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### WHEN AND WHERE DURING COVID-19: THE EFFECT OF AT-HOME SEMEN COLLECTION ON SPERM PARAMETERS, FERTILIZATION RATE, AND BLASTOCYST RATE.

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**OBJECTIVE:** In order to maintain social distancing and reduce risk of transmission of coronavirus disease 2019 (COVID-19) amongst patients at an academic fertility center, semen collection for semen analyses and treatments such as intrauterine insemination (IUI) and in vitro fertilization (IVF), were converted to "at home." Our aim was to assess whether at-home semen collection altered sperm parameters, fertilization rates, or day 5 usable quality blastocyst rates in patients undergoing IVF.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** Semen parameters and embryo outcomes were compared in 42 patients between their IVF cycle prior to COVID-19 (on-site "clinic" collection) and their subsequent cycle after COVID-19 protocols necessitated "at-home" collection. On-site collection was performed in a room adjacent to the andrology laboratory, and processing occurred within approximately 30 minutes. The post-COVID-19 collections were performed at home with the standard specimen cup, delivered to the andrology laboratory within 2 hours of collection, and then processed. Patient demographics, semen parameters, fertilization rate (number of 2 pronuclear embryos/number metaphase II oocytes), and day 5 usable quality blastocyst rate (number transferable and freezable blastocysts/number 2 pronuclear embryos) in fresh transfer cycles were compared between clinic and at-home collections from each patient with a paired T-test. The effect of time between semen production and processing on sperm parameters and embryo outcomes was assessed with linear regression modeling.

**RESULTS:** Mean male age was 38.1 years in the clinic group and 38.9 years in the at-home group ( $p < 0.001$ ). On average, men were abstinent for 2.9 days (SD 1.3) in the clinic group and 3.3 days (SD 3.6) in the at-home group ( $p = 0.576$ ). Mean time to semen processing was 34.0 minutes (SD 11.4) in the clinic group and 78.7 minutes (SD 28.5) in the at-home group ( $p < 0.001$ ). Semen concentration, percent motility, total motile count, and forward progression score were similar between the clinic and at-home groups. While there was no change in sperm parameters by the amount of time to processing in clinic samples, those collected at home demonstrated an increase in motility of 0.357% ( $p = 0.002$ ), an increase in total motile count by 1.6 million ( $p = 0.007$ ), and an increase in forward progression score of 0.01 ( $p = 0.006$ ) for each extra minute from production to processing. There were no differences in mean fertilization rates (clinic 77.0%, SD 22.5 vs. at-home 77.9%, SD 18.2;  $p = 0.813$ ) or usable day 5 blastocyst rates (clinic 47.2%, SD 21.3 vs. at-home 54.6%, SD 24.8;  $p = 0.218$ ). Longer time between semen production and processing had no effect on fertilization rates or day 5 usable quality blastocyst rates.

**CONCLUSIONS:** Our data suggest that at-home semen collection within 2 hours of processing does not negatively impact sperm parameters or embryo outcomes within the same patient. Therefore, at-home collection is a reasonable alternative to on-site collection in clinics seeking to encourage increased social distancing of patients during the COVID-19 pandemic.

**SUPPORT:** None

P-1014 3:30 PM Wednesday, October 21, 2020

### PATERNAL EXPOSURE TO NON-ESSENTIAL HEAVY METALS AFFECTS EMBRYO EFFICIENCY INDICATORS IN INTRACYTOPLASMIC SPERM INJECTION (ICSI) CYCLES: EVIDENCE IN FAVOR OF A PARADOXICAL EFFECT.

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**OBJECTIVE:** While preconception health remains an essential component of fertility counseling, the association between paternal exposure to pollutants and reproductive endpoints in intracytoplasmic sperm injection (ICSI) cycles remains uncertain and poorly explored. The primary aim of this study was to address this existing data gap and generate hypotheses by identifying associations between paternal levels of non-essential metals in blood and semen, and reproductive endpoints in ICSI cycles.

**DESIGN:** This is a prospective cohort study of heterosexual couples undergoing ICSI treatment using autologous oocytes at a university fertility

center. Ninety-five heterosexual couples undergoing fresh ICSI cycles were evaluated.

**MATERIALS AND METHODS:** Metal levels (lead Pb, cadmium Cd, arsenic As, mercury Hg, barium Ba, and uranium U) in semen and blood samples from male partners were analyzed using Ion-Coupled Plasma-Mass Spectrometry (ICP-MS; Agilent 7500 ce, Agilent Technologies, Germany) equipped with cell dynamic range. Adjusted associations between paternal concentrations of metals and embryo-level outcomes (embryo quality/fragmentation score, cleavage, and implantation) were evaluated using multiple linear regression models and natural log transformed metal data. Associations between paternal exposure and reproductive endpoints (live births) were investigated using modified Poisson regression employing a sandwich variance estimator after adjusting for co-variables.

**RESULTS:** High blood Cd, As and U levels in men were associated with significantly lower proportions of cleaved embryos ( $\beta = -0.30$ ; 95% CI: -0.11, -0.02;  $P = 0.01$ ) ( $\beta = -0.26$ ; 95% CI: -0.16, -0.11;  $P = 0.02$ ) ( $\beta = -0.22$ ; 95% CI: -0.24, -0.02;  $P = 0.05$ ), respectively. Counterintuitively, paternal blood and semen Pb concentrations were positively associated with higher embryo implantation ( $\beta = 0.26$ ; 95% CI: 0.01, 0.22;  $P = 0.03$ ) ( $\beta = 0.25$ ; 95% CI: 0.03, 0.14;  $P = 0.04$ ), respectively. Semen U concentrations were also positively associated with embryo implantation ( $\beta = 0.27$ ; 95% CI: 0.01, 0.19;  $P = 0.03$ ). Paternal metal concentrations in both body compartments did not predict the likelihood of livebirth in ICSI treatment cycles.

**CONCLUSIONS:** These findings highlight the potential effects of sperm metal exposure on embryo efficiency indicators after ICSI, laying support to possible molecular pathways which could impact specific pre- and post-implantation embryonal events. This may point to the likelihood of a trans-generational effect of paternal exposure to pollutants with long-term bearing on obstetrical and postnatal outcomes. These results also underline a paradoxical favorable association between specific metal pollutants at low-exposure levels and some reproductive outcomes, shedding light on different pattern effects through pathophysiological pathways unique to each trace element. Whereas counseling of women is common practice in fertility care, this study emphasizes the importance of paternal health on reproductive outcomes in ICSI treatment cycles and the need for more male partner inclusive counseling in fertility practice.

**SUPPORT:** Medical Practice Plan MPP - American University of Beirut

P-1015 3:30 PM Wednesday, October 21, 2020

### COMPARISON OF THE EMBRYO QUALITY OBTAINED AFTER AN UNSTIMULATED AND STIMULATED CYCLE IN THE SAME INFERTILE PATIENT UNDERGOING IN VITRO FERTILIZATION.

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**OBJECTIVE:** To analyze if ovarian stimulation increases the rate of aneuploidy compared to what occurs in the natural basal state.

We compared the probability of a MII oocyte becoming an euploid blastocyst in a natural and stimulated cycle in the same patient.

**DESIGN:** Prospective cohort study comparing embryo quality after a modified natural (MNC) and a stimulated cycle (SC) in the same infertile IVF patient. Registration Number: NCT03128580.

**MATERIALS AND METHODS:** Patients provided written informed consent prior to any procedure. No exogenous gonadotropins were given in the MNC. The requirement to continue in the study was to obtain at least one MII oocyte in the MNC. The SC consisted of a fixed combo GnRH antagonist protocol with a daily dose of 225 IU of rFSH and 75 IU of hp-HMG. In both cycles, ovulation was triggered 36h prior to oocyte retrieval with triptoreline (0.1mg) when at least one (MNC) or 3 follicles (SC)  $\geq 17$  mm were observed.

Embryo quality was assessed through morphological (following the ASEBIR criteria), morphokinetic (by time-lapse technology) and genetic evaluation (using NGS for the embryo chromosomal analysis).

Student's t tests and ANOVA were used for quantitative variables, for comparisons between 2 or more than 2 groups, respectively.  $\chi^2$  was used for categorical variables. Correlation between quantitative variables was evaluated by Pearson's correlation analysis. P-value  $< 0.05$  is considered statistically significant.

Sample size was calculated assuming a 5% difference in the % of euploid embryos/ MII in favor of the MNC. Assuming that at least 2 MII oocytes are