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Title:

VARIATIONS IN RESPONSE TO OVARIAN STIMULATION, EMBRYO DEVELOPMENT AND EUPLOIDY RATE AMONG WOMEN OF DIFFERENT RACIAL BACKGROUNDS UNDERGOING IN VITRO FERTILIZATION (IVF)

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Objective:

Racial disparity is of clinical importance in all fields of medicine, as differences in the epidemiology of disease can influence response to medical therapy. While racial disparities in reproductive medicine have been well established with regard to access to care, differences among races in response to ovarian stimulation for in vitro fertilization (IVF) have not been well characterized. . In an era of pre-implantation genetic testing for aneuploidy (PGT-A), potential racial differences in embryo development, blastulation, and aneuploidy can be explored. This study aimed to determine if women of various racial backgrounds undergoing IVF demonstrate differential ovarian response to stimulation, and differential morphokinetic and chromosomal development of their resulting embryos.

Design:

Retrospective cohort study

Materials and Methods:

The study included patients who underwent IVF stimulation from 2003-2018. Oocyte donation cycles were excluded from analyses. Trophectoderm biopsy and pre-implantation genetic testing for aneuploidy (PGT-A) were performed on select blastocysts. The following data were determined: patient age, body mass index (BMI), self-reported race, gravidity, parity, anti-mullerian hormone (AMH) level, basal antral

follicle count (BAFC), estradiol (E2) and progesterone (P4) levels at the time of surge, total gonadotropin dose, number of total oocytes and metaphase II (MII) oocytes retrieved, number of oocytes fertilized, number of blastocysts, day of blastocyst biopsy, and number of euploid embryos. The rates of oocyte maturity (MII rate), fertilization, blastulation and euploidy were determined. Patients were separated into groups based on race: African American (AFAM), Asian, and Caucasian. Data were analyzed using a Student's T-test, Chi-square, Fisher's Exact test, and multivariate logistic regression.

Results:

A total of 2,171 autologous IVF cycles were performed during the study time frame. Compared to other racial groups, AFAM patients (n=132) were significantly older (38.1 ± 4.2 yrs, p <0.0001), had a higher BMI (27.8 ± 4.4, p < 0.0001) and higher E2 at time of surge (2374 ± 1201 pg/mL, p < 0.0001). Caucasian patients (n=1558) were more likely to be nulligravid (53.3%, p<0.0001) and have a higher BAFC (12.0 ± 6.6, p=0.02), and Asian patients (n=481) had a higher P4 at time of surge (0.92 ± 0.43 ng/mL, p<0.0001). While the number of oocytes retrieved and the MII rate were similar among groups, the number of MII oocytes (11.0 ± 7.5, p=0.01), blastocysts (6.3 ± 5.1, p=0.004) and the blastulation rate (77.1 ± 26.4%, p =0.003) were higher among AFAM patients as compared to other groups. The number of fertilized oocytes was highest among Caucasian patients (8.6 ± 6.2, P =0.03) but Asian patients had the highest fertilization rate (79.7 ± 16.3%, p<0.0001). Among patients undergoing PGT-A, AFAM women had more blastocysts biopsied (5.2 ± 4.2, p=0.0001) while Caucasian women had more euploid embryos (2.4 ± 2.7, p =0.004) following biopsy; however, the euploidy rate did not differ among groups after adjusting for observed confounders (p=0.26). Fertilization was 26% less likely for AFAM women as compared to Caucasian women (OR 0.74, 95% CI 0.7-0.9), yet blastulation was almost two times more likely for AFAM women (OR 1.7, 95% CI 1.4-2.0) as compared to Caucasian women after adjusting for confounders. Blastulation was also approximately 15% less likely for Asian women (OR 0.87, 95% CI 0.8-0.96) as compared to Caucasian women.

Conclusions:

This study shows that regardless of differences in age and gravidity, women of varying racial backgrounds also exhibit heterogeneity in ovarian response to stimulation, fertilization, embryo development and blastulation. This large database study revealed a greater response to ovarian stimulation in AFAM women, and a lower response in Asian woman, as compared to Caucasian women. The euploidy rate, however, did not appear to differ by race. While this variability may be inherent and possibly non-modifiable, understanding the underlying pathophysiologic mechanisms or contributing environmental factors may offer the opportunity to tailor ovarian stimulation protocols and potentially optimize laboratory conditions and procedures for women of different races.

Support:

None.

References:

1. Dieke, et al. "Disparities in Assisted Reproductive Technology Utilization by Race and Ethnicity, United States, 2014: A commentary." Journal of Women's Health, 2017 (26): 605-608.
2. Dhillon R. et al., "Investigating the effect of ethnicity on IVF outcome." RBMO, 2015 (31): 356-363.
3. Patel, et al. "Ethnicity is an independent predictor of IVF-ICSI outcome: a study of 5,549 cycles in Spain and India." Gynecological Endocrinology, 2016 (32): 819-822.

Table 1:

Demographics and Cycle Characteristics based on Self-Reported Race

	African American (n=132)	Asian (n=481)	Caucasian (n=1558)	P Value
Age (y)	38.1 ± 4.2	37.2 ± 4.0	36.6 ± 4.6	<0.0001
BMI (kg/m^2)	27.8 ± 4.4	23.2 ± 3.9	23.9 ± 4.5	<0.0001
Nulligravid	53 (40.2%)	232 (48.2%)	822 (53.3%)	<0.0001
Nulliparous	101 (76.5%)	377 (78.4%)	1187 (75.7%)	0.44
AMH (ng/mL)	3.1 ± 3.0	3.2 ± 4.3	3.0 ± 4.1	0.70
BAFC	11.6 ± 7.0	11.0 ± 5.8	12.0 ± 6.6	0.02
Surge E2 (pg/mL)	2374 ± 1201	2304 ± 1169	2068 ± 1129	<0.0001
Surge P4 (ng/mL)	0.78 ± 0.5	0.92 ± 0.43	0.80 ± 0.47	<0.0001
Total GND (units)	3829 ± 1247	3855 ± 1319	3798 ± 1351	0.71
Number of Oocytes Retrieved	14.3 ± 8.7	12.7 ± 7.8	13.8 ± 9.0	0.047
Number of MIIs	11.0 ± 7.5	9.7 ± 6.4	10.7 ± 7.7	0.01
MII Rate	78.0 ± 20.2%	78.8 ± 17.7%	79.6 ±17.7%	0.38
Number of Fertilized Oocytes	8.1 ± 5.9	7.8 ± 5.2	8.6 ± 6.2	0.03
Fertilization Rate	71.8 ± 22.1%	79.7 ± 16.3%	79.1 ± 18.5%	<0.0001
Number of Blastocysts	6.3 ± 5.1	5.4 ± 4.4	6.3 ± 5.3	0.004
Blastulation Rate	77.1 ± 26.4%	69.3 ± 24.9%	72.5 ± 24.3%	0.003
Number of Blastocysts Biopsied	5.2 ± 4.2	3.8 ± 2.9	4.6 ± 4.0	0.0001
% Day 5 Biopsy	59 (44.7%)	238 (49.5%)	809 (53.2%)	0.07
Number of Euploid Embryos	2.3 ± 2.7	1.9 ± 2.1	2.4 ± 2.7	0.004
Euploidy Rate	37.9 ± 31.7%	44.0 ± 35.0%	46.5 ± 34.8%	0.07