MATERIALS AND METHODS: The NASS database is comprised of data reported to the CDC for approximately 98% of ART cycles performed in the United States, including patient demographics, reproductive history, infertility diagnosis, clinical parameters for ART procedure, and cycle outcome data (e.g., number and weight of infants delivered). NASS data from years 2004-2018 were used to examine trends in use of FET and incidence of LGA. Also, all FET cycles between 2016 and 2018 resulting in singleton live births (N=127,916) were further analyzed to identify factors associated with LGA after FET. Clinical, demographic, and associated *retrieval* cycle characteristics were compared between the LGA and non-LGA groups. Modified Poisson regression was used to estimate adjusted relative risk (aRR) of LGA and 95% confidence intervals (CI) to determine possible factors associated with LGA after FET.

RESULTS: While the percentage of IVF transfers using frozen embryos steadily increased from 20% in 2004 to 74% in 2018, the rate of LGA infants following FET decreased from 18% to 12% during the same timeframe. Factors most strongly associated with increased risk of LGA after FET were higher than normal body mass index (BMI 25.0-29.9 kg/m^2 (aRR 1.31, 95% CI 1.26-1.36), BMI 30.0-34.9 kg/m^2 (aRR 1.48, 95% CI 1.41-1.55), and BMI >35 kg/m^2 (aRR 1.67, 95% CI 1.58-1.76)) and parity (1 prior birth (aRR 1.36, 95% CI 1.31-1.42) and >1 prior birth (aRR 1.39, 95% CI 1.31-1.47), compared to nulliparous patients). Use of gestational carrier (aRR 1.29, 95% CI 1.14-1.46) and use of donor sperm (aRR 1.20, 95% CI 1.12-1.29) were also positively associated with LGA after FET. In contrast, low BMI (<18.5 versus 18.5-24.9 kg/m^2), geographic region (NE and West compared to Midwest), low number of oocytes retrieved (5-9 versus 10-19 oocytes) and two or more fetal heartbeats were protective factors. In addition, compared to non-Hispanic (NH) White patients, NH Black, Hispanic, and Asian/Pacific Islander patients were at significantly lower risk of LGA infants born after FET.

CONCLUSIONS: BMI, parity, and race/ethnicity were the strongest independent risk factors for LGA infants following FET cycles. The annual rate of LGA after FET cycles decreased over the fifteen-year period studied.

IMPACT STATEMENT: Increased understanding of risk factors for LGA after FET can improve patient counseling and medical care for patients undergoing assisted reproductive technologies.

O-41 11:45 AM Monday, October 18, 2021

ENDOMETRIAL PREPARATION FOR FROZEN EMBRYO TRANSFER AND IMPACT ON BIRTH WEIGHT: A SYSTEMATIC REVIEW AND META-ANALYSIS. Kendal Frances Rosalik, Do,[1] Samantha Carson, MD,[2] Jacqueline Luizzi, MLIS, AHIP,[1] Justin Pilgrim, MD,[3] Gary Levy, MD,[2] Ryan Heitmann, DO,[4] Bruce D. Pier, MD[5] [1]Madigan Army Medical Center; [2]Tripler Army Medical Center; [3]Tripler Army Medical Center, Honolulu, HI; [4]West Virginia University Medical Center; [5]Division of Reproductive Endocrinology and Infertility, Tacoma, WA.

OBJECTIVE: Frozen embryo transfer (FET) has advantages over fresh embryo transfer IVF for certain patient populations and circumstances but may also increase some perinatal and maternal risks such as macrosomia, large for gestational age (LGA), cesarean section, hemorrhage, and hypertensive disorders of pregnancy. Given the growing number of studies comparing outcomes between natural (NFET) and programmed FET (PFET) cycles, we conducted a meta-analysis looking at the risk of fetal weight abnormalities in patients undergoing NFET and PFET cycles.

MATERIALS AND METHODS: A literature search using MEDLINE, SCOPUS, EMBASE and clinicaltrials.gov was conducted for published research comparing neonatal outcomes in NFET and PFET cycles. Primary outcomes interest were fetal weight, macrosomia, and large for gestational age. Studies were included if the following criteria were met: study contained cohorts of NFET and PFET with outcome data regarding birth weight, large for gestational data, and/or macrosomia data. Data are presented as average weight and odds ratio (OR) with 95% confidence interval (CI) with fixed- or random-effects meta-analysis between cohorts of NFET and PFET cycles. Given heterogeneity in defining NFET patients, a subgroup meta-analysis was performed using true natural cycle FET (TNFET) (no ovarian stimulation) and PFET cycles.

RESULTS: A total of 798 studies were identified, with 13 meeting inclusion criteria. Studies varied with respect to country of origin, definition of natural cycle FET, and type of progesterone supplementation used. Studies included had similar gestational age at time of birth. PFET cycles had a higher fetal weight (14.6gm, p = 0.03) compared to NFET cycles. PFET cycles were at higher risk for macrosomia (OR 1.16, 95% CI 1.09-1.23) and LGA (OR 1.13, 95% CI 1.07-1.19). In a subgroup meta-analysis, PFET cycles had a higher fetal weight (62.2gm, p = 0.0001) compared to TNFET cycles. PFET cycles were also at higher risk for macrosomia compared to TNFET cycles (OR 1.35, 95% CI 1.14-1.60).

CONCLUSIONS: Data demonstrates that programmed endometrial preparation for FET cycles has a small, yet significant increase effect on fetal birth weight, and increased risks of LGA and macrosomia. These effects appear to be more significant when comparing TNFET and PFET cycles.

IMPACT STATEMENT: Frozen embryo transfer is being used increasingly in the United States. Accurate and specific patient counseling as to risks associated with this specific procedure are important to discuss.

SUPPORT: None.

O-42 12:00 PM Monday, October 18, 2021

IVF OUTCOMES IN BRCA CARRIERS WITH AND WITHOUT ADDITION OF LETROZOLE TO STIMULATION. Chelsea M. Canon, MD,[1] Matthew A. Lederman, MD,[2] Carlos Hernandez-Nieto, MD,[2] Dmitry Gounko, MA,[2] Joseph A. Lee, BA,[2] Jeffrey Klein, MD,[2] Beth McAvey, MD,[2] Daniel E. Stein, MD,[2] Alan B. Copperman, MD[2] [1]Icahn School of Medicine at Mount Sinai, New York; [2]Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Women with BRCA 1/2 mutations are commonly referred to reproductive endocrinologists to discuss fertility preservation options prior to ovarian and breast cancer risk reducing surgery. Researchers remain divided about whether BRCA carriers might be predisposed to decreased ovarian reserve and accelerated ovarian aging compared to non-carriers, and debate optimal stimulation dosage and protocols.[1] The aromatase inhibitor letrozole is commonly used during controlled ovarian stimulation (COH) of breast cancer patients to minimize circulating Estradiol levels, but it is unclear whether its use negatively affects stimulation response, fertilization, and embryo quality. Our study aims to evaluate IVF outcomes in BRCA carriers who include or do not include Letrozole during stimulation.

MATERIALS AND METHODS: The study included BRCA mutation carriers without a diagnosis of cancer who underwent COH from March 2009 to April 2021. Study groups were segregated by stimulation type (Group A: IVF cycles with Letrozole; Group B: IVF cycles without Letrozole). Basic demographic and cycle characteristics were compared between the groups. Both cohorts included cycles in which preimplantation genetic testing for aneuploidy (PGT-A) and/or monogenic/single gene defects (PGT-M) via Next Generation Sequencing for both BRCA and aneuploidy screening was performed. Data was analyzed using student's t-test, chi-square and logistic regression.

RESULTS: A total of 72 IVF cycles for embryo cryopreservation (n=59) and egg freezing (n = 13) were included. Patients in which Letrozole was included during stimulation (n=22) were similar to group B (n=50) in baseline characteristics. Study groups were stimulated with an equivalent cumulative gonadotropin dose and had similar oocyte yield, number of mature oocytes, fertilization rate and number of embryos biopsied. 78 embryos from Group A and 219 embryos from Group B underwent PGT-A, which demonstrated equivalent rates of embryonic aneuploidy. 46 embryos from Group A and 47 embryos from Group B underwent PGT-M for BRCA, which demonstrated equivalent number of BRCA-free embryos. On multivariate logistic regression, after adjusting for age, BMI, D3 FSH, D3 E2, Gravidy, Parity, Gonadotropin Cumulative Dose, BAFC, and AMH, there was no association with use of Letrozole and lower number of oocytes retrieved (OR 1.41 (95% CI 0.47-4.19), lower number of mature oocytes (OR 0.951 95% CI 0.31-2.90), and lower number of usable euploid, BRCA embryos (1.76 95% CI 0.25-12.66).