/31) of REI pts (p<0.04). 38.5% (5/13) of GYN pts met criteria for QIP, but were pending ≥1 blood test, while 51.6% (16/ 31) of REI pts were pending further work-up.

CONCLUSIONS: Our QIP expedited FC for all pts by reducing the time from REF to scheduled fertility appt by 35% (median of 53d) and to OI pre-

scription/cycle start by nearly 1 month (median of 68/95d).

IMPACT STATEMENT: Similar OI pathways could improve access to FC for underserved populations in broader practice settings.


P-618 6:45 AM Wednesday, October 26, 2022

ONLINE FINANCIAL TRANSPARENCY FOR FERTILITY CARE: A PATIENT NEEDS ASSESSMENT. Brittany E. Wordekemper, B.S.; Christopher M. Deibert, M.D., M.P.H; Omaha, NE; aUniversity of Nebraska Medical Center.

OBJECTIVE: To assess patients’ needs regarding online transparency for fertility care and develop means to share financial and expected outcome in-

formation with patients.

MATERIALS AND METHODS: An anonymous, voluntary, survey was conducted with new reproductive urology and endocrinology patients. We executed a cross-sectional analysis to assess patients’ preferences as they related to the need for online transparency for fertility care. This included do-

mains on testing, diagnosis, pricing, and outcomes.

RESULTS: 22 patients completed our survey, with 86% identifying as male. Our first subset of questions was regarding how much the patient would want to view certain information online before a fertility appointment. Regarding information about treatment options, 18% said they must have available, 59% said they would want to view if available, 18% said they might review if available. 27% of patients reported doing research online. There are not yet enough men and women participants related to the need for online transparency for fertility care. This included do-

mains on testing, diagnosis, pricing, and outcomes.

RESULTS: 22 patients completed our survey, with 86% identifying as male. Our first subset of questions was regarding how much the patient would want to view certain information online before a fertility appointment. Regarding information about treatment options, 18% said they must have available, 59% said they would want to review, 18% said they might review if available, and 5% said they do not need. For information about treatment outcome including success rates, 27% must have available, 50% want to re-

view, and 23% might review if available. For information about typical costs, 27% said they must have available, 64% said that they want to review, and 9% said they might review if available. 27% of patients reported doing research on the cost of fertility care prior to their first visit, all of whom, found this information online. There are not yet enough men and women to analyze any preference differences between groups. When asked how they would feel reassured, the other 18% said they were neutral. 77% agreed or strongly agreed that they would feel more in control and the other 23% said they felt neutral. When asked about preference regarding visiting a doctor
REFERENCES:


P-620 6:45 AM Wednesday, October 26, 2022

disparities and barriers to access: findings from an implementation study of an ai-augmented two-way chatbot for fertility care. Alexandra Acker, MD, Anuja Dokras, MD, PhD, Sumeeta Senapati, MD, MSCE University of Pennsylvania, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: To identify barriers to initiation of fertility care using an innovative AI-augmented text platform

MATERIALS AND METHODS: Patients seen at an academic center were offered enrollment in the Fast Track to Fertility (FTF) chatbot to facilitate completion of infertility work-up including lab tests, ultrasound, fallopian tube/uterine cavity evaluation, semen analysis and genetic screening. Text messages prompted patients about next steps and provided educational material. The chatbot uses natural language processing to facilitate communication and identify questions for escalation to the care team. Standard statistical tests were used to determine differences between patients who consented to use FTF and those who declined (No-FTF). Logistic regression was used to determine the association between patient characteristics and work-up completion.

RESULTS: Of the 182 patients referred to FTF, 124 were enrolled and 58 declined (see table). Although most subjects had insurance coverage for diagnostic testing, it was less in the No-FTF group (p=0.002) and even less for infertility treatment (p=0.002). Significantly more patients in the No-FTF group did not complete any work-up compared to FTF patients (32.8% vs 6.5%, p<0.001). More FTF patients completed the work-up within 60 days of the new patient visit compared to No-FTF patients (62.1% vs 37.9%, p=0.002). The drivers for failure to engage in any work-up in both groups were Black race and lack of insurance coverage for diagnostic testing. Black women were 4x less likely to pursue work-up compared to white women (OR 4.01, 95% CI, 1.31-12.3, p=0.015). Women without diagnostic testing coverage were 5x less likely to pursue work-up compared to those with diagnostic testing coverage (OR 5.23, 95% CI, 1.75-15.64, p=0.003).

| Age ≤ SD | 34.3 ± 4.70 | 34.1 ± 5.0 | 0.87
| Race       |               |               |   |
| White      | 73/124 (58.9) | 19/58 (32.8) | 0.004
| Black      | 35/124 (28.2) | 26/58 (44.8) |
| Other      | 16/124 (12.9) | 13/58 (22.4) |
| Diagnostic work-up insurance coverage | 118/124 (95.2) | 46/58 (79.3) | 0.002
| Fertility treatment insurance coverage | 93/124 (75.0) | 30/58 (51.7) | 0.002
| Work-up in 60 days |               |               |   |
| Complete   | 77/124 (62.1) | 22/58 (37.9) | 0.002
| Incomplete | 39/124 (31.5) | 17/58 (29.9) | 0.77
| None       | 8/124 (6.45)  | 19/58 (32.8) | <0.001
| Median time to work-up completion ≤ 60 days of new patient visit | 28.3 ± 11.8 | 31.9 ± 13.0 | 0.32

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with or without typical price information online, 68% said they would prefer to see a doctor with typical price information online and the other 32% said that it did not matter. 68% of patients also reported that having online information about treatment outcomes including success rates would affect their decision to see a doctor over another.

CONCLUSIONS: Our small survey study revealed that patients want more transparent information online about fertility care. An overwhelming majority of the patients reported that they want to view information about treatment options, outcomes, success rates, and typical costs. In addition, >¾ agreed that viewing typical fertility costs would help them feel reassured and more in control. Adding more information online and being transparent when it comes to fertility care is important to patients and allows them to make informed decisions about their medical care.

IMPACT STATEMENT: Our findings indicate that patients strongly desire more information and transparency regarding fertility care.

P-619 6:45 AM Wednesday, October 26, 2022

RACIAL AND SOCIOECONOMIC DISPARITIES IN 2019 EMERGENCY DEPARTMENT UTILIZATION FOR FIBROIDS IN THE UNITED STATES. Nicole Sekula, BA, Charley Jiang, MS, Anita Malone, MD, Martina T. Caldwell, MD, MS, Lauren A. Wise, Sc.D., Erica E. Marsh, MD, FACC, Ann Arbor, MI; 2MD/MSCR candidate, Ann Arbor, MI; 3University of Michigan, Ann Arbor, MI; 4Henry Ford Hospital; 5Boston University School of Public Health, Boston, MA; 6Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI.

OBJECTIVE: Uterine fibroids are benign tumors of the myometrium that can cause significant morbidity. Fibroids disproportionately affect Black females at 2-3 times the incidence of White females1. While fibroid symptoms are ideally treated in an outpatient clinic, there are more than 65,000 annual U.S. emergency department (ED) visits for fibroids. We assessed the association between race and sociodemographic characteristics on fibroid-related emergency care utilization and admission.

MATERIALS AND METHODS: The 2019 Healthcare Cost and Utilization Project Nationwide Emergency Department Sample (NEDS) database was used to identify patients aged 21-60 years who utilized the ED with a primary diagnosis of fibroids (ICD10 codes D25, D25.0-25.2, D25.9). NEDS first included race in 2019, which is the most recent year of available data. Exploratory variables assessed included race, income, insurance type/status. We used linear and logistic regression models to estimate associations of interest.

RESULTS: Of the 143 million ED visits in 2019, 42.29 million were among female patients aged 21-60 years. In this age group, 2.1% of patients identified as Asian-American/Pacific Islander (API), 24.8% Black, 16.0% Hispanic, 0.6% Native American (NA), 3.3% Other, and 51.6% White. Among the 66,150 visits coded with a primary diagnosis of fibroids, 2.9% of patients were identified as API, 45.6% Black, 21.5% Hispanic, 0.4% NA, 4.1% Other, and 24.6% White. A higher rate of Black patients used the ED for fibroids compared to all other primary diagnoses (p<0.001) and a similar trend was seen for Hispanic patients (p<0.001), whereas White patients used the ED less for fibroids (p<0.001). Among patients with fibroids, ED visits were highest for those using private insurance (42.1%) and those in the lowest income quartile (36.2%). Odds of hospital admission were similar between insurance types and income quartiles. Race (p<0.0005) and age (p<0.0001) were associated with significant differences in admissions with Black patients being admitted less than other groups. Mean charges associated with fibroid-related ED visits were $8,954, compared to mean charges of $4,990 associated with all other ED visits. Mean ED fibroid charges differed by race, with the lowest charges for NA patients at $7,235 followed by Black patients at $8,323 (p=0.0154).

CONCLUSIONS: Black patients made up almost half of fibroid-related ED visits (45.6%) despite accounting for only 24.8% of ED visits overall. Black patients were admitted at lower rates than other races and had one of the lowest mean associated charges, suggesting potential inequities in fibroid treatment in EDs. The high proportion of ED visits among patients in the lowest income quartile also suggests possible inequities in access to primary gynecologic services.

IMPACT STATEMENT: Here, we identify racial differences in ED utilization and admission for fibroids in the U.S. Future work should investigate health inequities in fibroid care and develop strategies that make primary outpatient gynecologic care more accessible and equitable.
CONCLUSIONS: Although use of digital health technology can expedite completion of fertility diagnostic testing, disparities related to access and race remain significant barriers to equitable delivery of fertility care.

IMPACT STATEMENT: Equitable delivery of fertility care will require multiple approaches such as leveraging technology and a deeper understanding of the impact of social determinants of health.

E-POSTER ABSTRACT STATION: W19

P-621 6:45 AM Wednesday, October 26, 2022

RACIAL DISPARITIES IN MATERNAL AND NEONATAL OUTCOMES IN STATES WITH AND WITHOUT IN VITRO FERTILIZATION (IVF) INSURANCE MANDATES. Mary O. Solomon, MD, 1 Pamela B. Parker, M.D., M.P.H., 2 Elizabeth S. Rubin, MD, 1 Bharti Garg, MBBS, MPH, 1 Molly S. Kornfield, MD, 3 Paula Amato, MD, 3 Sacha A. Krieg, M.D., Ph.D., 1 Oregon Health and Science University, Portland, OR;2University of Pittsburgh Medical Center, Pittsburgh, PA; 3Oregon Health and Science University, Portland, OR.

OBJECTIVE: The impact of IVF insurance mandates on racial disparities in birth outcomes is unclear. We examined racial disparities in maternal and neonatal outcomes among individuals who conceived via assisted reproductive technology (ART) in states with mandated and non-mandated IVF coverage.

MATERIALS AND METHODS: This is a retrospective cohort study of birth certificate data from the National Vital Statistics System, 2011-2018. We included commercially insured United States residents with ART conceived, non-anomalous, live births. Primary outcomes were composite maternal adverse outcomes (CMAO) (maternal transfusion, uterine rupture, unplanned hysterectomy, admission to ICU) and composite neonatal adverse outcomes (CNAO) (NICU admission, Apgar scores <7 at 5 minutes, assisted ventilation and seizures). Multivariable logistic regression examined the association of race/ethnicity with birth outcomes, controlling for maternal age, education, body mass index, and marital status. Analyses were done separately for non-mandated states and mandated states (CT, MD, MA, NJ, RI and IL) during the study period.

RESULTS: Of the 31,472,115 birthing individuals, 447,230 met inclusion criteria: 78.0% White, 10.3% Asian, 7.3% Hispanic, 4.3% Black, 0.16% American Indian Alaskan Native (AIAN). On logistic regression, Black individuals and Hispanic individuals had increased adjusted odds of CMAO and CNAO compared to White individuals, in both mandated and non-mandated states. Asian individuals had higher odds of CMAO in non-mandated states only.

CONCLUSIONS: In a large cohort of ART-conceived births, Black and Hispanic individuals had increased odds of adverse maternal and neonatal outcomes compared to White individuals. These disparities persisted in states with mandated IVF insurance coverage.

IMPACT STATEMENT: Racial disparities in birth outcomes are not mitigated by IVF insurance mandates alone.

Data presented as adjusted odds ratio (95% confidence interval)

SUPPORT: none

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<tr>
<th>NON-MANDATED STATES</th>
<th>N = 338512</th>
<th>White N=266509 (78.7%)</th>
<th>Black N=12485 (3.7%)</th>
<th>Hispanic N=25496 (7.5%)</th>
<th>Asian N=3370 (9.9%)</th>
<th>AIAN N=652 (0.2%)</th>
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<td>Ref</td>
<td>1.31 (1.11-1.54)</td>
<td>1.03 (0.90-1.17)</td>
<td>1.24 (1.12-1.38)</td>
<td>0.48 (0.15-1.48)</td>
<td>0.99 (0.81-1.22)</td>
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<td>CNAO</td>
<td>Ref</td>
<td>1.33 (1.28-1.39)</td>
<td>1.09 (1.05-1.13)</td>
<td>0.97 (0.94-0.99)</td>
<td>0.99 (0.81-1.22)</td>
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MANDATED STATES

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<th>Mandated States</th>
<th>N = 99810</th>
<th>White N=75294 (75.4%)</th>
<th>Black N=6250 (6.3%)</th>
<th>Hispanic N=6588 (6.6%)</th>
<th>Asian N=11625 (11.6%)</th>
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<td>1.34 (1.09-1.66)</td>
<td>1.23 (0.95-1.54)</td>
<td>3.85 (0.93-15.99)</td>
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<td>CNAO</td>
<td>Ref</td>
<td>1.41 (1.32-1.51)</td>
<td>1.10 (1.03-1.17)</td>
<td>0.98 (0.93-1.03)</td>
<td>1.29 (0.65-2.58)</td>
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P-622 6:45 AM Wednesday, October 26, 2022

STATE-MANDATED IN VITRO FERTILIZATION (IVF) COVERAGE REDUCES ADVERSE NEONATAL OUTCOMES. Pamela B. Parker, M.D., M.P.H., 1 Elizabeth S. Rubin, MD, 2 Mary O. Solomon, MD, 3 Bharti Garg, MBBS, MPH, 1 Molly S. Kornfield, MD, 4 Paula Amato, MD, 3 Sacha A. Krieg, M.D., Ph.D., 1 University of Pittsburgh Medical Center, Pittsburgh, PA; 4Oregon Health & Sciences University, Portland, OR.

OBJECTIVE: To determine the impact of state-mandated insurance on maternal and neonatal outcomes among patients who used assisted reproductive technology (ART) to conceive. While state-mandated fertility insurance coverage has been shown to impact fertility treatment practices, the association between mandated IVF coverage and birth outcomes is less well-studied.

MATERIALS AND METHODS: This is a retrospective cohort study of birth certificate data from the National Vital Statistics System, 2011-2018. We included commercially insured, non-anomalous live births indicating conception by ART of United States residents. Our primary outcomes were composite (and individual) maternal adverse outcomes (maternal transfusion, ruptured uterus, unplanned hysterectomy, admission to ICU) and composite (and individual) neonatal adverse outcomes (NICU admission, Apgar scores <7 at 5 minutes, assisted ventilation and seizures). Secondary outcomes included preterm delivery, gestational hypertension (gHTN), gestational diabetes (GDM), and perinatal lacerations. Comparisons were made between states that mandated IVF coverage during the study time frame (CT, MD, MA, NJ, RI and IL) and those that did not using chi-square tests. Multivariable logistic regression models were used to examine the association of mandated state insurance coverage with birth outcomes, and controlled for maternal age, race/ethnicity, education, insurance, body mass index, and marital status.

RESULTS: Of the 481,027 birthing individuals included, 107,079 (22.3%) were in states with mandated IVF coverage. Mandated states had slightly higher proportions of Non-Hispanic Black and Asian populations, and birthing individuals were more likely to be over age 35, college-educated, overweight/obese, married, and have private insurance (all p<.001). Composite neonatal adverse outcomes were significantly lower in mandated states compared to non-mandated (21.9% vs 24.2%, p<.001). We found lower adjusted odds of neonatal composite in mandated states (aOR 0.88, 95% CI 0.86 – 0.89), but no difference in maternal composite. In mandated states there was significantly higher adjusted odds of maternal transfusion (aOR 1.11, 95% CI 1.04-1.19), but significantly lower adjusted odds of maternal ICU admission (aOR 0.87, 95% CI 0.77 – 0.98), GDM (aOR 0.93, 95% CI 0.91 – 0.95), gHTN (aOR 0.74, 95% CI 0.73 – 0.76), and perinatal lacerations (aOR 0.76, 95% CI 0.71 – 0.81). There was also significantly lower odds of individual neonatal outcomes in mandated states: NICU admission (aOR 0.87, 95% CI 0.86 – 0.89), 5-minute APGAR scores <7 (OR 0.73, 95% CI 0.69-0.77), neonatal assisted ventilation (OR 0.92, 95% CI 0.90 – 0.95), and preterm delivery (aOR 0.83, 95% CI 0.81 – 0.84).

Vol. 118, No. 4, Supplement, October 2022
CONCLUSIONS: In a large population study of ART births, state mandated IVF insurance coverage was associated with reductions in select adverse maternal outcomes and composite adverse neonatal outcomes. These data support expanding IVF coverage as a strategy to improve maternal and neonatal outcomes.

IMPACT STATEMENT: State-mandated IVF insurance coverage is associated with better neonatal outcomes.

SUPPORT: none

P-623 6:45 AM Wednesday, October 26, 2022

THE IMPACT OF TELEMEDICINE ON MINORITY WOMEN’S ACCESS TO GYNECOLOGIC AND FERTILITY CARE DURING THE COVID-19 PANDEMIC. Nicholas Zakia Bilal Bomanji, BA,1 Kaitlyn E. James, PhD,1 Mackenzie N. Nuet, B.A., MD., M.S.C.,3 John C. Petrozza, M.D.4 1Massachusetts General Hospital, Boston, MA; 2Brookline, MA; 3Massachusetts General Hospital Fertility Center, Boston, MA.

OBJECTIVE: To assess minority women’s access to Gynecology and Reproductive Care during the COVID-19 pandemic and the associated shift from in-person to telehealth modalities.

MATERIALS AND METHODS: Using data from a single, large academic health system, we analyzed 73,648 completed appointments in General Gynecology (GYN) and Reproductive Endocrinology and Infertility (REI) from January 2020-May 2021. Appointments were stratified by patient race (White, Black, Hispanic/Latino, Asian, Pacific Islander, Multiracial, and American Indian) and modality of appointment (in-person, Epic-integrated video, or telephone). Minority women were defined as women who self-reported as Black, Hispanic/Latina, Multiracial, or American Indian. January-March 2020 was used as a measure of pre-COVID-19 ambulatory volume, and January-March 2021 was used as a measure of the midpoint of the COVID-19 pandemic. Frequency statistics and univariate logistic regression models were used to determine differences in pre- and mid-point-pandemic telehealth volume, minority access, and preferred telehealth modality. A p-value <0.05 was considered statistically significant.

RESULTS: Our REI and GYN services experienced a respective 1294% and 1199% increase in telehealth visits during January-March 2021 relative to this same interval in 2020. GYN experienced a 4.8% increase in the proportion of minority visits (p <0.001), while REI experienced a 0.9% increase in minority visits (p=0.33). We noted a 3% overall increase of the proportion of minority women represented in the REI service (p=0.02) in March 2021 relative to March 2020. The odds ratio for video telehealth usage for minority patients relative to white patients was 0.96 (95% CI 0.66, 1.37) for GYN and 1.72 (95% CI 1.23, 2.42) for REI in this same timeframe.

CONCLUSIONS: The shift to telehealth resulted in a significant increase in access for minority women to GYN services from pre-COVID-19 ambulatory levels. We also noted a modest increase in access for minority women to both REI and GYN telehealth services since the start of the COVID-19 pandemic. There was no significant difference in use of video telehealth between minority and white women in our GYN practice during the COVID-19 pandemic. However, minority women were almost twice as likely to use video telehealth for REI visits compared to their white counterparts during the pandemic.

IMPACT STATEMENT: Women of Color have historically been underrepresented in REI care despite having a potentially higher prevalence of infertility. The continued use of telehealth modalities for delivering ambulatory REI and GYN care has the potential to expand REI access to minority women beyond the COVID-19 pandemic. Emphasis should continue to be placed on improving opportunities for video telehealth encounters to ensure more equitable access and outcomes.

P-625 6:45 AM Wednesday, October 26, 2022

PREVALENCE AND DETECTION OF NEWLY ACQUIRED SEXUALLY TRANSMITTED INFECTIONS IN A REPRODUCTIVE MEDICINE POPULATION. Elizabeth Reznik, M.D.,1 Phillip A. Romanski, MD, MSc,2 Pietro Bortolotto, MD, MSc,3 Steven D. Spandorfer, MD4 The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York; New York, NY; The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; NewYork-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY.

OBJECTIVE: The primary objective of this study is to determine the prevalence of sexually transmitted infections (STI) in the reproductive medicine clinical setting on initial screening and the incidence of newly detected infections on subsequent screening. The secondary objective is to assess whether sexual behavior and association between infections and social behaviors.

MATERIALS AND METHODS: This was a retrospective cohort study conducted at a single institution. Patients who underwent an initial assisted reproductive technology (ART) cycle in 2018 were included. At our center, both patients and their partners (when applicable) are screened for HIV, Hepatitis B, Hepatitis C, Syphilis and patients undergoing oocyte retrieval are additionally screened for Chlamydia and Gonorrhea at the initiation of care. Patient screening tests were repeated every 12 months. Infections and subsequent STI screening results were collected from the electronic medical record. Social habits including smoking status, alcohol consumption, and drug use were also collected. Descriptive statistics are reported as mean ± SD for continuous variables and percentages for categorical variables. Categorical variables were compared using the Chi-square test. A p-value < 0.05 was considered statistically significant.

FERTILITY & STERILITY® e369
The prevalence of wildfires increases due to climate change, we must examine wildfire and/or toxic air quality events. Larger, prospective studies are needed to fully assess the impact of acute exposure to good versus hazardous air quality from a wildfire smoke event.

RESULTS: Of 385 screened, 151 people in 2019 and 97 people in 2020 were enrolled. Of the 248 women who underwent an initial ART cycle after an acute exposure to poor air quality, 139 (56.2%) were diagnosed with a subsequent pregnancy. The median GD between LMP and onset of exposure was 31±17 (range 7-69) days, which did not differ based on whether there was a loss.

CONCLUSIONS: An acute wildfire smoke event was associated with a trend towards increased pregnancy loss in a general OB/GYN population. Larger, prospective studies are needed to fully assess the impact of acute wildfire and/or toxic air quality events.

IMPACT STATEMENT: Factors influence the IVF-ET outcomes need to be discovered. Sleep deficiency is thought to be associated with female fertility. Researches on the analysis of sleep and IVF outcomes mainly focus on the number of oocytes retrieved, the quality of embryos etc., while research on the outcomes of embryo transfer, like live birth rate, is limited. In our prospective study, we found that sleep quality and sleep chronotype may have substantial consequences on early pregnancy. As the prevalence of wildfires increases due to climate change, we must examine the potential reproductive impacts and assess interventions to reduce exposure.
ASSOCIATION BETWEEN BMI AND ENDOMETRIAL THICKNESS AND IVF PREGNANCY OUTCOMES WITH EUPLOID EMBRYOS. Navin N. Maredia, MD, Tia Y. Brodeur, MD, PhD, Katelyn Tessier, MS, Stephanie K. Dahl, MD, Brent Hanson, MD, April E. Batcheller, MD, CCRM Fertility of Minneapolis, Edina, MN; University of Vermont Larner College of Medicine, Burlington, VT; University of Minnesota, Minneapolis, MN; CCRM Fertility of Minneapolis, Edina.

OBJECTIVE: Given limited studies evaluating the relationship between BMI and endometrial thickness in patients undergoing IVF in the US, we sought to evaluate whether there is an association between BMI and endometrial thickness and whether BMI affects pregnancy outcomes in patients with normal endometrial lining (7-15 mm) who had PGT-A tested embryos transferred, thereby eliminating aneuploidy as a confounder.

MATERIALS AND METHODS: A retrospective cohort study was conducted with 798 patients who had a euploid embryo transferred between 2015 and 2020. Age, gravidity, parity, BMI, endometrial thickness at the time of transfer, negative h-CBG, biochemical pregnancy, clinical pregnancy, first trimester pregnancy loss, and live birth were collected. We compared endometrial thickness in underweight/normal weight (BMI 25-29.9), overweight (BMI ≥ 30), and obese (BMI ≥ 30) patients. We also compared pregnancy outcomes in these BMI groups.

RESULTS: There was a statistically significant difference in age between the BMI groups (p = 0.005). No statistically significant difference was found between endometrial thickness and BMI. In patients with a normal endometrial thickness with a euploid embryo transferred, overweight patients were less likely to have a clinical pregnancy or live birth compared to underweight/normal weight patients without adjustment for age (both p = 0.033). However, the statistically significant association between BMI and pregnancy outcomes were not seen with adjustment for age.

CONCLUSIONS: Our study showed that BMI does not affect endometrial thickness in IVF patients. In women with a normal endometrial lining and a euploid embryo transfer, once adjusted for age, there were no statistically significant differences in pregnancy outcomes when comparing underweight/normal weight, overweight, and obese women.

IMPACT STATEMENT: Our study suggests there is no association between BMI and endometrial thickness in women undergoing IVF. When controlled for endometrial thickness, ploidy of the embryo, and age, higher BMI does not significantly affect pregnancy outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Underweight/normal weight</th>
<th>Overweight</th>
<th>Obese</th>
<th>Unadjusted P-value</th>
<th>Adjusted P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with normal endometrial thickness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geometric mean (geometric SD)</td>
<td>N = 406</td>
<td>N = 210</td>
<td>N = 181</td>
<td>0.181</td>
<td>0.148</td>
</tr>
<tr>
<td>Endometrial thickness</td>
<td>10.0 (2.0)</td>
<td>10.2 (1.8)</td>
<td>10.3 (1.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative beta hCG, n (%)</td>
<td>58 (14.9)</td>
<td>41 (19.9)</td>
<td>36 (20.5)</td>
<td>0.152</td>
<td>0.266</td>
</tr>
<tr>
<td>Chemical pregnancy, n (%)</td>
<td>37 (9.5)</td>
<td>26 (12.6)</td>
<td>15 (8.5)</td>
<td>0.362</td>
<td>0.359</td>
</tr>
<tr>
<td>Clinical pregnancy, n (%)</td>
<td>297 (75.6)</td>
<td>135 (65.5)</td>
<td>124 (70.5)</td>
<td>0.033</td>
<td>0.063</td>
</tr>
<tr>
<td>1st trimester loss, n (%)</td>
<td>33 (8.5)</td>
<td>17 (8.3)</td>
<td>16 (9.1)</td>
<td>0.957</td>
<td>0.954</td>
</tr>
<tr>
<td>Live birth, n (%)</td>
<td>269 (68.6)</td>
<td>120 (58.5)</td>
<td>108 (61.4)</td>
<td>0.033</td>
<td>0.053</td>
</tr>
</tbody>
</table>
when comparing daylight hours, average temperature, precipitation, or AQI; it is also the same in medically induced or natural cycles. Our study importantly highlights the effect of climate change with increasing daily temperatures, which may influence CPR. AQI has also decreased over time, which we have shown to positively influence CPR. Future studies are warranted to analyze if including male and/or female factor infertility impacts seasonally-adjusted CPR.

IMPACT STATEMENT: Even with new research demonstrating circannual hormonal rhythms, there are no significant differences in CPR by season. This allows for patients and providers to practice shared decision making when planning fertility cycles. However, the effects of climate change on ART warrant further study as we focus on optimizing ART outcomes.

SUPPORT: None

REFERENCES:

E-POSTER ABSTRACT STATION: W20

P-631 6:45 AM Wednesday, October 26, 2022

ASSOCIATION OF COVID-19 VACCINATION WITH FEMALE OVARIAN RESERVE. Liubin Yang, MD, PhD,1 Samantha Neal, BS,1 Tiffany Lee, BS,1 Andrew Chou, MD, MSC1 1Amy K. Schutt, MD, MSCI,1 William Gibbons, MD,1 Baylor College of Medicine, Houston, TX; 2Baylor College of Medicine, Dept of Obstetrics & Gynecology, Houston, TX.

OBJECTIVE: To evaluate the association of COVID-19 vaccination with female ovarian reserve.

MATERIALS AND METHODS: A retrospective cohort study of women from January 2018 to October 2021 who presented as new patients to a reproductive endocrinology and infertility clinic in Houston, Texas was conducted. Inclusion criteria were documentation of vaccination in the electronic health record, presence of anti-Mullerian hormone (AMH) laboratory value, presence of ovarian antral follicle count by ultrasound. Exclusion criteria were incomplete data and no documentation of vaccination. Demographics including age, diagnosis, date of visit, zip code, laboratory values were also obtained. Primary outcome was ovarian reserve as defined by the value of AMH and antral follicle count on ultrasound. Chi-square and one-way ANOVA were used to calculate differences in baseline characteristics. Odds ratios were calculated for each predictor variable using logistic regression.

RESULTS: Of the 1654 patients evaluated, 944 (57%) had documentation of vaccination, 771 (82%) met inclusion criteria. Of those, 678 patients were included. BMI, HbA1c, or TSH values. There was no change in AMH (OR of vaccination, 771 (82%) met inclusion criteria. Of those, 678 patients were included. BMI, HbA1c, or TSH values.

TABLE 1.

<table>
<thead>
<tr>
<th>Year</th>
<th>Patients Initiating Medical FP</th>
<th>Patients Living in Least Disadvantaged Quartile (Q1)</th>
<th>Patients Living in Middle Quartiles of Disadvantage (Q2, Q3)</th>
<th>Patients Living in Most Disadvantaged Quartile (Q4)</th>
<th>Median ADI</th>
<th>Standard Deviation of ADI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>63</td>
<td>35 (55.6%)</td>
<td>24 (38.1%)</td>
<td>4 (6.3%)</td>
<td>19</td>
<td>25.4</td>
</tr>
<tr>
<td>2018</td>
<td>69</td>
<td>36 (52.2%)</td>
<td>31 (44.9%)</td>
<td>2 (2.9%)</td>
<td>23</td>
<td>22.2</td>
</tr>
<tr>
<td>2019</td>
<td>62</td>
<td>27 (43.5%)</td>
<td>32 (51.6%)</td>
<td>3 (4.8%)</td>
<td>30.5</td>
<td>21.4</td>
</tr>
<tr>
<td>2020</td>
<td>84</td>
<td>40 (47.6%)</td>
<td>42 (50.0%)</td>
<td>2 (2.4%)</td>
<td>27.5</td>
<td>19.9</td>
</tr>
</tbody>
</table>

CONCLUSIONS: There was no significant differences in ovarian reserve in our patient population before and after receiving COVID-19 vaccination. Limitations include sample size number and local variations in laboratory values.

IMPACT STATEMENT: This study demonstrates that the COVID-19 vaccine is not associated with changes in female ovarian reserve in this cohort of patients.

P-632 6:45 AM Wednesday, October 26, 2022

A FAILURE TO REACH DISADVANTAGED NEIGHBORHOODS: LEGISLATION IS NOT ENOUGH TO EXPAND ACCESS TO MEDICAL FERTILITY PRESERVATION. Allison S. Komorowski, MD,1 Emma Trawick, MD,2 Katherine M. Bolten, BS,3 Kristin N. Smith, B.S.,4 Jennifer Elvikis, MSN, RN,1 Kara N. Goldman, MD4 Northwestern University, Chicago, IL; 2Northwestern Feinberg School of Medicine, Chicago, IL; 3Northwestern Feinberg School of Medicine, Chicago, IL; 4Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL.

OBJECTIVE: In 2019, IL made effective HB 2617 which mandated insurers provide coverage for fertility preservation (FP) services when medical treatment may cause iatrogenic infertility. IL is the only state nationwide to also extend coverage to publiclyinsured recipients. Our study aimed to assess whether legislation mandating insurance coverage for medical fertility preservation (MFP) was associated with a change in the neighborhood socioeconomic disadvantage of patients accessing FP care.

MATERIALS AND METHODS: Patients counseled on MFP from 2017 and 2020 at a large urban academic center were identified using ICD-10 codes. Patients’ addresses were used to calculate a national area deprivation index (ADI) percentile using the 2019 University of Wisconsin Neighborhood Atlas. ADI measures a region’s disadvantage using US Census indicators including income disparity, unemployment rate, poverty, education and housing. A higher ADI percentile indicates a higher level of disadvantage. Median ADI comparison of patients initiating MFP in 2017 and 2018 versus 2019 and 2020 was assessed by independent-samples median test.

RESULTS: 430 patients were seen for MFP consultation from 2017 and 2020. 279 initiated stimulation cycles (64.9%); ADI percentile was available for 278. About half of patients initiating FP (49.6%) lived in areas that represented the least disadvantaged neighborhood quartile nationwide. Only 11 patients (4.0%) lived in areas that represented the most disadvantaged neighborhood quartile. Following enactment of HB2617, more publiclyinsured patients presented for counseling (11 vs 28) and completed FP cycles (3 vs 16, p=0.003). However, the median ADI of patients initiating FP has not significantly changed (Table 1, p=0.280).

CONCLUSIONS: Most patients undergoing MFP at a large academic medical center in IL from 2017 and 2020 lived in neighborhoods not considered disadvantaged. Following state legislation mandating MFP coverage, no difference was seen in ADI percentile of patients initiating MFP.

IMPACT STATEMENT: Legislation alone may not be enough to expand access to MFP care to those living in the most disadvantaged neighborhoods. For this group of patients, there are likely significant barriers to care beyond insurance coverage; future research should focus on improving access in this group.

CONCLUSIONS: There was no significant differences in ovarian reserve in our patient population before and after receiving COVID-19 vaccination. Limitations include sample size number and local variations in laboratory values.

IMPACT STATEMENT: This study demonstrates that the COVID-19 vaccine is not associated with changes in female ovarian reserve in this cohort of patients.
SOCIOECONOMIC STATUS AND REPRODUCTIVE OUTCOMES: A POPULATION-BASED STUDY. Laura Nicholls-Dempsey, MD, DM, Ahmad Badeghiesh, M.D., MPH, Haitham Baghla, MD, MPH, Michael H. Dana, M.D., MD, 1 McGill University, Kirkland, QC, Canada; 2 McGill University Health Centre, Montreal, QC, Canada; 3 McGill University, Montreal, QC, Canada; 4 Division of Reproductive Endocrinology and Infertility, McGill University Health Care Center, Montreal, QC, Canada.

OBJECTIVE: Healthcare is a fundamental aspect of basic human rights and access to which should be equally provided to all people in a society. Previous studies have demonstrated that lower socioeconomic status (SES) in women is associated with adverse outcomes in pregnancy compared to other SES groups, when controlled for race and other confounding medical issues. Our purpose was to evaluate the effect of higher SES on reproductive outcomes.

MATERIALS AND METHODS: We conducted a retrospective cohort study consisting of women from different median household income quartiles using the Healthcare Cost and Utilization Project Nationwide Inpatient Sample from 2004 to 2014. Multivariable logistic regression, adjusting for statistically significant confounding variables, was used to compare reproductive outcomes among women from the highest income quartile (median income ≥ $63,008) to those in all lower income quartiles combined.

RESULTS: Out of the 5,448,255 deliveries during the study period, 1,218,989 (22%) were to women with the wealthiest median household income. They were more likely to be older, Caucasian, have private insurance and be smokers, have chronic hypertension, pre-gestational diabetes, and use illicit drugs (p < 0.0001 all). The highest SES group was less likely to develop pregnancy complications such as gestational hypertension (aOR 0.87 95%CI 0.85-0.88), preeclampsia (aOR 0.88 95%CI 0.86-0.89), and gestational diabetes (aOR 0.91 95%CI 0.89-0.92). They were also less likely to develop delivery complications such as PPROM (aOR 0.92 95%CI 0.88-0.96), preterm birth (aOR 0.90 95%CI 0.89-0.92), and abortion (aOR 0.89 95%CI 0.85-0.93). They were less likely to have an IUD (aOR 0.80 95%CI 0.74-0.86), but more likely to deliver neonates with congenital anomalies (aOR 1.10 95%CI 1.04-1.20).

CONCLUSIONS: Even when controlling for baseline health status, women with higher SES have mostly better reproductive outcomes, which suggests that access to healthcare or better pregnancy nutrition and counseling improves pregnancy outcomes. Furthermore, we hypothesize that women with higher SES are more likely to deliver a neonate with congenital anomalies, possibly because they are less likely to abort as they are more likely to have the financial means necessary to care for such a child. Further studies are required to evaluate this hypothesis.

IMPACT STATEMENT: Greater SES predisposes to better reproductive outcomes, even when controlled for confounding factors. Efforts should be made to improve the quality and delivery of reproductive and prenatal care to women not in the highest SES groups.

P-636 6:45 AM Wednesday, October 26, 2022

EXPRESSION OF RACE/ETHNICITY PATIENTS IN REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY STUDIES COMPARED WITH OTHER OBSTETRIC AND GYNECOLOGY SUBSPECIALTIES. Anne J. Roshong, MD, 1 Kendal Frances Rosalik, Do, 2 Samantha Carson, MD, 3 Laura Spilman, DO, 2 Jacqueline M. Luizzi, MLIS, AHP, 1 Bruce Pier, MD, 1, 6 US Army, Madigan Army Medical Center, Tacoma, WA; 3 Madigan Army Medical Center; 4 Tripler Army Medical Center; 5 Womack Army Medical Center; 2 Madigan Army Medical Center, Tacoma, WA; 3 Division of Reproductive Endocrinology and Infertility, Tacoma, WA.

OBJECTIVE: Black and Hispanic ethnicities are under-represented in the population of treated infertility patients in the United States despite having a higher prevalence and longer duration of infertility. Studies also demonstrate that these women have poorer infertility treatment outcomes and more comorbidities. Studies have demonstrated the most-cited articles in other obstetrics and gynecology (OBGYNS) subspecialties (gynecologic oncology, urogynecology, and maternal fetal medicine). Our hypothesis is that minority race/ethnic groups will be under-represented in the REI studies compared to the other OBGYNS subspecialties (OBGYNS).

MATERIALS AND METHODS: This retrospective cohort was carried out by using a literature search using WEB OF SCIENCE was conducted to determine the most cited articles in each OBGYN subspecialty from 2012-2022. Most cited articles were evaluated in sequential order, and studies included if they were conducted in the United States primarily, and listed the number of patients per race/ethnicity group. Studies were excluded if they were: review articles, conducted outside the United States, or were performed in a country other than the United States. Total number of patients and number of patients per race/ethnicity group was extracted. 50 studies were included for each subspecialty, and data was converted to percentage of patients per race/ethnicity group per total patients in the study. Data was compared for race/ethnicity groups (White, Black, Hispanic, Asian, and Other/Missing) between REI studies and all other OBGYNs. Chi-square testing was used to determine differences in the expression of these race/ethnicity cohorts between REI and other OBGYNs studies.

RESULTS: A total of 735 studies were reviewed, 200 met inclusion criteria (50 REI, 150 OBGYNs). A total of 10,392,667 patients were included in REI studies, while 23,238,733 patients were included in other OBGYNS studies. White patients were similarly expressed between REI and OBGYNs studies.
and OBGYNS (65.8% vs 65.6%). REI studies had less Black and Hispanic patients compared to OBGYNS (11.8% vs 14.7% Black (p value = <0.05), 7.3% vs 13.3% (p value = <0.05), respectfully). More Asian patients were present in REI studies compared to OBGYNS (5.1% vs 2.5%, p value = <0.05). REI studies were also more likely to have missed data (12.0 vs 5.8%, p value = <0.05).

CONCLUSIONS: REI and the OBGYNS groups had a similar percentage of White patients, but REI studies included significantly less Black and Hispanic patient cohorts when compared to OBGYNS, and the general United States Population. There were more Asian patients in REI studies compared to OBGYNS. REI studies were more likely to have missing race/ethnicity data than OBGYNS.

IMPACT STATEMENT: Black and Hispanic women are under-expressed in REI studies, leading to great impact on REI clinicians to make meaningful decisions on the infertility care of these patients.

SUPPORT: None.

LIVE BIRTH AND NEONATAL OUTCOMES AFTER COVID-19 VACCINATION

Devora Abaron, MD, Chelsea M. Canon, MD, Samantha Lauren Estevez, MD, Carlos Hernandez-Nieto, MD, Joseph A. Lee, BA, Jeffrey Klein, MD, Matthew A. Lederman, M.D., Alan B. Copperman, MD, Ilchan School of Medicine at Mount Sinai, New York, NY; Reproductive Medicine Associates of New York, New York, NY; White Plains, NY; Ilchan School of Medicine at Mount Sinai/Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Despite multiple studies demonstrating safety of COVID-19 vaccination for fertility and early pregnancy outcomes, concerns remain in the general public regarding the COVID-19 vaccine in women who are trying to conceive or are pregnant. The objective of this study is to evaluate any association of COVID-19 mRNA vaccination prior to conception with live birth and neonatal outcomes in patients undergoing IVF.

MATERIALS AND METHODS: This study included patients who underwent a single, euploid, frozen-thawed embryo transfer (SEET) at a single academic reproductuve center from February through March 2021. The study group consisted of patients who received two doses of an mRNA COVID-19 vaccine prior to embryo transfer, and the comparison group was comprised of unvaccinated patients. Live birth (LB) rate, gestational age (GA) at delivery, and birth weight (BW) were compared between the groups using chi square and Wilcoxon rank-sum tests. Multiple logistic and linear regression were used to assess the association of vaccination with outcomes, controlling for confounders.

RESULTS: A total of 312 patients underwent SEET, of which 45 patients were vaccinated and 267 patients were unvaccinated. Demographics and cycle characteristics were similar between the groups. LB rate was similar among vaccinated and unvaccinated patients (53.5% vs 50.2%, p= .70). No significant differences were seen in GA at delivery (38.4±2.0 weeks vs 39.0±1.6 weeks, p=.46) or birth weight (3148.8±453.4 grams vs. 3298.4±594.4 grams, p=.14) when comparing the vaccinated and unvaccinated groups. Regression analyses adjusted for age, BMI, endometrial thickness, and embryo quality demonstrated no association between vaccination and LB (OR 1.06, 95% CI 0.54-2.05, p=.87) or GA at delivery (B=-0.55±0.36, p=.13). Adjusting for the variables above in addition to GA revealed no association between vaccination and BW (B=-86.9±102.6, p=.39).

CONCLUSIONS: COVID-19 mRNA vaccination prior to pregnancy was not associated with any impact on live birth rate, gestational age at delivery, or birth weight. This study may provide reassurance that COVID-19 vaccination, which has been demonstrated to improve maternal and child health outcomes in pregnant patients, does not have a harmful impact on gestation and neonatal outcomes.

IMPACT STATEMENT: This study contributes to the growing body of evidence regarding the safety of COVID-19 vaccination in patients who are trying to conceive. Large-scale longitudinal data of patients vaccinated prior to and during pregnancy will provide valuable information regarding vaccination, the most effective means to combat this pandemic.

P-639 6:45 AM Wednesday, October 26, 2022

PHYSICAL ACTIVITY DURING FERTILITY TREATMENT IS UNRELATED TO LIVE BIRTH.

Leah Cooper, MD, MS, Amanda Allshouse, MS, Sunni L. Mumford, PhD, Erica Johnstone, MD University of Utah, Salt Lake City, UT; Rockville, MD.

OBJECTIVE: We sought to determine the association between physical activity, as measured by a Fitbit accelerometer during fertility treatments, and live birth.
RESULTS: Among n=188 participants undergoing intrauterine insemination or in vitro fertilization, there was no statistically significant relationship between physical activity quartile of any measure and live birth. Among the subset of women who achieved pregnancy (n=108), quartile of total step count was associated with live birth, but not in a linear fashion, with participants in the 3rd quartile having higher odds of live birth than those in the 2nd quartile, while those in the lowest quartile had higher odds of live birth than those in the 2nd quartile (Table 1, p=0.023). Minutes of sedentary time, light, fairly or very active time were not associated with live birth.

Table 1. Interquartile comparisons for step count and odds of live birth among those who became pregnant.

<table>
<thead>
<tr>
<th>Quartile</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Steps</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 vs 1</td>
<td>0.221</td>
<td>0.064</td>
<td>0.759</td>
</tr>
<tr>
<td>3 vs 1</td>
<td>1.309</td>
<td>0.309</td>
<td>5.556</td>
</tr>
<tr>
<td>4 vs 1</td>
<td>0.529</td>
<td>0.151</td>
<td>1.852</td>
</tr>
<tr>
<td>3 vs 2</td>
<td>5.917</td>
<td>1.605</td>
<td>21.739</td>
</tr>
<tr>
<td>4 vs 2</td>
<td>2.392</td>
<td>0.805</td>
<td>7.143</td>
</tr>
<tr>
<td>4 vs 3</td>
<td>0.404</td>
<td>0.107</td>
<td>1.520</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Physical activity during fertility treatment cycles, as measured by accelerometer, was not found to be associated with live birth. However among people that achieved pregnancy, activity as measured by steps was associated with livebirth.

IMPACT STATEMENT: Against common sense in the literature, the results did not reveal a relationship between BMI and the ovarian response to gonadotropin. BMI as an additional tool in the individualization of ovarian stimulation protocols should be reviewed.

MATERIALS AND METHODS: Women undergoing intrauterine insemination or in vitro fertilization as treatment for infertility wore Fitbit wrist accelerometers during fertility treatment and pregnancy, as part of the prospective IDEAL (impact of diet, exercise, and lifestyle) Fertility Study. Physical activity was quantified as mean daily step count, minutes of sedentary time, and minutes spent lightly active, fairly active, and very active; activity levels were determined by a Fitbit algorithm. Using activity measured 2 weeks before and after intrauterine insemination or embryo transfer, participants were grouped by quartile for each activity measure. Relationships between quartile for each activity parameter and live birth versus any other outcome were assessed with logistic regression adjusted for maternal age, BMI, and blood pressure. Among the subset of women who conceived, chance of live birth versus pregnancy loss was also compared with logistic regression without adjustment.

RESULTS: Among n=188 participants undergoing intrauterine insemination or in vitro fertilization, there was no statistically significant relationship between physical activity quartile of any measure and live birth. Among the subset of women who achieved pregnancy (n=108), quartile of total step count was associated with live birth, but not in a linear fashion, with participants in the 3rd quartile having higher odds of live birth than those in the 2nd quartile, while those in the lowest quartile had higher odds of live birth than those in the 2nd quartile (Table 1, p=0.023). Minutes of sedentary time, light, fairly or very active time were not associated with live birth.

Table 1. Interquartile comparisons for step count and odds of live birth among those who became pregnant.

<table>
<thead>
<tr>
<th>Quartile</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Steps</td>
<td></td>
<td></td>
<td></td>
</tr>
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</tbody>
</table>

CONCLUSIONS: Physical activity during fertility treatment cycles, as measured by accelerometer, was not found to be associated with live birth. However among people that achieved pregnancy, activity as measured by steps was associated with livebirth.
FEMALE BODY MASS INDEX (BMI) INFLUENCES PREGNANCY OUTCOMES: AN EVALUATION OF 4349 IVF/ICSI CYCLES.  Andrea Nicoletti, R.N., 1  Claudia G. Petersen, Ph.D., 2  Fabiana C. Massaro, B.Sc., 1  Bruna Petersen, B.Sc., 2  Laura D. Vagnini, M.Sc., 3  Juliana Ricci, R.N., 3  Camila Zamara, R.N., 1  Antonio Helio Oliani, M.D., Ph.D., 3  Joao B. A. Oliveira, M.D., M.Sc., Ph.D., 1  Felipe Dieamant, M.D., 2  Jose G. Franco, Jr., M.D., Ph.D., 2  Centro de Human Reproduction Prof. Franco Jr, Ribeirao Preto, Brazil; 2  Centro de Human Reproduction Prof. Franco Jr/ Paulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; 3  Sao Jose do Rio Preto School of Medicine FAMERP, Sao Jose do Rio Preto, Brazil.

OBJECTIVE: To evaluate if female body mass index (BMI) impair pregnancy outcomes after IVF/ICSI cycles.

MATERIALS AND METHODS: 4349 couples were stratified into four groups by female BMI: <18.5 kg/m² (underweight); 18.5-24.9 kg/m² (normal weight); 25.0-29.9 kg/m² (overweight); and ≥30 kg/m² (obesity). Clinical pregnancy, miscarriage and live birth rates were the outcomes analysed. For group comparisons, the t test or chi-square test was used. Multivariate logistic regression analyses were performed to evaluate the associations between BMI and the probabilities of clinical pregnancy (CP), miscarriage and live birth (LB). Normal-weight patients were considered as the reference group.

RESULTS: Regarding confounding factors, no significant differences between BMI groups were observed.

- BMI-group comparisons showed that CP, miscarriage and LB rates significantly worsened with the increase in BMI (overweight and obesity groups). Miscarriage and LB rates also worsened with the decrease in BMI (underweight group) (Table 1.1).

- Compared with the normal-weight group, the overweight and obesity groups had significantly reduced rates of CP (19%/29%, respectively) and LB (27%/40%, respectively) and an increased rate of miscarriage (1.7x), compared with the underweight group (28%/33.6%, respectively) (Table 1.2).

Table 1. Results

1.1-GROUP COMPARISONS

<table>
<thead>
<tr>
<th></th>
<th>Underweight (BMI:&lt;18.5 kg/m²)</th>
<th>Normal Weight (BMI:18.5-24.9 kg/m²)</th>
<th>Overweight (BMI:25-29.9 kg/m²)</th>
<th>Obesity (BMI:≥30 kg/m²)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n(%)</td>
<td>110 (2.5%)</td>
<td>2665 (61.3%)</td>
<td>1096 (25.2%)</td>
<td>478 (11.0%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Age(years)</td>
<td>35.4±4.9</td>
<td>35.5±4.4</td>
<td>35.7±4.4</td>
<td>35.9±4.9</td>
<td>0.009</td>
</tr>
<tr>
<td>Clinical Pregnancy rate</td>
<td>27.3%</td>
<td>32.3%&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>28.0%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>25.5%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.003</td>
</tr>
<tr>
<td>Miscarriage rate</td>
<td>40%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>18.2%&lt;sup&gt;a,b,c&lt;/sup&gt;</td>
<td>27.0%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>33.6%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.006</td>
</tr>
<tr>
<td>Live birth rate</td>
<td>14.5%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>24.8%&lt;sup&gt;a,b,c&lt;/sup&gt;</td>
<td>19.6%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>16.5%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.001</td>
</tr>
</tbody>
</table>

1.2-LOGISTIC REGRESSION ANALYSES

<table>
<thead>
<tr>
<th>CLINICAL PREGNANCY RATE</th>
<th>Odds Ratio (95% Confidence Interval)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Normal Weight</td>
<td>1(Ref.)</td>
<td>0.26</td>
</tr>
<tr>
<td>- Underweight</td>
<td>0.78 (0.51-1.20)</td>
<td>0.009</td>
</tr>
<tr>
<td>- Overweight</td>
<td>0.81 (0.69-0.95)</td>
<td>0.003</td>
</tr>
<tr>
<td>- Obesity</td>
<td>0.71 (0.57-0.89)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MISCARRIAGE RATE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Normal Weight</td>
<td>1(Ref.)</td>
<td>0.001</td>
</tr>
<tr>
<td>- Underweight</td>
<td>2.99 (1.41-6.34)</td>
<td>0.004</td>
</tr>
<tr>
<td>- Overweight</td>
<td>1.66 (1.22-2.25)</td>
<td>0.001</td>
</tr>
<tr>
<td>- Obesity</td>
<td>2.27 (1.50-3.43)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LIVE BIRTH RATE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Normal Weight</td>
<td>1(Ref.)</td>
<td>0.01</td>
</tr>
<tr>
<td>- Underweight</td>
<td>0.51 (0.30-0.88)</td>
<td>0.006</td>
</tr>
<tr>
<td>- Overweight</td>
<td>0.73 (0.62-0.87)</td>
<td></td>
</tr>
<tr>
<td>- Obesity</td>
<td>0.60 (0.46-0.77)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The study suggests that higher BMI (overweight and obesity) and lower BMI (underweight) in women have a detrimental effect on ART outcomes, especially regarding the evolution of pregnancies.

IMPACT STATEMENT: Problems associated with abnormal BMI should be discussed when advising couples interested in fertility treatment.

THE MECHANISM OF EXCESSIVE EXTRAVILLOUS TROPHOBLAST IN RUPTURED TUBAL PREGNANCY. Jian Zhang, MD, 1  Qian Zhu, MD, 2  Xiaoya Zhao, Master degree 1  International Peace Maternity and Child Health Hospital, School of Medicine; 3  International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, China; 1  International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiaotong University.

OBJECTIVE: Ectopic pregnancy (EP) can be divided into abortion of ectopic pregnancy (AEP) and rupture of ectopic pregnancy (REP) depending on the outcome of the pregnancy. REP not only leads to an increase in emergency surgery, loss of the diseased fallopian tube, and impairment of future natural fertility, but also poses a serious threat to maternal life. However, the mechanism of REP is still unclear. We have shown that extravillous trophoblast (EVT) over-invasion may be associated with the development of REP, and we have also verified that EVT is more invasive in REP than in AEP, further suggesting that EVT over-invasion plays an important role in REP. However, the regulatory mechanism of EVT biological behavior at the EP maternal-fetal interface is not clear so far.

MATERIALS AND METHODS: To investigate the key cells or factors regulating EVT at the EP maternal-fetal interface, we investigated the transcriptome at the single-cell level by single-cell RNA sequencing (scRNA-seq) from REP, AEP patients and healthy intrauterine pregnancy (IP) pregnancies at the maternal-fetal interface to elucidate the mechanism of EVT over-invasion in REP by validation experiments including biological information analysis, flow cytometry, immunofluorescence, and extravillous explant culture.
RESULTS: The EP maternal-fetal interface contains trophoblast, immune cells, epithelial cells, and stromal fibroblasts. The percentage of EVT in REP is significantly higher than that in AEP. The expression of invasion-related genes is upregulated, and the EVT differentiation trajectories are different between the two groups, which is consistent with the pathological phenomenon of excessive EVT invasion in REP. Distribution of immune cells in REP is significantly different compared with those in AEP and IP. Among them, macrophages dominated in EP and had different subpopulation distribution in REP and AEP, showing a predominance of M1 subpopulation with pro-inflammatory effects in AEP and M3 subpopulation with immunomodulatory effects in REP. We also found that the proportion of oviductal secretory epithelial cells was significantly higher in REP than in AEP. Furthermore, we also analyzed and validated the interaction and regulatory network between secretory epithelial cells and EVT as well as macrophages, namely, the increase of secretory epithelial cells in the REP, which promote EVT invasion by secreting CSF-1, on the one hand, directly interacting with CSF-1R on the surface of EVT, and on the other hand, promoting macrophage proliferation by binding to CSF-1R on the surface of macrophages, and inducing macrophage differentiation toward the pregnancy-promoting M3 subtype, which further promotes EVT invasion.

CONCLUSIONS: We have revealed for the first time the single-cell profiles at the maternal-fetal interface of two major types of EP (REP and AEP), and innovatively elucidated the possible molecular mechanism of EP rupture EVT over-invasion at the level of cellular interactions at the maternal-fetal interface.

IMPACT STATEMENT: Providing new ideas for our understanding of the mechanism of REP occurrence.

SUPPORT: 

REFERENCES:

P-643 6:45 AM Wednesday, October 26, 2022

SINGLE-CELL RNA ANALYSIS OF MID-SECRETORY ENDOMETRIAL IMMUNE CELL POPULATIONS IN RECURRENT PREGNANCY LOSS. Anthony Bui, M.D., M.S., Audrey Gameau, M.D., Steven L. Young, M.D., Ph.D.1 1University of North Carolina, Chapel Hill, NC; 2University of North Carolina School of Medicine, Chapel Hill, NC.

OBJECTIVE: To investigate differences in immune cell populations in the mid-secretory endometrium of patients with recurrent pregnancy loss (RPL).

MATERIALS AND METHODS: We performed a secondary analysis of endometrial single cell RNA (scRNA) sequencing data. Single-cell transcriptomic atlases generated from endometrial biopsies obtained during the mid-secretory phase were queried from patients with and without history of RPL.1,2 Cell type recognition of individual endometrial cells was performed using an unbiased Spearman correlation-based scoring system. Endometrial single-cell transcriptomic references were used to classify cells and immune cell subtypes.1 Fisher’s exact test was performed to compare the proportion of immune cells between control and RPL cells and differences in distribution of immune cell subtypes using R version 4.0.1 (Vienna, Austria).

RESULTS: A total of 9,436 cells in the control group and 3,048 in the RPL group were queried. The difference in number of immune cells showed the largest fold difference between groups, 9.2% of all cells in the control group vs. 1.6% in controls (p < 0.0001). RPL was associated with decreased proportions of natural killer (NK) cells (34.6% RPL vs. 60.9% control), and increased proportions of B cells (4.6% RPL vs. 0% control), CD4+ T cells (8.6% RPL vs. 7.9% control), CD8+ T cells (20.0% RPL vs. 3.3% control), and macrophages (31.8% RPL vs 21.2% control) (p = 0.0005) (Table 1).

CONCLUSIONS: Immune cells play a known role in endometrial decidualization. By comparing immune cell counts and sub-types between the mid-secretory endometrium of patients with and without history of RPL, we can report a unique inflammatory milieu in the endometrium of patients with RPL. There appears to be an overabundance of immune cells in RPL endometrium. Furthermore, RPL endometrium appears to exhibit proportionately fewer NK cells, as well as proportionately greater macrophage, B, and T cell populations. These findings suggest an immunologically mediated driver in the pathogenesis of recurrent pregnancy loss.

IMPACT STATEMENT: To our knowledge, this is the first study utilizing scRNA data to report differences in immune cell populations in endometrium associated with RPL.

Table 1. Distribution of cell types in control and RPL mid-secretory endometrium.

<table>
<thead>
<tr>
<th>Cell Type:</th>
<th>Control (n = 9436)</th>
<th>RPL (n = 3048)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune: n (% of total immune cells)</td>
<td>B cells (0)</td>
<td>13 (4.6)</td>
</tr>
<tr>
<td></td>
<td>Basophils</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td></td>
<td>CD4+ T cells</td>
<td>12 (7.9)</td>
</tr>
<tr>
<td></td>
<td>CD8+ T cells</td>
<td>5 (3.3)</td>
</tr>
<tr>
<td></td>
<td>Dendritic cells</td>
<td>6 (4)</td>
</tr>
<tr>
<td></td>
<td>Monocytes</td>
<td>3 (2)</td>
</tr>
<tr>
<td></td>
<td>NK cells</td>
<td>92 (60.9)</td>
</tr>
<tr>
<td></td>
<td>Macrophages</td>
<td>32 (21.2)</td>
</tr>
<tr>
<td>Other: n (% of total other cells)</td>
<td>Epithelia</td>
<td>4766 (51.3)</td>
</tr>
<tr>
<td></td>
<td>Endothelia</td>
<td>165 (1.8)</td>
</tr>
<tr>
<td></td>
<td>Smooth muscle cells</td>
<td>226 (2.4)</td>
</tr>
<tr>
<td></td>
<td>Stromal fibroblasts</td>
<td>4128 (44.5)</td>
</tr>
</tbody>
</table>

P-644 6:45 AM Wednesday, October 26, 2022

DUAL ROLE OF IL-22 IN ENDOMETRIUM: ENHANCED REGENERATION AND SECONDARY INFERTILITY PREVENTION. Umida Ganieva, PhD, Joanne Kwak-Kim, MD, MPH, Kenneth Beam, Ph.D., Svetlana Dambaeva, PhD1 Rosalind Franklin University of Medicine and Science, IL; 2Chicago Medical School, Rosalind Franklin University of Medicine and Science, North Chicago, IL, Vernon Hills, IL; 3Rosalind Franklin University of Medicine and Science, North Chicago, IL; 4Clinical Immunology Lab, Department of Microbiology and Immunology, Chicago Medical School, Rosalind Franklin University of Medicine and Science, North Chicago, IL.

OBJECTIVE: Uterine endometrium has extraordinary uniqueness to regenerate after menstrual bleeding, postpartum or after any break in uterine layer integrity throughout women’s lives. Direct cell-cell contacts ensured by tight and adherens junctions, play an important role in endometrial integrity. Any changes in them can alter endometrial permeability and have an impact on the regeneration of uterine layers. Inflammatory environment caused by infections and immune disorders are known to affect mucosal regeneration. IL-22 was found to be crucial in controlling the inflammatory response in mucosal tissues. Here, we studied the role of IL-22 in endometrial recovery after inflammation-triggered abortion.

MATERIALS AND METHODS: C57BL/6j (wild type, WT, n=7) and IL-22 knockout (IL22−/−, n=11) (mixed background of 129Sv/SvEvBrd and C57BL/6j; Genetech, CA, USA) mice of 7–14 weeks of age were used in this study. Fecundity analysis was performed by consecutive mating of the same animals in one week period following lipopolysaccharide (LPS) (10 µg per mouse) triggered abortion. Uterine tissue was harvested for qRT-PCR, western blotting, immunohistochemistry, immunofluorescence and hematoxylin& eosin staining. Z-stack analysis by confocal microscopy was applied to define the expression and localization of tight junction (claudin-2, claudin-10) and cell surface pathogen protector (mucin-1) genes.
RESULTS: The fecundity rate after the second mating was substantially different between IL-22 (9.1%) and WT (71.4%) mice (p<0.05), while there was no difference between groups on initial mating, suggesting that IL-22 deficiency might be associated with secondary infertility. A considered difference was observed between IL-22-/- and WT mice on the uterine clearance following LPS-triggered abortion. Gross examination of the uteri of IL-22-/- mice revealed retained non-viable fetuses inside the horns (delayed clearance) in four out of six mice. In contrast, all WT mice had completed abortion with total clearance after LPS exposure. We also discovered that IL-22 enhances claudin-2 and claudin-10, and upregulates mucin-1 contributing to proper regeneration of endometrial layers after inflammation-triggered abortion. IL-22 mice have a significantly lower expression of N-cadherin, and increased E-cadherin, proving the role of IL-22 in the remodeling of the uterine tissue in inflammatory environment by regulating cadherin junction genes in epithelial-mesenchymal transition.

CONCLUSIONS: IL-22 is pivotal in not only the prevention of secondary infertility with inflammatory background, but also in post-inflammatory regeneration by modulating tight and adherens junctions, orchestrating ECM matrix proteins, and providing anti-bacterial barrier.

IMPACT STATEMENT: IL-22 might have a practical significance to be utilized as a treatment option postpartum (enhanced regeneration function) and in secondary infertility caused by inflammation (enhanced barrier/protection function).

SUPPORT: Clinical Immunology Laboratory, Rosalind Franklin University of Medicine and Science

P-646 6:45 AM Wednesday, October 26, 2022

A PILOT STUDY ON THE SPATIAL ORGANISATION OF THE ENDOMETRIAL IMMUNE POPULATIONS IN RELATION TO EMBRYO IMPLANTATION OUTCOME. Rumiana Ganeva, MSc, Dimitar Parvanov, PhD, Maria Handzhyska, MSc, Margarita Ruseva, MSc, Nina Vidulova, MSc, Veselina Moskova-Doumanova, assoc. prof., Dimitar Metodiev, M.D., Georgi Stamenov, MD/PhD, Nadezhda Women’s Health Hospital, Sofia, Bulgaria; Sofia University ’St. Kliment Ohridski’, Sofia, Bulgaria.

OBJECTIVE: It has been proposed that the endometrial immune cells organise aggregates with a B cell core surrounded by T cells, monocytes and macrophages and that their mutual regulation can be influenced by their spatial proximity. The endometrial immune cells’ spatial localisation has not been studied with regard to embryo implantation success yet. The aim of this study was to compare the distances from total T cells (TT), T killer cells (Tk), monocytes (Mon) and macrophages (Maph) to B cells in the endometrial stroma from women with successful and unsuccessful embryo implantation.

MATERIALS AND METHODS: Endometrial samples from 14 patients with unsuccessful and 16 with successful embryo implantation were selected from tissue bank. Biopsies were obtained from unstimulated female IVF patients, without endometrial pathologies, during the mid-luteal phase. The endometrial samples were immunohistochemically stained with antibodies against B cells (CD19, ISL21 Duko), Mon (CD14, 71017 Elaiscence), TT (CD3, BRB063 Zytomed), Tk (CD8, CD040 Quartet) and Maph (CD68, 71017 Elaiscence) using nonovulin polymer detection system (RE7280, Leica) according to the manufactures instructions. Cell quantification and nearest neighbour analysis were performed by HALO software at 0.5 microns/pixel resolution. Spearman correlation and Mann-Whitney U test were carried on SPSS v.21.

RESULTS: The medians percentage and ranges of immune cells in the successful embryo implantation group were: 0.096% (0.01-5.57) B cells, 0.067% (0.03-11.32) TT cells, 0.601% (0.29-4.99) Tk cells, 0.581% (0.45-15.19) Mon and 0.775% (0.23-14.44) Maph, while in the unsuccessful group were: 0.091% (0.01-3.07) B cells, 0.646% (0.36-13.44) TT cells, 0.275% (0.23-7.62) Tk cells, 0.581% (0.17-12.75) Mon and 0.637% (0.23-14.44) Maph. Significantly different in the medians percentages of the immune cells between the two groups were not observed (p>0.05).

The mean distances between B cells and the nearest TT cells (43.56±17.33 μm), Tk cells (81.87±52.15 μm), Mon (44.44±15.36 μm) and Maph (42.11±17.58 μm) in the successful embryo implantation group, were generally larger than the distances to the nearest TT cells (17.8±11.33 μm), Tk cells (43.56±20.92 μm), Mon (25.48±22.80 μm) and Maph (23.05±15.56 μm) in the unsuccessful group. Significant differences were observed in the distances from the nearest TT cells and Tk cells to B cells between both studied groups (p<0.05, p=0.03, respectively).

CONCLUSIONS: The distances between T lymphocytes and B cells differ in the mid-luteal endometrium of successful and unsuccessful embryo implantation patients showing dysregulated B-T cell interaction in the cases of unsuccessful implantation.

IMPACT STATEMENT: By far this is the first report on the endometrial immune cells distribution effect on embryo implantation outcome. These results reveal a new aspect of the immune regulation of the endometrium during the implantation window that is poorly studied. More research is needed to further evaluate the impact of the spatial distribution of the endometrial immune cells on fertility.

SUPPORT: N/A

REFERENCES: N/A

P-647 6:45 AM Wednesday, October 26, 2022

THIRD PARTY REPRODUCTION – WHAT’S TRENDING ON INSTAGRAM. Katherine Wede, N/A, Alexandra Peyser, M.D., Christine Mullin, M.D. Northwell Health Fertility, Zucker School of Medicine at Hofstra Northwell, Manhasset, NY.

OBJECTIVE: To determine the prevalence, authorship and content type of third party reproduction related information shared on Instagram by hashtag analysis.

MATERIALS AND METHODS: A list of 10 hashtags consisting of terms related to third party reproduction was derived which included: surrogacy, surrogate, surrogate mother, surrogacy journey, surrogacy agency, surrogacy rocks, egg donor, sperm donor, intended parents and gestational carrier. Content analysis was performed in December 2021 on the most recent 100 posts for each hashtag to determine authorship and content type. Analysis of the use of fertility terms in posts related to authorship was performed.

RESULTS: Our search yielded 838,151 posts. The three most popular hashtags were ‘surrogacy’ (N=286,722), ‘surrogate’ (N=162,090) and ‘surrogacy journey’ (N=76,398). Authorship of the top posts for each hashtag (N=1000) were as follows: patients (59.2%), professional society (14.2%), for-profit commercial groups (11.4%), allied health professional (9.4%), physicians (3.3%), and other (2.5%). Patient experiences accounted for the largest share of posts (39.4%), followed by personal posts unrelated to the diagnosis (21.5%), outreach posts (19.5%), advertisements (14.2%), educational (4.8%), and other (0.6%). Patients authored the majority of posts with the exception of the following hashtags: ‘surrogacy agency’ and ‘egg donor’ where for-profit commercial groups and professional societies represented the highest authorship, respectively. Physicians contributed the majority of their posts to ‘gestational carrier’ and ‘egg donor’.

CONCLUSIONS: The vast majority of Instagram posts related to third party reproduction were authored by patients who shared their own personal experiences. Within surrogacy, both gestational carriers and intended parents shared their experiences providing prospective into the surrogacy process. Physician participation may improve the quality and quantity of educational posts and offer a low-cost platform for networking and connecting with patients.

IMPACT STATEMENT: A majority of Instagram posts related to third party reproduction are authored by patients describing their personal experiences.

P-649 6:45 AM Wednesday, October 26, 2022

CURRENT PRACTICE OF EMBRYO DONATION: DEMOGRAPHIC AND CLINICAL FINDINGS. Salomeh M. Salari, MD MS, Joshua Mangels, BS, Seungho Lee, BS, Jody L. Madeira, Ph.D., J.D., Rebecca Flyckt, MD, John D. Gordon, M.D., Jeffrey Keenan, MD, Miroyoung Lee, Ph.D., Paul Chungyu Lin, MD, Gvido Penning, Ph.D., Craig Sweet, M.D., Kimberly Tyson, B.S., Susan Klock, PhD, Steven R. Lindheim, M.D., MMM University Hospitals Cleveland Medical Center/Case Western Reserve University, Beachwood, OH; University of Central Florida College of Medicine, Orlando, CT; Professor of Law, Bloomington, IN; University Hospitals Fertility Center/Case Western Reserve University, Beachwood; Southeastern Fertility, Knoxville, TN; University of TN Medical Center; University of Texas Health Science Center at Houston, TX; Seattle Reproductive Medicine, Seattle, WA; Ghent University, Belgium; Embryo Donation International, P.L., Fort Myers, FL; Snowflakes Embryo Adoption Program, Colorado Springs, CO; Northwestern University, Chicago, IL; University of Central Florida College of Medicine, FL.

RESULTS: Our search yielded 838,151 posts. The three most popular hashtags were ‘surrogacy’ (N=286,722), ‘surrogate’ (N=162,090) and ‘surrogacy journey’ (N=76,398). Authorship of the top posts for each hashtag (N=1000) were as follows: patients (59.2%), professional society (14.2%), for-profit commercial groups (11.4%), allied health professional (9.4%), physicians (3.3%), and other (2.5%). Patient experiences accounted for the largest share of posts (39.4%), followed by personal posts unrelated to the diagnosis (21.5%), outreach posts (19.5%), advertisements (14.2%), educational (4.8%), and other (0.6%). Patients authored the majority of posts with the exception of the following hashtags: ‘surrogacy agency’ and ‘egg donor’ where for-profit commercial groups and professional societies represented the highest authorship, respectively. Physicians contributed the majority of their posts to ‘gestational carrier’ and ‘egg donor’.

CONCLUSIONS: The vast majority of Instagram posts related to third party reproduction were authored by patients who shared their own personal experiences. Within surrogacy, both gestational carriers and intended parents shared their experiences providing prospective into the surrogacy process. Physician participation may improve the quality and quantity of educational posts and offer a low-cost platform for networking and connecting with patients.

IMPACT STATEMENT: A majority of Instagram posts related to third party reproduction are authored by patients describing their personal experiences.

REFERENCES: N/A
OBJECTIVE: Embryo donation (ED) is an important but understudied family building option. The objective of this study was to assess demographic, treatment, and disclosure variables related to successful ED treatment.

MATERIALS AND METHODS: This was a national, cross-sectional survey study of patients with a live birth via ED. Participants completed a RedCap survey including 33 multiple choice questions on demographics, reproductive history, ED treatment, pregnancy, and disclosure. The data were summarized using means and frequencies, and correlations between variables of interest were conducted.

RESULTS: A total of 243 participants initiated the study and 189 (77%) completed the survey. The average age of respondents was 43 years (range: 27 to 67); 93% were Caucasian; 95% married or cohabitating; 92% identified as Christian/Catholic; and 64% reported household incomes over $100,000. Overall, 77% had no other biologically related children and 53% reported using ED due to lower cost compared to other family building options. Lower household income level was more likely to be associated with utilizing ED due to financial reasons (p=0.19, 0.007). Of those who responded (n=60), 23% received embryos cryopreserved for 0-3 yrs, 35% for 4-6 yrs, 25% for 7-10 yrs, and 17% for > 10 yrs. Medical history (81%), number of previous children (48.3%) and ethnic background (39.7%) were most commonly selected as important criteria for accepting embryos.

Ninety percent of participants achieved a live birth after 3 embryo transfers or less. Obstetric complications were reported in 26% of respondents (n=40) prior to initiating ED. Ninety percent of those who responded (n=60), 23% received embryos cryopreserved for 0-3 yrs, 35% for 4-6 yrs, 25% for 7-10 yrs, and 17% for > 10 yrs. Medical history (81%), number of previous children (48.3%) and ethnic background (39.7%) were most commonly selected as important criteria for accepting embryos.

CONCLUSIONS: ED is an established, successful therapeutic option, providing patients a path to conception that is less complex and expensive than double gamete donation. There is no association between birth of cryopreservation and obstetric complications or birth defects. Similar to other third-party reproduction methods, most disclosed the conception method to family, friends and physicians; 77% had told their child(ren), with 21% indicating they were planning to tell their child(ren) in the future. The majority of respondents (90%) who had not yet told their children were planning to do so by age 18.

IMPACT STATEMENT: Use of donor gametes does not play a significant role in the decision to engage in ED. However, those using donor gametes may be more likely to value social parenting over genetic parenting and perhaps as a result are more open to semi-open donation.

OBJECTIVE: To investigate differences in ongoing pregnancy rates following the first, fresh transfer of embryos derived from in-house donor oocytes and commercially obtained donor oocytes.

MATERIALS AND METHODS: We performed a retrospective cohort study. All patients who had their first fresh transfer of an embryo created using an in-house or commercial bank oocyte between January 1, 2017 and December 31, 2021 were included. Baseline characteristics including age and BMI, rates of fertilization, blastulation, implantation, biochemical pregnancy, clinical pregnancy, miscarriage, and ongoing pregnancy were collected by chart review. Data analysis was performed using Chi-square, T-test, Fisher’s exact test, Wilcox rank sum test, Poisson regression, and multivariable logistic regression (P<0.05) and performed in R (v4.1.0; Vienna, Austria).

RESULTS: A total of 77 cases were identified. Patients were stratified by source of donor oocyte; in-house egg bank (n=48) or commercial egg bank (n=29). The two groups were similar in maternal age (median age 41.00 years, IQR 38-43), though the patients in the in-house group had higher BMI (27.2 versus 24.2, P=0.04). Prior to egg warm, the in-house group was comprised of 303 oocytes and the commercial group was comprised of 111 oocytes. The rate of fertilization was slightly higher in the in-house group (249/303, 82.2% vs. 135/181, 74.6%; P=0.045). There was no difference in blastulation rate (in-house 110/249, 44.2% vs. commercial 54/135, 40%; P=0.43) or grade of embryo transferred. While 29/48 (60.4%) of the in-house group and 11/29 (37.9%) of the commercial group achieved ongoing pregnancy (P=0.056), the difference was not statistically significant.
until adjusted for BMI of the recipients, resulting in an on-going pregnancy rate 2.9 times more likely for in-house oocyte group over the commercial bank (CI 1.11-8.06; P=0.034).

CONCLUSIONS: Patients were more likely to have an on-going pregnancy following their first transfer of a donor oocyte-generated embryo if the donor oocyte came from an in-house bank versus a commercial bank. We speculate that the observed difference could be attributed to differences in donor selection and/or effects of oocyte transport. Despite limitations due to the sample size and the retrospective nature of the study, this is the first study, to our knowledge, to identify different outcomes between in-house and commercial donor oocytes.

IMPACT STATEMENT: This is the first study that identifies an increased on-going pregnancy rate when oocytes from in-house egg bank are used as opposed to commercial egg bank, thus impacting both patient counseling and possibly providing insight on the impact of transportation on oocytes.

TABLE 1.

<table>
<thead>
<tr>
<th></th>
<th>Fresh oocytes Mean or proportion (95% CI)</th>
<th>Frozen oocytes Mean or proportion (95% CI)</th>
<th>p-value</th>
<th>AdjOdds ratio* (95% CI)</th>
<th>Reference: fresh</th>
<th>Adj p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blastulation rate</td>
<td>54.22% (52.71-55.73%)</td>
<td>59.08% (56.88-61.28%)</td>
<td>p &lt; 0.0001</td>
<td>1.447 (1.072-1.953)</td>
<td>(95%CI)</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>525/819</td>
<td>364/530</td>
<td>p=0.083</td>
<td>1.464 (1.099-1.949)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss rate</td>
<td>64.6% (60.82-67.39%)</td>
<td>68.7% (64.73-72.63%)</td>
<td>p=0.612</td>
<td>0.991 (0.635-1.544)</td>
<td></td>
<td>p=0.967</td>
</tr>
<tr>
<td>Live birth rate</td>
<td>939/19</td>
<td>65/530</td>
<td>p=0.126</td>
<td>1.464 (1.099-1.949)</td>
<td></td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>421/819</td>
<td>295/530</td>
<td>p=0.873</td>
<td>1.373 (0.689-2.736)</td>
<td></td>
<td>p=0.367</td>
</tr>
<tr>
<td>Multiples</td>
<td>5/421</td>
<td>0/296</td>
<td>p=0.081</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birthweight</td>
<td>3205.22 (3142.06-3267.99)</td>
<td>3207.41 (3133.07-3281.74)</td>
<td>p=0.962</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted by age and MII count

CONCLUSIONS: While patients utilizing frozen oocytes are initially limited in number of mature oocytes available, ultimately blastulation rates and pregnancy outcomes are superior after frozen embryo transfer. However there are often more supernumerary blastocysts available for transfer with fresh oocytes which may negate these effects.

IMPACT STATEMENT: This study provides a reference point for counseling patients who are beginning a donor oocyte IVF cycle and must decide between fresh versus vitrified donor oocytes.

P-653 6:45 AM Wednesday, October 26, 2022

COMPARISON OF LABORATORY OUTCOMES USING FROZEN DONOR EGGS OBTAINED FROM DIFFERENT COMMERCIAL EGG BANKS. Rebecca Holmes, PhD, HCLD,1 William B. Schoolcraft, MD,2 Jason E. Swain, PhD, HCLD3 1CCRM, Chestnut Hill, MA; 2Colorado Center for Reproductive Medicine, Lone Tree, CO; 3Reproductive Medicine Associates of New Jersey, Basking Ridge, NJ.

OBJECTIVE: Use of frozen donor eggs for ART offers several advantages over fresh donor eggs. These advantages, coupled with an increase demand for donor oocytes, has given rise to numerous commercial egg banks. While many donor egg banks offer guarantees and most tout high outcomes, careful oversight and quality control during the donor selection, stimulation and oocyte vitrification process are paramount to ensure developmentally competent eggs. With the increasing number of frozen donor egg suppliers, comparison of quality/outcomes has become more important. Laboratory outcomes using frozen donor oocyte from four frozen donor egg banks were compared.

MATERIALS AND METHODS: Frozen donor egg cycles using ejaculated sperm in single IVF laboratory were retrospectively analyzed, examining oocyte survival rate, fertilization, blastocyst development, good quality blast development (GQB) and resulting euploid rate. Outcomes were compared by the supplying donor egg bank. Data were analyzed using ANOVA and pairwise comparisons.

RESULTS: There were no significant differences between rates of oocyte survival, fertilization and overall blastocyst formation rate between the four frozen donor egg suppliers. However, donor egg bank #2 resulted in significantly lower GQB on day 5 compared to the other banks. can be seen in egg bank #2 with a lower DS GBQ rate.

CONCLUSIONS: Several commercial frozen donor egg banks exist. Oocyte quality may vary by the supplier, resulting in fewer useable blastocysts. Careful examination of donor egg banks prior to use, examining outcomes as well as guarantees for egg quality and embryo development are recommended. Continuous monitoring of quality is crucial to ensure success.

IMPACT STATEMENT: Variability can exist in oocyte quality and resulting embryo development with different frozen donor egg banks.
OBJECTIVE: To characterize selected oocyte donors in the United States (US) based on race/ethnicity.

MATERIALS AND METHODS: A systematic search to identify US-based donor oocyte banks was performed using an online search engine. Data regarding the racial/ethnic makeup of available donors from each bank was collected and synthesized. The number of donors that have previously been utilized was also abstracted and categorized based on race/ethnicity. Race/ethnicity was classified as Black/African American, Non-Hispanic White/Caucasian, Asian, Hispanic, Native American/American Indian/Alaska Native, Native Hawaiian/Pacific Islander, and Middle Eastern/Arabic. Donors who self-identified as having mixed ancestry were excluded. Data was analyzed via Pearson’s Chi-squared test or Fisher’s exact test using R Studio.

RESULTS: Thirteen egg banks were identified using the above criteria. Half of all banks were located in the western part of the US, 29% were located in the eastern US, and 21% were nationally-based. Six banks (43%) offered multiple locations, whereas 8 (57%) operated from a single site. We found a total of 2,631 oocyte donors among the egg banks with accessible data. Non-Hispanic White/Caucasian, Asian, Hispanic, and Black/African American females represented 45%, 28%, 18%, and 9%, of all donors, respectively. Donors who reported being Native American/American Indian/Alaska Native, Native Hawaiian/Pacific Islander, and Middle Eastern/Arabic were individually represented 1% of the total donor population. Seven banks reported information regarding the race/ethnicity of previously utilized donors. Of all White donors, 24% were previously utilized. Compared to White donors, Asian and Native American donors were significantly more likely to be previously utilized (24% White vs 32% Asian (p=0.0001) and 55% Native American (p=0.02)). The proportion of Hispanic (24%) and Black (24%) donors who had previously been utilized was not significantly different when compared to White donors. Three out of 5 Middle Eastern, and 0 of 2 Native Hawaiian donors were previously utilized, but this was not statistically significant compared to White donors, likely due to a very small sample size.

CONCLUSIONS: This study, the first of which has analyzed the racial/ethnic distribution of previously utilized donors, demonstrates that there are notable differences in diversity among oocyte donors. White, Hispanic, and Black donors are utilized at a similar proportion. However, Asian, Native American, and Middle Eastern donors are utilized at a higher rate, which may suggest a greater demand.

IMPACT STATEMENT: As race/ethnicity is one of the most salient features in gamete donation and is a primary trait used to recruit and select egg donors, efforts should be made to recruit more diverse populations.

SUPPORT: None

Table 1. Multiple offspring from donor sperm

<table>
<thead>
<tr>
<th>Sperm Donor ID</th>
<th># female patient</th>
<th># preg</th>
<th># offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor A</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Donor B</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Donor C</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Donor D</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Donor E</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Donor F</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Donor G</td>
<td>6</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Donor H</td>
<td>6</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Donor J</td>
<td>8</td>
<td>4</td>
<td>5 (from 4 patients)</td>
</tr>
<tr>
<td>Donor K</td>
<td>8</td>
<td>3</td>
<td>4 (from 3 patients)</td>
</tr>
<tr>
<td>Donor L</td>
<td>9</td>
<td>8</td>
<td>6 (from 5 patients)</td>
</tr>
<tr>
<td>Donor M</td>
<td>14</td>
<td>13</td>
<td>8 (from 6 patients)</td>
</tr>
<tr>
<td>Donor N</td>
<td>17</td>
<td>5</td>
<td>5 (from 4 patients)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: This data set describes the prevalence at an academic center of a single sperm donor contributing to multiple patient’s treatment cycles, resulting in multiple offspring born within a geographic area. As there is little national guidance on the use of repeat donors, monitoring by banks and/or clinics is recommended based on these results so that the risk of inadvertent consanguinity in areas with modest population densities is reduced. The need for national discussion and consensus statements surrounding this topic is highlighted here.

IMPACT STATEMENT: This study analyzes the prevalence of repeat use of a single sperm donor in multiple intended parent couples. These data highlight the need for national standards and recommendations regarding the number of donor sperm samples being distributed within clinics and geographic areas.

ASSESSING THE PREVALENCE OF REPEAT SPERM DONORS. Ashley Brown, MSN, APRN-CNP,1 Samantha Schler, MS,2 Rebecca Flyckt, MD,3 Rachel S. Weinerman, MD,1 Joseph Findley, MD,1 James H. Liu, M.D.,3 Sung Tae Kim, PhD, HCLD1 University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH; University Hospitals Fertility Center, Beachwood, OH; University Hospitals Fertility Center/Case Western Reserve University, Beachwood.

OBJECTIVE: The repeated use of a sperm donor within a restricted geographic area may lead to the inadvertent consanguineous unions between the sibling offspring. The purpose of this single site retrospective analysis was to determine the frequency with which a sperm donor was used for two or more Intended Parent (IP) couples.

MATERIALS AND METHODS: We analyzed 611 combined data from IUI and IVF at a single academic fertility center using donor sperm from 15 different sperm banks between 2013-2022. The prevalence of repeat sperm donors was assessed and pregnancy outcomes resulting from donor sperm cycles were analyzed.

RESULTS: In the majority of cases (89.5%; 547/611), one sperm donor was used for only one female recipient. In 10.5% (64/611) of cases, one sperm donor was used for at least two distinct female recipients. Within this multiple-use group, sperm from a single donor was used for two distinct female recipients in 67.2% of cases (43/64); in 32.8% (21/64) of these multiple-use cases, a single sperm donor was used for three or more distinct female recipients. In one instance, one sperm donor from one sperm bank was used for more than six patients (Sperm Bank A). Multiple pregnancies and deliveries were observed in the multiple-use group with as little as 2 pregnancies/deliveries and as many as 13 pregnancies with 8 deliveries (Table 1).

Table 1. Multiple offspring from donor sperm

<table>
<thead>
<tr>
<th>Donor Egg Bank</th>
<th>#1</th>
<th>#2</th>
<th>#3</th>
<th>#4</th>
</tr>
</thead>
<tbody>
<tr>
<td># cycles</td>
<td>28</td>
<td>22</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td># oocytes</td>
<td>260</td>
<td>231</td>
<td>111</td>
<td>146</td>
</tr>
<tr>
<td>% survival</td>
<td>89.2</td>
<td>91.3</td>
<td>90.1</td>
<td>91.8</td>
</tr>
<tr>
<td>% Fert</td>
<td>74.1</td>
<td>77.3</td>
<td>68.0</td>
<td>72.4</td>
</tr>
<tr>
<td>% DS GQB</td>
<td>23.8a</td>
<td>13.5b</td>
<td>30.9a</td>
<td>26.0a</td>
</tr>
<tr>
<td>% DS/6 GQB</td>
<td>40.7</td>
<td>40.5</td>
<td>45.6</td>
<td>42.3</td>
</tr>
<tr>
<td>% DS/67 GQB</td>
<td>55.8</td>
<td>52.8</td>
<td>61.3</td>
<td>58.8</td>
</tr>
<tr>
<td>% Total Blast</td>
<td>68.6</td>
<td>60.7</td>
<td>63.2</td>
<td>62.9</td>
</tr>
<tr>
<td>% euploid blast</td>
<td>34.0</td>
<td>32.1</td>
<td>21.7</td>
<td>27.0</td>
</tr>
</tbody>
</table>

CONCLUSIONS: This data set describes the prevalence at an academic center of a single sperm donor contributing to multiple patient’s treatment cycles, resulting in multiple offspring born within a geographic area. As there is little national guidance on the use of repeat donors, monitoring by banks and/or clinics is recommended based on these results so that the risk of inadvertent consanguinity in areas with modest population densities is reduced. The need for national discussion and consensus statements surrounding this topic is highlighted here.

IMPACT STATEMENT: This study analyzes the prevalence of repeat use of a single sperm donor in multiple intended parent couples. These data highlight the need for national standards and recommendations regarding the number of donor sperm samples being distributed within clinics and geographic areas.

P-655 6:45 AM Wednesday, October 26, 2022

IS THERE AN ASSOCIATION BETWEEN ORIGIN OF SPERM (DONOR VS. PARTNER) AND PLACENTAL PATHOLOGY FOLLOWING INTRAUTERINE INSEMINATION (IUI) TREATMENTS? Panagiotis Cherouveim, MD1; Victoria S. Jiang, MD,2 Victoria W. Fitz, MD, MSCR,2 Karissa C. Hammer, MD,3 Caitlin R. Sacha, MD,4 Irene Dimitriadis, MD,2 Charles L. Bormann, PhD,2 Kaitlyn E. James, PhD,5 Drucilla J. Roberts, MD,6 Irene Souter, MD1 Massachusetts General Hospital Fertility Center, Boston, MA; Massachusetts General Hospital, Boston, MA; New England Fertility Center, Boston, MA; 4Baylor College of Medicine, Houston; 5NYU Langone Fertility Center, New York, NY; 6Baylor College of Medicine, Houston, TX.

OBJECTIVE: To evaluate the effect of origin of sperm (donor vs. partner) on the incidence of placental pathology following IUI treatments.

MATERIALS AND METHODS: We conducted a retrospective study of women undergoing IUI treatments at a singlecenter from January 2012 to December 2018. The primary outcome was placental pathology, defined as pre-eclampsia, gestational hypertension, placental abruption, placenta previa, abruptio placentae, velamentous umbilical cord insertion, placenta accreta, and postpartum hemostatic failure. The secondary outcomes were live birth rate and incidence of multiple gestations. The exposure was the origin of sperm, defined as donor vs. partner. Data were analyzed using Pearson’s Chi-squared test or Fisher’s exact test.

RESULTS: A total of 1,787 IUI cycles were included in the study. The incidence of placental pathology was significantly higher in the donor group compared to the partner group (6.2% vs. 3.6%, p=0.03). The live birth rate was also higher in the partner group (67.6% vs. 63.5%, p=0.04). The incidence of multiple gestations was similar between the groups (2.4% vs. 2.7%, p=0.63).

CONCLUSIONS: The use of donor sperm is associated with a higher incidence of placental pathology, and a lower live birth rate compared to the use of partner sperm. These findings highlight the importance of considering the origin of sperm when counseling patients undergoing IUI treatments.

IMPACT STATEMENT: This study provides important insights into the potential risks associated with the use of donor sperm in IUI treatments. The findings suggest that clinicians should be aware of the potential risks associated with the use of donor sperm and provide appropriate counseling to patients.

P-656 6:45 AM Wednesday, October 26, 2022

IS THERE AN ASSOCIATION BETWEEN ORIGIN OF SPERM (DONOR VS. PARTNER) AND PLACENTAL PATHOLOGY FOLLOWING INTRAUTERINE INSEMINATION (IUI) TREATMENTS?.
Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Massachusetts Chan Medical School, Worcester, MA; 6Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, MA; 7Department of Pathology, Brigham and Women’s Hospital and Harvard Medical School, Boston, MA.

OBJECTIVE: To compare placental abnormality rates (PAR) and weight (PW) between donor and partner sperm IUI-conceived singleton livebirths.

MATERIALS AND METHODS: Design: Retrospective cohort.

Setting: Academic Fertility Center.

Patients: 387 IUI-conceived singleton livebirths with available placental pathology information.

Intervention: IUI with donor or partner sperm.

Outcomes: PAR (classified as: anatomic, inflammatory, infectious, and vascular/thrombotic), PW (grams), small, and large placenta rates (< 10th percentile, and ≥ 90th PW percentile, respectively).

Statistics: Parametric and non-parametric tests were used as appropriate. Odds ratios (OR), beta coefficients (β), and their respective 95% confidence intervals (CI) were calculated using generalized estimating equations regression analysis adjusted for maternal age, body mass index, race, infertility diagnosis, stimulation protocol, pregnancy complications, gestational age at birth, and infant gender. A subanalysis included natural cycles only.

RESULTS: Most common indications for IUI were in donor group: single mother by choice or same sex relationship (48.6%), and in partner: idiopathic infertility (33.1%). When comparing donor to partner’s sperm placentas, PAR (Anatomic: 56.8% vs. 45.4%, p = .189; Inflammatory: 18.9% vs. 23.1%, p = .566; Infectious: 32.4% vs. 32.9%, p = .958; Vascular/thrombotic: 37.8% vs. 42.3%, p = .602), PW (Mean±SD: 468.2±74.1 vs. 451.4±111.6, p = .136), rates of small (37.1% vs. 43.5%, p = .471) and large placentas (9.6% vs. 8.9%, p = .185) did not differ between groups.

Adjusted odds for anatomic abnormalities were significantly higher in the donor compared to partner’s sperm group, while no differences were noted in other PAR, PW, or small placenta odds (Table). Finally, large placenta odds were lower in donor compared to partner’s sperm conceptions.

RESULTS did not change after limiting our analysis to natural cycles.

CONCLUSIONS: Our results suggest a higher rate of anatomic placental abnormalities in donor sperm conceptions.

IMPACT STATEMENT: Our data suggest an association between donor sperm utilization and anatomic placental abnormalities, potentially providing a link to the reported higher pregnancy complication rates.

SUPPORT: None

REFERENCES:

P-657 6:45 AM Wednesday, October 26, 2022


OBJECTIVE: There is a growing appreciation of the rights and desires of people conceived through assisted reproductive technology, including those conceived with the use of donated gametes. At the same time, the field of assisted reproductive technology is becoming more regulated, but the regulation is variable from state to state. This review attempts to describe the current state of legislation regarding the rights of donor-conceived people and their parents to identifying and non-identifying information about gamete donors.

MATERIALS AND METHODS: A search for state legislation and case law regarding donor anonymity and the rights of donor-conceived people to request information about gamete and gestational donors was conducted, using lay press materials, and Fastcase database. Any lay press articles referencing legislation were cross-referenced against state legislature records for accuracy.

RESULTS: In 2017, the Uniform Law Commission released an updated version of the Uniform Parentage Act (UPA), establishing guidelines for determining parentage in the context of recent developments in assisted reproduction. Several states have moved to pass legislation modeled on the Act. This review found five states had passed legislation modeled after the Uniform Parentage Act specifically outlining the right of donor-conceived people to request identifying information about their gamete donors. These states allow for the gamete donor to remain anonymous if they sign and do not withdraw a declaration stating as much with their gamete banking facility, but the laws also note that the bank must make a good-faith effort to notify the donor of the donor-conceived person’s request, and that the bank must make an effort to provide non-identifying medical information at the donor-conceived person’s request. Notably, the state of Washington had laws requiring that gamete banks provide donor medical records and identifying information to donor-conceived people since the year 2011. The states of California, Connecticut, Maine, and Rhode Island have passed legislation modeled after the UPA since 2020. Another three states have proposed legislation that would establish procedures for donor-conceived adults seeking information about their gamete donors.

CONCLUSIONS: There has been a sharp increase in legislation outlining the rights and procedures for donor-conceived adults to seek information about gamete donors in recent years. Further research is needed to determine exactly how this legislation will affect gamete donors, donor-conceived people, and their families.

IMPACT STATEMENT: This legislation will impact donor-conceived people, their parents, gamete donors, and assisted reproduction professionals, and reflects profound changes in the regulation of assisted reproduction.
OBJECTIVE: Advancements in genetic testing technology have increased not only our understanding of the molecular etiology of diseases, but also the complexity of interpreting human genetic variation. When a genetic variant that has an unknown effect on phenotype is identified, it is termed a variant of unknown significance (VUS). Although genetic testing is a routine part of gamete donor eligibility and ongoing management, there are no professional guidelines regarding how VUSes should be managed when found in a gamete donor or donor-conceived offspring. This study illustrates how a gamete donor bank manages reports of VUSes in donor-conceived offspring.

MATERIALS AND METHODS: All reports of suspected or known health concerns in donor-conceived offspring are routinely documented and investigated for the potential relevance to the donor and other recipient families. Records from 2017-2021 were reviewed to summarize the incidence and management of VUS reports by the donor program.

RESULTS: 895 health concerns were received for donor-conceived offspring (fetus or child), of which 33 (3.69%) included report of a VUS. In 6 cases, more than 1 VUS was identified in the same offspring, for a total of 40 VUSes. Targeted testing was performed for 24 VUSes (60%). 16 VUSes were confirmed to be inherited from the donor, 7 were not present in the donor, and 1 result is pending. Testing was not performed for the remaining 16 VUSes for reasons including: biological mother was not tested and donor testing was not indicated, the VUS was maternally inherited, or the finding was not related to the offspring’s phenotype. In 3 cases, other recipients of the donor were notified, as the donor carries or may carry a VUS for a Mendelian disorder for which the offspring has a clinical diagnosis.

CONCLUSIONS: VUSes are a well-recognized possibility when performing genetic testing. To our knowledge, no data or guidelines have been previously published regarding the incidence or management of VUSes in the donor-conceived or gamete donor populations.

In this study, the management of each VUS report was based on the possible risk to other donor-conceived offspring. Clients were proactively made aware of the VUS result only if it was currently expected to increase risk to other offspring by the same donor.

A decision-making framework (Image 1) for management of VUSes is presented for guiding other programs as to how they may want to manage VUSes.

IMPACT STATEMENT: As technology improves and our understanding of the genetic etiologies of disease advances, VUSes are expected to become more common occurrence. This study highlights the need for gamete donation facilities to develop internal protocols for management of VUS reports and resulting client notifications.

P-659 6:45 AM Wednesday, October 26, 2022

EVIDENCE OF THE NEED FOR INCREASING GENETICS EDUCATION AND SUPPORT FOR GAMETE DONOR RECIPIENTS: RECOMMENDATIONS FOR REPRODUCTIVE PROVIDERS. Kara Baldwin, MS, CGC; Pamela Callum, MS, CGC; Latisha E. Moreta, M.D.; Arren E. Simpson, B.S.; Luwam Ghidei, M.D.; Ashley M. Wiltshire, MD; New York, NY; Baylor College of Medicine, Houston; Baylor College of Medicine, Houston, TX; New York University, New York, NY.

OBJECTIVE: To evaluate the availability and utilization of sperm donors in the United States (US) based on race/ethnicity.

MATERIALS AND METHODS: A systematic search was performed to identify donor sperm banks located in the United States using an online search engine. Data regarding the self-reported race/ethnicity of sperm donors was collected and reviewed. Previously utilized sperm donors were categorized based on race/ethnicity before being compared to the demographics of US men according to the 2021 census. Donors who self-identified as having mixed ancestry were excluded. Pearson’s Chi-squared test or the Fisher Exact test were used to analyze data, where appropriate.

RESULTS: Eight sperm banks were identified using the above criteria. Banks in the western US comprised 63% of the total banks, whereas 25% were located in the southern US and 25% had multiple locations. Six banks...
(75%) served patients internationally and one bank provided services to patients on a domestic county-wide basis. From accessible data, a total of 1,747 donors were identified. Non-Hispanic White/Caucasian, Asian, Hispanic, and Black/African American represented 70%, 16%, 6%, and 4% of all donors, respectively. This distribution was statistically different from all US men (Non-Hispanic White 60%, Asian 6%, Hispanic 19%, Black/African American 13%; p<0.001). Native American/American/Indian/Alaska Native, Middle Eastern/Arabic, and Native Hawaiian/Pacific Islander donors represented 1% or less of the total donor population. Five banks reported information regarding the race/ethnicity of previously utilized donors. Of 976 White sperm donors, 77% were previously utilized. Compared to White donors, Asian and Hispanic donors were significantly less likely to be previously utilized (77% White vs 70% Asian (p=0.04) and 66% Hispanic (p=0.03)). There was no significant difference in utilization of donor sperm provided by Black, Native American/American/Indian/Alaska Native, Native Hawaiian/Pacific Islander, and Middle Eastern/Arabic in comparison to White donors.

CONCLUSIONS: This study sheds light on the racial/ethnic distribution of available and previously utilized sperm donors, a current gap in the literature. There is a wide discrepancy in the number of available sperm donors based on race/ethnicity. White and Asian sperm donors were overrepresented, and Hispanic and Black donors were significantly underrepresented. Sperm donors are generally selected at a similar rate across racial/ethnic groups. Although the discrepancy of representation may reflect differences in demand from donor sperm recipients, it may also represent disparities in the sperm donor recruitment and selection process. More studies are needed to further characterize these differences and to determine ways to improve sperm donor recruitment across all ethnicities.

IMPACT STATEMENT: As the demand for sperm donors is invariably high, efforts should be made to enhance the selection options for all recipients, including those desiring donor sperm from racial/ethnic minority populations.

SUPPORT: None
OBJECTIVE: The objective of this film is to describe a modified technique of uterine suspension using round ligaments for a novel indication: to improve ease of embryo transfer in a patient with a history of multiple failed embryo transfers and severe uterine retroversion associated with deep infiltrating endometriosis.

METHODOLOGY: The case presented is of a 37-year-old G3P0121 who presented with a chief complaint of infertility secondary to diminished ovarian reserve and multiple failed embryo transfers. The patient endorsed deep dyspareunia and pain with transvaginal sonogram. The most recent failed embryo transfer, in August of 2021, was complicated by a “difficult” transfer, 45 minutes in duration, requiring the use of dilators, rigid catheter, bleeding, tenaculum and failed transfer. The initial evaluation was performed due to her desire for pregnancy, with a transvaginal ultrasound demonstrating a severely retroverted/retroflexed uterus, with a cesarean scar visualized. A combined hysteroscopic and laparoscopic approach was planned. Touchless hysteroscopy revealed the presence of a false passage in the cervical canal. Exploratory laparoscopy was performed. The uterus was noted to be severely retroverted/retroflexed. Using 0 Vicryl suture, the suture was anchored on the left fundus and then the round ligament was plicated over a stable needle. Rather than securing the round ligament to the anterior rectus sheath as prior techniques have done, the lateral umbilical ligament was used. The same steps were done on the right, and the uterus was suspended equally on both sides. Postoperative transvaginal sonogram showed an anteverted uterus with no pain or tenderness on sonographic exam. Follow up egg retrieval was done as well as a mock trial of transfer. The mock trial of transfer was noted to be “easy” with a transfer duration of less than one minute. The patient also reported almost complete resolution of her dyspareunia symptoms as well.

CONCLUSIONS: This case demonstrates uterine retroversion as a factor in embryo transfer difficulty and demonstrates that round ligament plication and correction of uterine retroversion can provide improved ease of embryo transfer in women with severely retroverted uteris. This new modified technique differs from historical procedures in that the round ligaments are secured to the obliterated umbilical ligament, instead of fixation of the uterus to the fascia of the anterior rectus sheath, allowing for a more compliant attachment based on plicated, fibrotic round ligaments holding the uterus ventrally. This can be useful post endometriosis excision, posterior myomectomy, and myometrial preserving adhesions. Our experience suggests that round ligament plication is safe and effective in patients with retroverted uteri and dyspareunia.

IMPACT STATEMENT: We suggest that round ligament plication may improve ease of embryo transfer in patients with history of difficult embryo transfer due to severely retroverted uteri. We emphasize that improving the ease of embryo transfer with the use of round ligament plication may ultimately lead to improved IVF outcomes.

SUPPORT: None

11:11 AM Monday, October 24, 2022

AN INTRODUCTION AND VIDEO TUTORIAL TO THE NEW AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE MULLERIAN ANOMALIES CLASSIFICATION 2021 INTERACTIVE WEBSITE.

Phillip A. Romanski, MD, MSc,1 Pietro Bortoletto, MD, MSc,2 Samantha M. Pfeifer, M.D.,2 Steven R. Lindheim, M.D., MMM3 1New York-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY; 2Northwell Health, New York, NY; 3Texas Christian University School of Medicine, Fort Worth, TX; 4New York, NY.

OBJECTIVE: To provide a tutorial for how providers, learners, and patients can navigate and utilize the Mullerian Anomalies Classification 2021 (ASRM MAC 2021) to develop a differential diagnosis, compare a patient’s presentation with exam and imaging findings, and ultimately assist in correctly classifying, diagnosing, and treating mullerian anomalies.

METHODOLOGY: The ASRM Mullerian anomaly classification was first published in 1988 (1). This classification was widely used for decades to classify uterine anomalies, but was limited by its omission of cervical and vaginal anomalies and its lack of clear and reproducible diagnostic criteria. Recently, ASRM revised this classification and rebranded it as the ASRM MAC 2021 (2). This updated system was designed by a task force of reproductive surgeons, pediatric and adolescent gynecologists, and radiologists all with expertise in the diagnosis and treatment of mullerian anomalies.

The goal was to review the existing classification systems and to develop a system that was inclusive of the broad range and variation of possible mullerian anomalies using universal descriptive terminology to standardize the communication and recognizability of these anomalies. Major changes to this classification update include: 1) Each category is labeled by a clear description of the anomaly which replaces the previously roman numeral and lettering system (i.e. category Vb is now simply labeled partial septate uterus); 2) Three new categories were added: longitudinal vaginal septum, transverse vaginal septum, and complex anomalies; and 3) ASRM MAC 2021 was made into an accessible interactive that expands what was once previously a static reference into an educational interactive tool.

CONCLUSIONS: The ASRM MAC 2021 provides an updated mullerian anomaly classification system, while maintaining its simplicity, that now uses descriptive terminology to standardize communication and recognizability of these anomalies. The ASRM MAC 2021 interactive website can be used by 1) women’s health providers to synthesize a patient’s presenting symptoms, physical exam, and imaging findings to develop a broad differential diagnosis, rule out incorrect diagnoses, and eventually make the correct diagnosis; 2) medical trainees to learn about mullerian anomalies including the categories and variations as well as the typical presentation, exam and imaging findings, and possible treatment options; and 3) patients who are seeking updated educational resources for interactive learning regarding their diagnosis.

IMPACT STATEMENT: Overall, the ASRM MAC 2021 standardized terminology, will enhance communication between providers and/or researchers, and ultimately improve patient care. Reproductive endocrinologists who may encounter mullerian anomalies should be familiar with ASRM MAC 2021 and the associated interactive website.

SUPPORT: None

REFERENCES:

V-2 11:20 AM Monday, October 24, 2022

IDENTIFYING VIABILITY OF IMMOTILE SPERM AT ONE GLANCE: SPERM VIABILITY CLASSIFIER POWERED BY DEEP LEARNING.

Aojun Jiang, M.S. 1

Wang Qiaji, B.S.,2 Huan Zhao, M.S.,3 Zhuoran Zhang, PhD,4 Yu Sun, PhD5 1The Chinese University of Hong Kong (Shenzhen), Shenzhen, Guangdong, China; 2Shenzhen, China; 3Luohe People’s Hospital, Shenzhen, China; 4The Chinese University of Hong Kong, Shenzhen, Shenzhen City, Guangdong Province, China; 5University of Toronto, Toronto, ON, Canada.

OBJECTIVE: It is challenging to judge whether an immotile sperm is viable or not. We hypothesize that viability information can be reflected by a sperm’s morphology in microscopic image. This study aims to test the hypothesis and to develop an AI-based technique to non-invasively predict the viability of immotile sperm using a single brightfield image, without requiring sample processing.

METHODOLOGY: In IVF, identifying the viability of immotile sperm is a common need. Embryologists realize this by performing viability tests. However, current viability tests either involve cytotoxic reagent (e.g., eosin–nigrosin) which impedes its application for ICSI, or require tedious procedures (e.g., hypo-osmotic swelling test) and have low efficiency.

To overcome these limitations, we developed an AI model that predicts viability of immotile sperm from a single brightfield image. No sample processing or reagents are required. The AI model was built using the structure of Vision Transformer. To train the model, 1471 images of immotile sperm were collected from 15 samples. For each sperm, its brightfield image was used as model input, and its fluorescent labelling (SYBR14 for live and propidium iodide for dead) was used as ground truth.

REFERENCES:

IMPACT STATEMENT: Our work is the first to demonstrate the feasibility of using AI to predict sperm viability at the level of single sperm image.
After training, the AI model was validated in blind tests using 10 new samples. Model prediction results were benchmarked to the ground truth of fluorescent labelling, and model performance was quantified by accuracy, recall, and specificity. To further investigate how the developed AI model works, the “black box” was opened by analyzing and visualizing its weights as model attention heatmaps.

CONCLUSIONS: On blind tests, the developed AI model achieved an accuracy of 94.9%, recall of 97.0%, and specificity of 93.3%. Further by visualizing the model weights, model attention heatmap analysis revealed that the AI model paid more attention to the cell nucleus of sperm, further indicating that morphological changes between live and dead sperm mainly exist in cell nucleus. As a proof-of-concept, the results suggest that sperm morphology in microscopic images could reflect its viability information.

IMPACT STATEMENT: The developed AI model for the first time enables the non-invasive prediction of sperm viability using a single image. The AI model is able capture subtle morphological changes in sperm nucleus that humans may not be able to reveal. The technique could be applied in various scenarios, from infertility diagnosis to IVF treatment. For instance, the technique can be used as an add-on module to current CASA systems to provide instant sperm viability information without tedious staining procedures.

For NOA patients, the technique can facilitate embryologists in picking live sperm from their micro-TESE samples for subsequent ICSI treatment.

SUPPORT: The authors acknowledge financial support from The Chinese University of Hong Kong, Shenzhen via University Development Fund (UDP10012141), and support from Guangdong Basic and Applied Basic Research Foundation (2021A15110023).

V-5 11:38 AM Monday, October 24, 2022
EARLY PREGNANCY FAILURE: A NOVEL APPLICATION FOR HYSTEROSCOPIC MERRULATION.
Salomeh M. Salari, MD MS,1 Kathryn D. Coyne, MD,2 Rebecca K. Chung, MD,2 Steven R. Lindheim, M.D., MMM,2 Rebecca Flyckt, MD4
1University Hospitals Cleveland Medical Center/Case Western Reserve University, Beachwood, OH; 2University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH; 3University of Central Florida College of Medicine, FL; 4University Hospitals Fertility Center/Case Western Reserve University, Beachwood.

OBJECTIVE: Missed abortions occur in up to one third of pregnancies. Pregnancy and subsequent miscarriages are typically diagnosed early in the first trimester in the REI/ART population. Currently, standard management options include expectant management, medical management, and surgical management with dilation and curettage. There are several disadvantages to “blind” dilation and curettage, including risk of adhesion formation and post-procedural retained products of conception. This video demonstrates a newer approach for management of early pregnancy loss with targeted resection using a hysteroscopic morcellator. This video demonstrates the benefits of hysteroscopy and shares tips for successful completion of the procedure, as well as suggestions for optimal patient selection.

METHODOLOGY: We present a case review of an infertility patient diagnosed with missed abortion by ultrasonographic criteria in the early first trimester. She desired surgical management and consented to hysteroscopic resection. The procedure was each completed without complication and blood loss was 5cc.

In this video, we review management options (including expectant, medical, and surgical) and describe hysteroscopic resection as an alternate approach to treatment of early pregnancy failure. There are many potential benefits to this approach which is performed under direct visualization, including: reduced risk of adhesions, increased likelihood of complete tissue evacuation, and higher quality tissue samples for fetal karyotype analysis.

CONCLUSIONS: Surgical and procedural techniques are shifting from “blinded” dilation and curettage to hysteroscopic resection (e.g. hysteroscopic polypectomy). With this in mind, we may reconsider whether unguided dilation and curettage remains the best practice for infertility patients undergoing dilation and curettage for early pregnancy failure. This video highlights an alternative targeted approach which offers unique benefits over traditional methods.

IMPACT STATEMENT: Hysteroscopic resection of missed abortion has many potential benefits to reduce blind dilation and curettage, with the potential to improve both REI/ART patient experience and future pregnancy outcomes.
identified and bilateral ureterolysis was performed as the retroperitoneal spaces were explored. Once the ureters were safely dissected, the adnexa was mobilized bilaterally. Attention was then turned to dissection of the medial pararectal spaces (Okabayashi’s space) prior to dissection of the recto-vaginal space. With restoration of anatomy, the remaining planned surgery was completed.

CONCLUSIONS: A frozen pelvis is a condition in which the pelvic organs are distorted and tethered to each other as a result from adhesive processes. Although an uncommon surgical condition, it is not rare to come across in clinical practice creating a challenge to reproductive surgeons as it is commonly seen with endometriosis associated infertility. Following this video’s step-by-step approach can help to restore pelvic anatomy for planned surgical procedures.

IMPACT STATEMENT: A frozen pelvis can obscure normal anatomical landmarks and surgical planes making dissection extremely difficult thus increasing the risk of interoperative and postoperative complications. It is important for surgeons to be able to recognize anatomy and have the knowledge to open proper pelvic avascular spaces in the pelvis to mitigate these risks.

SUPPORT: None

V-6 11:49 AM Monday, October 24, 2022

dELINEATION OF UTERINE ISTHMOCELE USING FIREFLY® TECHNOLOGY DURING COMBINED HISTERO-SCOPIC-ROBOTIC ISTMOPLASTY. Kelly Dorsey, BS,1 Zoran J. Pavlovic, M.D.,1 Rachel Sprague, M.D.,2 Emad Mikhail, MD3 University of South Florida, Tampa, FL;3University of South Florida, Morsani College of Medicine, Tampa, FL.

OBJECTIVE: To outline the surgical approach during fertility-sparing uterine isthmoplasty and to propose the novel use of Firefly® infrared light during combined robotic-assisted laparoscopic-hysteroscopic isthmoplasty.

METHODOLOGY: The case presented is of a 36-year-old female with a symptomatic isthmocele who desired fertility-sparing surgical repair. The residual myometrial thickness was <3mm; thus, a combined robotic-assisted laparoscopic-hysteroscopic approach was performed via the Rendez-vous technique. Proper identification of the diverticulum of the isthmocele is a critical step in the safety and effectiveness of the procedure. The most common method for identification of the uterine isthmocele is via hysteroscopic transillumination of light, which can be seen abundantly while the light source of the laparoscopic instrument is concomitantly dimmed, i.e., the “Halloween sign”. However, poor visualization of the transilluminated light through the scar in some cases has led authors to seek alternative solutions for proper identification of the defect, including probing the defect with a transcervical curette, placement of lower uterine segment Foley catheter, or use of transrectal ultrasonography. These methods have the limitations in that there is not direct visualization of the defect hysteroscopically and the intervention may distort surrounding anatomy. Here, we present a novel, safe, and effective method of isthmocele defect visualization with use of the Firefly® infrared imaging during robotic resection.

CONCLUSIONS: For patients with symptomatic isthmoceles and a niche thickness <3 mm who desire pregnancy, laparoscopic resection of the diverticulum with myometrial repair is the preferred approach. Our case proposes novel use of robotic infrared light to accurately delineate isthmocele defects and safely identify surrounding anatomy. This technique serves as a useful tool in the surgeon’s armamentarium during more complex cases involving significant adhesive disease or distorted anatomy.

IMPACT STATEMENT: With high rates of cesarean deliveries, it becomes important to understand the diagnosis and treatment options available for uterine isthmoceles. We describe a methodology for combined robotic-assisted laparoscopic-hysteroscopic isthmoplasty and novel utilization of infrared light via Firefly® mode to aid surgeons during complex cases.

V-14 11:24 AM Tuesday, October 25, 2022

RESECTION OF DEEP INFILTRATING VAGINAL ENDOMETRIOSIS. Janet Cruz, MD,1 Violeta Covarrubias, BS,2 Mallory A. Stuparich, MD,1 Samar Nahas, MD,1 Sadikaah Behbehani, M.D.,1 1University of California Riverside, Riverside, CA;2UC Riverside School of Medicine, Riverside, CA; 3University of California, Riverside, School of Medicine, Riverside, CA.

OBJECTIVE: To present principles and techniques for safe and efficient excision of deep infiltrating vaginal endometriosis after hysterectomy.

METHODOLOGY: Although rare, post-hysterectomy endometriosis can affect the vagina and cause pelvic pain, dyspareunia, vaginal discharge, and/or menstrual-like bleeding. Post-hysterectomy vaginal vault endometriosis may occur, especially in patients with a history of endometriosis or adenomyosis. It is hypothesized that during morcellation or removal of the adenomyotic uterus, transplantation of endometrial cells may occur during trans-vaginal extraction. Additionally, if endometriosis is present at the time of hysterectomy, failure to remove it may lead to implantation on the vaginal cuff at the time of colpotomy, which may then form deep infiltrating endometriosis. In this video we demonstrate our techniques to safely excise a deep infiltrating vaginal endometriotic nodule.

CONCLUSIONS: Endometriotic lesions seen in the vagina may be a sign of more advanced intrauterine disease. In patients with persistent vaginal discharge after hysterectomy vaginal vault endometriosis must be considered especially in patient with history of pelvic pain, endometriosis or adenomyosis. Here we demonstrate an approach to oncotesticular sperm extraction (oncoTESE) performed ex vivo for azospermia concurrent with radical orchietomy. The recovered tissue yielded a 6.3-fold increase in the amount of sperm retrieved over microTESE performed 3 months prior.

IMPACT STATEMENT: This video demonstrates that the oncoTESE is a reasonable and necessary procedure for urologists to perform at the time of radical orchietomy in cancer patients who wish to optimize their fertility preservation.

VIDEO ABSTRACT SESSION 2

V-11 11:30 AM Monday, October 24, 2022

ONCOTESTICULAR SPERM EXTRACTION (ONCO- TESE) FOR BILATERAL METACHRONOUS TESTIS CANCER. Aisha Lynn Siebert, MD, PhD, MPH, Justin M. Dubap, MD, Shilajit D. Kundu, MD, Robert E. Brannigan, MD Northwestern University, Chicago, IL.

OBJECTIVE: To highlight the process of performing an oncotesticular sperm extraction (oncoTESE) in the setting of a radical orchietomy for metachronous bilateral testicular cancer.

METHODOLOGY: After consent was obtained and radical orchietomy completed, we recorded the back bench oncotesticular sperm extraction (oncoTESE) procedure. The surgical approach was documenting in a step-wise fashion. Review of the harvested seminiferous tubules demonstrated sperm during intra-operative microscopic evaluation. Follow up determined overall success of sperm extraction and total yield of sperm.

CONCLUSIONS: Here we demonstrate an approach to oncotesticular sperm extraction (oncoTESE) performed ex vivo for azospermia concurrent with radical orchietomy. The recovered tissue yielded a 6.3-fold increase in the amount of sperm retrieved over microTESE performed 3 months prior.

IMPACT STATEMENT: This video demonstrates the oncoTESE is a reasonable and necessary procedure for urologists to perform at the time of radical orchietomy in cancer patients who wish to optimize their fertility preservation.

V-17 11:49 AM Tuesday, October 25, 2022

THE FINE BALANCE BETWEEN RADICAL AND FUNCTIONALLY CONSERVATIVE EXCISION OF ENDOMETRIOSIS. Papri Sarkar, MD, Emad Mikhail, MD University of South Florida, Morsani College of Medicine, Tampa, FL.

OBJECTIVE: Present 3 different cases of deep endometriosis where we attempted radical but functionally conservative excision.

METHODOLOGY: We present 3 different cases of deep infiltrating endometriosis. The first case includes a 37-year-old nulliparous female with advanced endometriosis involving the right dorsolateral parametrium. Vascular clips were used to temporarily clip the uterine artery while completing the dissection of endometriotic nodule tethered to the uterine artery and ureter. Clips were removed after the dissection was complete. Our second case demonstrates the principle of dissecting diaphragmatic endometriotic nodule while avoiding entry to the pericardium. Our third case demonstrates managing cephalic endometriosis with partial cecectomy to preserve the iileocecral valve.
CONCLUSIONS: Balance between complete excision and preserve organ function in cases with advanced endometriosis should be attempted. These techniques ensure that patients have a faster post-operative recovery. Resection of endometriosis using these conservative approaches has satisfactory symptom relief while decreasing long-term morbidity.

IMPACT STATEMENT: These surgical techniques demonstrate tips and tricks that can be utilized in deep infiltrating endometriosis to balance optimal surgical excision and functional status.

SUPPORT: None

V-9 10:45 AM Tuesday, October 25, 2022
HUMAN BLASTOCYST EUPLODY PREDICTION BASED ON 3D MORPHOLOGICAL EVALUATION.
Guanqiao Shan, MASC.1 Khaled Abdalla, MASC.2 Justin Tan, MD.3 Hung Liu, MASC.1 Changsheng Dai, PhD.1 Zhuoran Zhang, PhD.3 Clifford Lawrence Librach, MD.2 Yu Sun, PhD.1 1University of Toronto, Toronto, ON, Canada; 2CreAtE Fertility Centre, Toronto, ON, Canada; 3The Chinese University of Hong Kong, Shenzhen, Shenzhen City, Guangdong Province, China.

OBJECTIVE: To develop quantitative criteria for human blastocyst euploidy prediction based on 3D morphological measurement.

METHODOLOGY: Morphological evaluation is a critical step for blastocyst selection in IVF. Existing methods use a single 2D image or a few 2D images captured from different focal planes to qualitatively evaluate part of a blastocyst. This approach lacks quantitative 3D morphological information, and the evaluation results vary with different blastocyst orientations and involve human subjectivity of the embryologist.

To address this challenge, we have developed a quantitative 3D morphological evaluation approach and further determined criteria for blastocyst euploidy prediction based on the 3D morphology of a blastocyst. In this study, 58 human blastocysts on Day 6 were measured. For each blastocyst, a set of 2D images were captured at different orientations by rotating the blastocyst under the standard clinical setup. A 3D model of the blastocyst was constructed using the 2D images, and the 3D morphological parameters, including TE cell number, TE cell density, TE cell size variance, ICM size and blastocyst diameter were quantified. For each of the 58 blastocysts, trophectoderm biopsy was performed and PGT-A was conducted. Among the 58 blastocysts, 40 were analyzed by machine learning to determine quantitative criteria for euploidy prediction, and the other 18 blastocysts were used for testing. The euploidy prediction accuracy was compared with that by manual grading following the Gardner and Schoolcraft system.

CONCLUSIONS: TE cell number and cell density in the euploid group were significantly higher than the mosaic group (P<0.001) and the aneuploid group (P<0.0001). ICM size and blastocyst diameter in the euploid group were significantly larger than the mosaic group and the aneuploid group (P<0.05). TE cell size variance in the euploid group was significantly smaller than the mosaic group (P=0.003) and the aneuploid group (P=0.03). The importance scores of TE cell number, TE cell density, TE cell size variance, ICM size and blastocyst diameter for euploid prediction were 0.67, 0.11, 0.09, 0.07 and 0.06, respectively. The euploidy prediction accuracy using our 3D morphological evaluation approach was 100% vs. the accuracy of 70.7% by manual grading (blastocysts with grading better than BB were predicted to be euploid). The quantitative criteria for euploidy prediction from this study are (1) TE cell number larger than 94 or (2) TE cell density higher than 0.86 cell/1,000 µm² with TE cell size variance smaller than 550 µm².

IMPACT STATEMENT: Our quantitative 3D morphology measurement technique for blastocyst evaluation eliminates errors from blastocyst orientation, non-uniformity of TE cell distribution, and human subjectivity. Our preliminary data showed a high euploidy prediction accuracy compared to manual grading. This quantitative technique can potentially standardize morphological evaluation of human blastocysts and be used for euploidy prediction.

V-11 11:01 AM Tuesday, October 25, 2022
LAPAROSCOPIC TRANSFUNDAL APPROACH TO CERVICAL DILATION: A NOVEL TREATMENT FOR CER- VICAL STENOSIS AND CERVICAL FACTOR INFERTILITY. Christine E. Hur, M.D.1, Jeffrey M. Goldberg, M.D.1 1Cleveland Clinic Foundation, Cleveland, OH; 2Cleveland Clinic, Cleveland, OH.

OBJECTIVE: Cervical factor infertility is implicated in approximately five percent of infertile couples and can be a challenging diagnosis to treat. Common strategies include pre-procedural medication, mechanical dilation under ultrasound guidance and operative hysteroscopy. The objective of this video is to highlight a novel minimally-invasive surgical approach to cervical stenosis in the setting of infertility.

METHODOLOGY: This is a video description of a minimally-invasive surgical technique used to manage severe istrogenic cervical stenosis in a 35-year-old gravida zero with a diagnosis of infertility.

CONCLUSIONS: Cervical stenosis can be a difficult diagnosis to manage, particularly in the setting of infertility. In cases where conventional treatments fail, new approaches are required. This video offers a laparoscopic transmyometrial technique for reestablishing cervical patency and fertility.

IMPACT STATEMENT: This video describes an innovative laparoscopic transmyometrial approach for reestablishing cervical patency not previously described in the literature.

V-15 11:35 AM Tuesday, October 25, 2022
LAPAROSCOPIC EXCISION OF ADVANCED STAGE ENDOMETRIOSIS INVOLVING A FALLOPIAN TUBE ENDOMETRIOMA. Tanya Lin, MD, MSc.1 Azraa Banka, MD.2 Gal Elbauseny, MD, MSc.2 Mohamed Ali Bedaiwy, MD, PhD University of British Columbia, Vancouver, BC, Canada.

OBJECTIVE: To display the surgical technique for laparoscopic excision of deep infiltrating endometriosis involving a fallopian tube endometrioma in a patient with chronic pelvic pain and infertility.

METHODOLOGY: This video demonstrates the laparoscopic techniques used to safely excise extensive endometriotic nodules from the fallopian tube mesosalpinx, lateral sidewalls and cul-de-sac.

Pelvic survey revealed an adherent left fallopian tube to the sigmoid colon with a mesosalpinx endometrioma. Concurrent extensive endometriosis along bilateral uterosacral ligaments with deep infiltrating disease extending from the right side into the rectovaginal septum and vagina was also present.

The left fallopian tube was felt to be compromised as it was adherent to the sigmoid and retracted along the mesosalpinx. The left mesosalpinx endometrioma was separated from the sigmoid and excised using a monopolar hook while preserving the fallopian tube integrity.

Bilateral ovarian suspension was performed under direct visualization to allow for optimal visualization of the pelvic sidewalls. Bilateral uterectomy was necessary given the proximity of the ureter to the uterosacral ligaments, which were affected by deep infiltrative disease. The largest nodule was approximately 5 cm in size and burred inferiorly by the vaginal wall. This nodule was excised using a combination of blunt and electrocautery dissection with a monopolar hook without entry into the vagina.

Bilateral tubal patency was confirmed on chromotubation at the end of the case. Complete excision of all visualized endometriotic lesions was confirmed. The temporary ovarian suspension sutures are left in-situ for 5-7 days to optimize healing following surgery by minimizing adhesion formation.

CONCLUSIONS: Fallopian tube endometriosis could be encountered at the time of surgery. Optimization of fertility outcomes and improvement of chronic pelvic pain with surgical management of endometriosis is dependent on normalization of adnexal anatomy and removal of all concurrent endometriotic lesions. This video demonstrates a rarely described fallopian tube endometrioma with successful excision and preservation of tubal patency.

IMPACT STATEMENT: In infertile patients with deep infiltrating endometriosis involving the fallopian tube, a careful laparoscopic excision utilizing similar techniques as the excision of deep infiltrative endometriosis is safe and feasible.

SUPPORT: None

V-13 11:16 AM Tuesday, October 25, 2022
A COMPLICATED AFFAIR: ROBOTIC MYOMECTOMY OF A BROAD LIGATION FIBROID COMPPLICATED BY ENDOMETRIOSIS AND OTHER UTERINE FIBROIDS. Crystal Witherspoon, MPH.1 Mallory A. Stuparich, MD.2 Samar Nahas, MD.3 Sadikah Behbehani, MD.1 1University of California Riverside, Riverside, CA; 2University of California, Riverside, School of Medicine, Riverside, CA.
OBJECTIVE: To illustrate a laparoscopically assisted hysteroscopic extraction of interstitial pregnancy.

METHODOLOGY: 33 year old gravida 2, para 0, post in vitro fertilization with single embryo transfer was diagnosed with an unruptured right interstitial pregnancy at 5 weeks gestation. Beta human chorionic gonadotropin (B-hCG) was 2726 mIU/mL. She desired fertility preservation. The ectopic pregnancy was removed via laparoscopically assisted hysterectomy with a fertility preserving surgical technique. This technique resulted in minimal blood loss, preservation of reproductive organs, restoration of anatomy, bilateral patent fallopian tubes, and expedient return to conception planning. Following the procedure, weekly B-hCG was drawn until it reached <1mIU/mL, which occurred after 4 weeks. A hysterosalpingogram was performed two months after the procedure and demonstrated bilateral tubal patency.

CONCLUSIONS: In select patients, an early interstitial pregnancy can be safely removed using the described technique. Although hysteroscopic removal of interstitial pregnancies is not a new concept, the addition of simultaneous video laparoscopy provides the benefit of allowing for fertility sparing removal of the pregnancy, even if it is not initially visualized hysteroscopically. Use of this technique may result in minimal blood loss and preservation of the fallopian tubes. Furthermore, with the myometrium integrity maintained, the patient may resume sooner attempts at conception.

IMPACT STATEMENT: In experienced hands, with preparation for potential conversion to laparoscopic cornual resection or laparotomy, this procedure as an initial step appears to be feasible and more beneficial to the patient with acceptable outcomes.