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ASSISTED REPRODUCTION TECHNOLOGIES

Correlation of self-reported racial background to euploidy status and live birth rates in assisted reproductive technology cycles

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Abstract

Purpose To determine whether the embryonic euploidy rate and live birth outcomes following single, euploid embryo transfer (SEET) differ among women of self-reported racial and ethnic backgrounds.

Methods This retrospective cohort study included all infertile patients of different self-reported racial backgrounds who underwent In vitro fertilization (IVF) with preimplantation genetic testing for aneuploidy (PGT-A) and an autologous single euploid embryo transfer (SEET) from December 2015 to December 2019 at a single private and academic assisted reproduction technology center. Primary outcome measures included ploidy rates among different racial groups. Secondary outcomes included clinical pregnancy, clinical pregnancy loss, and live birth rates.

Results Five thousand five hundred sixty-two patients who underwent an IVF cycle with ICSI-PGT-A were included. A total of 24,491 blastocysts were analyzed. White participants had on average more euploid embryos and higher euploidy rates when compared to their counterparts ($p \leq 0.0001$). However, after controlling for confounding factors, there was no association between race and the odds of having a higher euploidy rate (aOR 1.31; 95% CI 0.63–2.17, $p = 0.42$). A total of 4949 patients underwent SEET. Pregnancy outcomes did not differ among patients of varying self-reported races.

Conclusions Euploidy rates and pregnancy outcomes were comparable among patients of different racial backgrounds who underwent a SEET.

Keywords Self-reported racial background · In vitro fertilization · Preimplantation genetic testing · Euploidy · Live birth rate

Introduction

In the ever-evolving landscape of assisted reproductive technology (ART), the quest for understanding predictors of in vitro fertilization (IVF) success is imperative for advancing our field. This pursuit becomes even more nuanced as a growing body of evidence suggests that reproductive and obstetrical outcomes may diverge among different racial groups. Within the context of ART, racial disparities in access to care and outcome have been addressed by several studies [1, 2]. Chandra et al. reported that non-White women are less likely to utilize IVF services, despite higher infertility rates among black (7.2%) and Hispanic (6.1%) women, compared with White women (5.5%) [3]. Seifer et al. demonstrated that Black women produced fewer mature oocytes, fertilized oocytes, and blastocysts for cryopreservation when compared to White women [4]. McQueen et al. documented higher spontaneous abortion rates and lower live birth rates (LBR) in Black and Asian women when compared with White women after undergoing IVF without preimplantation genetic testing (PGT-A) [5].

These racial differences in reproductive outcomes may result from a combination of diverse risk factors and conditions known to influence embryonic ploidy and ART success. For instance, Black, Hispanic, and Asian populations have been documented to have an increased exposure to endocrine-disrupting chemical (EDCs) recognized as deleterious to the ovaries and gametogenesis [6, 7]. In addition, research indicates that Black and Hispanic women

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have lower anti-Mullerian hormone (AMH) levels when compared to White women, even after adjusting for age and body mass index (BMI) [8, 9]. Importantly, AMH has been recognized as an independent factor to predict aneuploidy rates and ART outcomes [10, 11]. Finally, Black and Hispanic women have been reported to have a higher frequency of polycystic ovarian syndrome (PCOS) when compared to other races [12]. PCOS diagnosis itself has been proposed as possible cause of higher aneuploid embryos by causing a disruption of the endocrine control of meiosis which could result in an impaired extrusion of the first polar body and compromise the chromosomal normality of oocytes [13].

Given that non-White women have been documented to exhibit a higher prevalence of factors known to be associated with increased embryonic aneuploidy rates [10, 11, 13], and recognizing that previous data, and racial disparities in infertility have failed to fully elucidate a plausible cause for the association between race and ART outcomes by being limited in sample size, incomplete reporting of race data, and by transferring embryos without PGT-A, we sought to determine whether the embryonic euploidy rate differs among patients of different self-reported racial backgrounds. We hypothesized that when compared to White patients, patients from other racial backgrounds would have different euploidy rates, explaining at least some of the differences associated with lower LBR and higher miscarriage rates reported in previous studies where untested embryos were used.

Material and methods

Study design and patient population

This retrospective, single-center study included all infertile patients who underwent IVF with preimplantation genetic testing for aneuploidy (PGT-A) at RMA NY using next generation sequencing, from December 2015 through December 2019. Cases of patients harboring chromosomal rearrangements, undergoing preimplantation genetic testing for monogenic defects (PGT-M), Asherman syndrome, and/or using donor gametes were excluded from the analysis.

As part of the new patient intake form, patients were provided the opportunity to choose between the following racial groups: White, Black, Asian, Native Hawaiian, American Indian or Alaskan Native, Hispanic, and Other. All White, Black, Asian, Native Hawaiian, American Indian, or Alaskan Native were non-Hispanic. Due to the low number of responses, Native Hawaiian and American Indian or Alaskan Native were included with others as part of the analysis. Patients who chose not to answer were categorized as "not specified" their race. Demographic characteristics such as age, BMI, gravidity, and ovarian reserve metrics were collected. Infertility diagnoses were explored in 8 categories: tubal factor, uterine factor (including fibroids, adenomyosis, septum, or history prior uterine surgery), diminished ovarian reserve, ovulatory dysfunction (including polycystic ovary syndrome), recurrent pregnancy loss (RPL), male factor, idiopathic, and others (including cervical factor, gender selection, vaginitis, sexual dysfunction, etc.). Cycle characteristics and embryologic data, including total number of oocytes retrieved, number of mature oocytes (MII), oocyte maturity rate (total number of MII over the total number of oocytes retrieved), fertilization rate, blastulation rate (total number of viable blastocysts over the total number of fertilized oocytes), day of biopsy, embryo quality, and ploidy rates (number of euploid/aneuploid/indeterminate blastocysts over the number of biopsied blastocysts) were compared between cohorts.

A subsequent sub-analysis evaluated the live birth (LB) outcomes of patients who underwent a synthetic endometrial preparation and single-euploid embryo transfer (SEET).

Stimulation protocol

Patients underwent controlled ovarian hyperstimulation (COH) for IVF as previously described [14]. Briefly, the COH protocol was selected at the discretion of the reproductive endocrinologist and involved the administration of follicle-stimulating hormone (FSH) and human menopausal gonadotropin (hMG) with a gonadotropin-releasing hormone (GnRH) agonist downregulation protocol with leuprolide acetate (Lupron, AbbVie Inc., North Chicago, IL), a GnRH antagonist protocol (Ganirelix Acetate, Organon USA Inc., Roseland, NJ or Cetrotide, EMD Serono, Rockland, MA), or a microflare protocol with leuprolide acetate (Lupron, AbbVie Inc., North Chicago, IL). These protocols have been described previously [15]. Follicular development was monitored using transvaginal ultrasonography. When at least two follicles reached 18 mm in diameter, final oocyte maturation was induced with either hCG (5000–10,000 IU, Novarel, Ferring Pharmaceuticals, Parsippany, NJ, USA), recombinant human chorionic gonadotropin (250–500 μg, Ovidrel, EMD Serono, Rockland, MA), or, in high responders at risk of ovarian hyperstimulation syndrome undergoing a GnRH antagonist protocol, a dual trigger with 2 mg of leuprolide acetate and 1000 IU of hCG or leuprolide acetate alone. Thereafter, patients underwent vaginal oocyte retrieval under transvaginal ultrasound guidance 36 h after oocyte maturation was triggered.

Laboratory procedures

Embryo culture

All metaphase II (MII) oocytes underwent intracytoplasmic sperm injection (ICSI). Embryos were cultured to the

blastocyst stage as previously described [14]. On day 3 of embryo development, all embryos underwent laser-assisted zona hatching by creating a 25–30 µm opening in the zona pellucida with a 200–300 ms pulse using ZILOS-tk Laser (Hamilton Thorne Biosciences, MA, USA) to facilitate posterior trophectoderm herniation. Blastocyst trophectoderm biopsies were performed on days 5–7 of development, contingent upon morphologic eligibility (modified Gardner scoring system) [16]. Biopsy was performed as described previously [14]. The biopsy samples were placed in hypotonic wash buffer and submitted for analysis. Embryos were vitrified after the biopsies. Five to seven cells were analyzed by next generation sequencing (NGS) in order to determine chromosome, copy number, and assigned to the following categories: euploid, aneuploid, or inconclusive by the reference laboratory (during the study period mosaicism was not yet reported).

Cryopreservation and rewarming techniques

The cryopreservation and rewarming techniques have been described previously [14]. After the embryos had been rewarmed, their survival was determined according to the appearance of the blastomeres and zona pellucida and the ability of the blastocoel to re-expand. Degenerated embryos were deemed as failed to survive and not used for embryo transfer.

Endometrial preparation and FET

For standardization and per typical clinical practice, every SEET in this study was performed in a synthetic preparation cycle. For each patient, the uterine cavity was prepared with micronized oral estradiol (Estrace, Teva Pharmaceuticals, NJ) 2 mg twice daily for 4 days, then 2 mg three times daily. After a minimum of 12 days of estradiol administration, transvaginal ultrasonography was performed to assess endometrial thickness. When a minimum thickness of at least 7 mm was achieved, 50 mg of intramuscular progesterone in oil (Watson Pharma Inc., Parsippany, NJ) was administered daily. For all clinical cases, thawing and transfer of the embryos were carried out on the sixth day of progesterone supplementation regardless of the day of embryo development at the time of cryopreservation. Euploid embryos with the highest morphological grade were selected for transfer [14].

Outcome measures

The primary outcome was ploidy rates among different racial groups, defined as the number of euploid and/or aneuploid blastocysts over the total number of biopsied blastocysts. Secondary outcome measures included clinical pregnancy rate (CPR), defined as the proportion of patients with fetal cardiac activity detected by ultrasound; clinical pregnancy loss (CPL), defined as pregnancy loss occurring after the presence of a confirmed fetal cardiac activity; finally, LBR, defined as live birth per embryo transfer [17].

Statistical analysis

Continuous data were reported as mean + -SD or median (IQR) as appropriate with Clopper-Pearson binomial 95% confidence intervals (95% CI). Groups were compared using ANOVA for continuous normally distributed data and Kruskal–Wallis when the conditions of normality were not met. Categorical data were analyzed using Fisher exact or Chi-squared tests as appropriate. Adjusted odds ratios (aORs) with 95% confident intervals (CI)s were calculated using a multivariate logistic regression analysis to adjust for confounding variables, and the models were fitted with a generalized estimating equation (GEE) to account for patients who underwent multiple IVF and SEET cycles. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). All p values were two-sided and were considered significant if less than 0.05.

Power analysis

A post hoc power analysis was performed. For our primary outcome, a sample size of 506 embryos per group was needed to detect a difference of 10% in euploidy rate with 80% power (alpha = 0.05).

For the sub-analysis, to detect a difference in LB rates from a SEET, a sample size of 110 SEET per group was calculated to detect a difference of 10% in LB rates with 80% power (alpha = 0.05).

Regulatory approval

This retrospective study was approved by the Icahn School of Medicine at Mount Sinai Institutional Review Board, Inc. Date 6/2/2022–6/1/2023. Study-18–00441-CR002.

Results

Twelve thousand seven hundred and eighty-eight patients underwent an initial consultation for ART treatment during the study period (7301 identified as White (57%), 1205 as Black (9%), 1366 as Hispanic (11%), 1826 as Asian (14%), 907 as other (7%), and 183 did not specify their race (2%). Of these, 8175 were recommended to undergo IVF with PGT (4741 identified as White (58%), 654 as Black (8%), 1145 as Asian (14%), 736 as Hispanic (9%), 490 as other (6%), and 409 did not specify their race (5%)). Six thousand

six hundred and forty-four women underwent IVF with PGT during the study time (4010 self-reported as White (60%), 325 as Black (5%), 1086 as Asian (16%), 540 as Hispanic (8%), 298 as other (5%), and 385 did not specify their race (6%) (Fig. 1). A total of 5562 patients who underwent an IVF cycle with ICSI and embryo biopsy for PGT-A during the study period and met inclusion criteria were included in the analysis. Of these, 3342 self-reported as White (60%), 291 as Black (5%), 1018 as Asian (18%), 472 as Hispanic (9%), 142 as other (3%), the most common being Hawaiian, and 297 did not specify their race (5%) (Fig. 1). One thousand and eighty-two women were excluded: 137 women due to PGT-M, 70 due to PGT-SR, 480 used donor gametes, 60 were canceled prior to a vaginal oocyte retrieval (VOR) due to personal reasons or poor response and did not continue treatment, and 335 did not have embryos for biopsy (Fig. 1).

Patient demographic and cycle characteristics are described in Table 1. When analyzing age, Black, Asian, and Hispanic, women who self-reported as other and that did not specify their race were older than White women (38.0 ± 3.1, 37.3 ± 3.1, 37.3 ± 4.0, 38.1 ± 3.4, 37.2 ± 4.6, 36.6 ± 3.5, respectively, $p < 0.0001$). Black women had a significantly higher BMI when compared to White and Asian women (27.3 ± 3.9 vs. 24.1 ± 3.5, and 23.4 ± 3.9, respectively, $p \leq 0.0001$). No differences were noted in gravidity nor ovarian reserve markers among groups. When analyzing the etiology of infertility, a significantly higher proportion of Black women had infertility due to tubal and uterine factor when compared to White women (14.8% vs. 4.5%, $p < 0.0001$; 9.9% vs. 2.1%, $p \leq 0.0001$, respectively). Women who did not specify their race had the lowest incidence of ovulatory dysfunction infertility (1.9%, $p \leq 0.0001$). The occurrence of RPL and male factor infertility was greater in women who

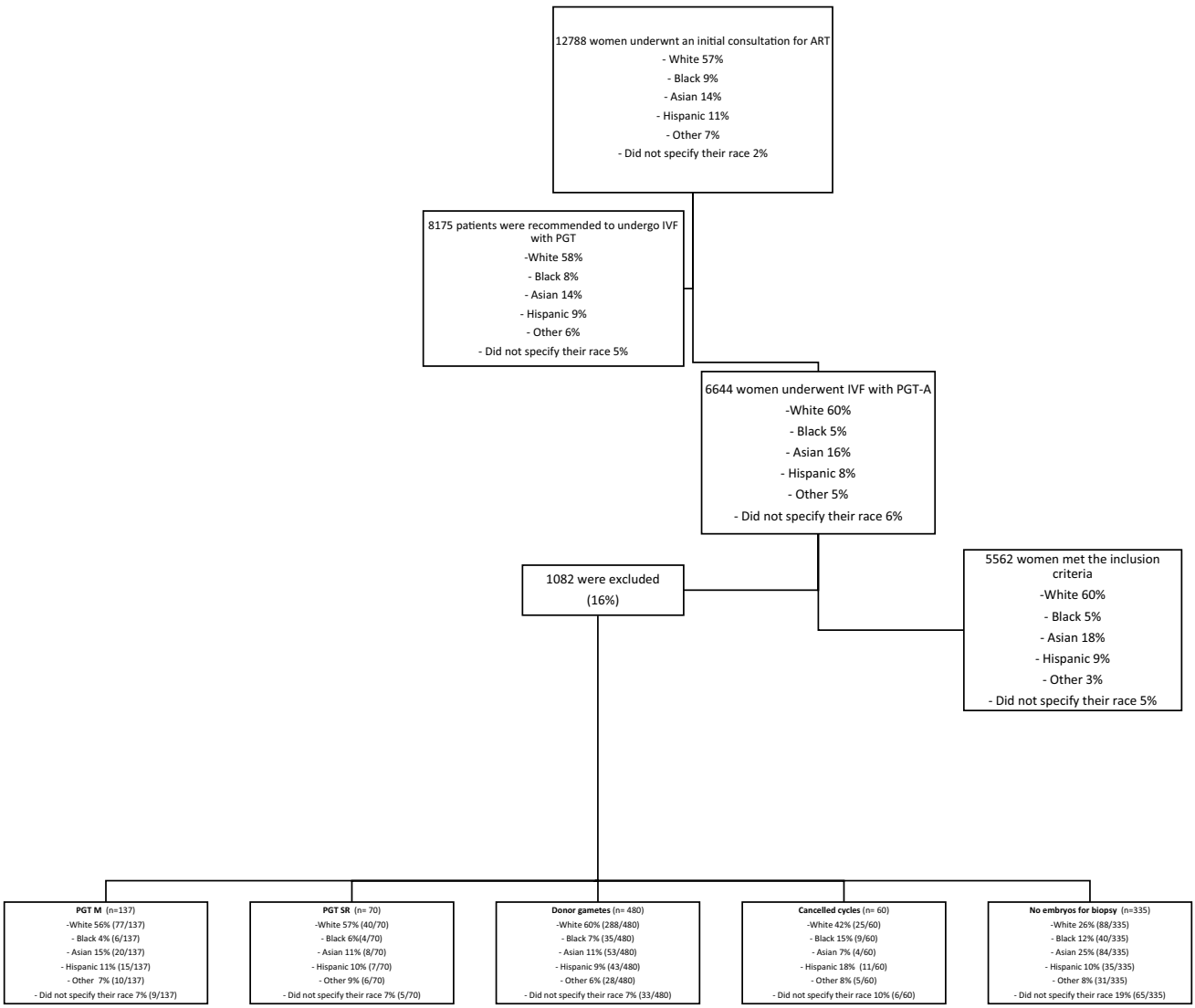

Fig. 1 Flow chart showing the distribution of women who completed an IVF+PGT cycle

Table 1 Demographic and cycle characteristics of patients categorized by self-reported racial background

	White (*n*=3342)	Black (*n*=291)	Asian (*n*=1018)	Hispanic (*n*=472)	Other (*n*=142)	Not specified (*n*=297)	*P* value
Age at oocyte retrieval (years)	36.6 ± 3.5	38.0 ± 3.1[a]	37.3 ± 3.1[a]	37.3 ± 4.0[a]	38.1 ± 3.4[a]	37.2 ± 4.6	< 0.0001*
BMI (kg/m2)	24.1 ± 3.5	27.3 ± 3.9[a]	23.4 ± 3.9	25.4 ± 4.4	24.7 ± 3.3	25.1 ± 3.2	< 0.0001*
Gravidity	1.9 ± 1.3	1.8 ± 2	1.7 ± 1. 2	1.9 ± 0.9	1.8 ± 1.3	1.9 ± 1.4	0.5
AMH (ng/ml)	2.9 ± 3	2.8 ± 3.4	3.0 ± 2.3	2.7 ± 3.3	3.0 ± 4.3	2.9 ± 2.3	0.11
Baseline FSH (IU/mL)	6.4 ± 4	6.9 ± 3.5	6.7 ± 4.8	6.6 ± 4	6.9 ± 4.5	6.4 ± 3.4	0.44
Baseline antral follicle count	12.4 ± 6.8	11.9 ± 6	12.6 ± 5.8	12.1 ± 7	12.0 ± 5	12.1 ± 3	0.39
Etiology of Infertility %							
Tubal Factor	4.5	14.8[a]	8.2[c]	8.4[c]	6.6[c]	6.8	< 0.0001*
Uterine factor	2.1	9.9[a]	2.5	4.6[b]	2.0	3.4	< 0.0001*
Diminished ovarian reserve	19.5	19.9	19.4	18.7	20.3	18.4	0.56
Ovulatory disfunction	5.2	6.5	6.5	6.1	6.2	1.9[a]	< 0.0001*
Recurrent pregnancy loss	5.6	4.1	5.7	5.0	9.3[b]	6.9	< 0.01*
Male factor	13.8	10.7	12.5	15.3[c]	17.3[a]	13.6	< 0.0001*
Idiopathic infertility	12.1	7.1[a]	15.8	12.5	12.6	13	< 0.0001*
Other	37.2	27[b]	29.4	21.9[a]	25.7[a]	36	< 0.0001*
Cycle characteristics							
Cumulative GND dose (Units)	3890 ± 1301	4166 ± 1339[a]	3838 ± 1276	4008 ± 1278	3878 ± 1185	3947 ± 1371	< 0.002*
Day of ovulation trigger	12.0 ± 1.6	12.6 ± 2.4	12.1 ± 1.7	12.1 ± 2	12.4 ± 1.7	12.0 ± 1.9	0.22
Surge E2 (pg/mL)	2295.1 ± 1036.8	2214.3 ± 1148.7	2268 ± 1129	2176.5 ± 1086.3	2141.1 ± 1215.4	2173.13 ± 1136.3	0.09
Surge P4 (ng/mL)	0.9 ± 0.5	0.9 ± 0.5	1.2 ± 0.5	1.0 ± 1	1.0 ± 0.7	1.0 ± 0.4	0.006*

Data presented as mean and ± standard deviations, unless stated otherwise

BMI, body mass index; *AMH*, anti Mullerian hormone; *FSH*, follicle stimulating hormone; *GND*, gonadotropins; *E2*, estradiol; *P4*, progesterone

[a]$p < .0001$ compared to White group

[b]$p < .01$ compared to White group

[c]$p < .05$ compared to White group

*Statistical significance is defined as $p < .05$

self-reported as other when compared to White women (9.3% vs. 5.6%, $p < 0.01$; 17.3% vs. 13.8%, $p \leq 0.0001$, respectively). Finally, White women had the highest prevalence of other causes of infertility when compared to the other 5 groups (37.2%, $p < 0.0001$).

Differences were observed in cycle characteristics. Black women required higher doses of gonadotropins (4166 IU ± 11,339) compared to White and Asian women (3890 ± 13,010 and 3838 ± 1276, respectively, $p = 0.02$). The average day of ovulation trigger was on day 12 for all groups. No statistical differences were noted on serum estradiol levels at the time of surge among cohorts despite the higher dose of total gonadotropins required in Black women. Asian women had higher serum progesterone (ng/ml) levels at trigger than their counterparts ($p = 0.006$).

While Black women had the highest number of oocytes retrieved (15.0 ± 10.9, $p = 0.003$), they had the lowest rate of mature oocytes ($p = 0.003$). Fertilization rate was higher in White women, albeit this was not statistically significant. Blastulation rate (78.6%) and the percentage of biopsied embryos (70.6%) were highest among Black women when compared to other groups ($p \leq 0.0001$ vs. $p < 0.0001$, respectively). The average day of embryo biopsy was similar in all groups ($p = 0.71$) (Table 2).

A total of 24,491 blastocysts were analyzed (Table 2). White women had on average more euploid embryos and higher euploidy rates when compared to their counterparts (White 2.4 ± 2.7 and 52.9%, Black 2.0 ± 2.3 and 44.3%, Asian 1.9 ± 2.1 and 50.2%, Hispanic 2.0 ± 2.2 and 48.7%, other 2.1 ± 2.0 and 49.1%, not specified 2.1 ± 1.9 and 49.8%, $p \leq 0.0001$ and $p \leq 0.0001$, respectively). The inconclusive embryo rate ranged from 5 to 7.2%, being highest among White women. The aneuploidy rate was highest among Black women (48.7%) vs. White (39.9%), Asian (44.3%), Hispanic (45%), other (44.2%), and not specified (45%), $p \leq 0.0001$) (Table 2). However, after controlling for patient

Table 2 IVF outcomes by self-reported racial background

	White (*n*=3342)	Black (*n*=291)	Asian (*n*=1018)	Hispanic (n*n*472)	Other (n*n*=142)	Not specified (*n*=297)	*P* value
Oocytes retrieved	14.5 ± 9.6	15.0 ± 10.9[a]	13.4 ± 8.7[a]	13.8 ± 9.5	14.3 ± 8.1	13.9 ± 9.0	0.003*
Number of MII	11.4 ± 7.3	10.2 ± 5.3	10.3 ± 7.2	10.5 ± 7.0	11.1 ± 7.2	10.7 ± 7.0	0.004*
Oocyte maturity rate	77.8	68.7[a]	75.6	76.3	78.0	77.0	< 0.0001*
Fertilization rate	78.0	77.3	77.3	77.0	77.3	76.1	0.084
Blastulation rate	75.6	78.6[a]	73.9[a]	76.5	76.0	74.3	< 0.0001*
Biopsied blastocysts rate	66.2	70.6[a]	64.7[a]	67.3	67.5	68.3	< 0.0001*
Average embryo biopsy day	5.4 ± 1.6	5.4 ± 1.8	5.5 ± 1.9	5.4 ± 1.8	5.2 ± 1.6	5.5 ± 1.9	0.71
Embryo quality at biopsy % (24514)							
Good (≥ 4BB)	68 (10507/15451)	62 (824/1329)	63.1 (2417/3837)	65 (1292/1988)	62.1 (378/610)	65 (844/1299)	0.81
Moderate (4 BC or 4 CB)	25 (3863/15451)	25 (332/1329)	23.9 (921/3837)	27 (537/1988)	25 (153/610)	24.5 (325/1299)	0.46
Fair (4 CC)	7 (1081/15451)	13 (173/1329)[a]	13 (499/3837)[a]	8 (159/1988)	12.9 (79/610)[a]	10.5 (130/1299)[a]	< 0.001*
PGT-A results (24514)							
Number of euploid embryos	2.4 ± 2.7	2.0 ± 2.3	1.9 ± 2.1	2.0 ± 2.2	2.1 ± 2.0	2.1 ± 1.9	0.004*
Euploid embryo rate	52.9 (8176/15451)	44.3 (589/1329)[a]	50.2 (1930/3837)	48.7 (969/1988)	49.1 (300/610)	49.8 (648/1299)	< 0.0001*
Number of aneuploid embryos	1.8 ± 2.1	2.2 ± 2.4	1.6 ± 2.0	1.8 ± 2	1.9 ± 2.1	1.9 ± 2.2	0.003*
Aneuploid embryo rate	39.9 (6169/15451)	48.7 (648/1329)[a]	44.3 (1701/3837)	45.0 (895/1988)[b]	44.2 (270/610)	45.0 (585/1299)[b]	< 0.0001*
Number of inconclusive embryos	0.3 ± 0.2	0.3 ± 0.3	0.2 ± 0.4	0.2 ± 0.4	0.3 ± 0.2	0.2 ± 0.2	0.17
Inconclusive embryo rate	7.2 (1106/15451)	6.9 (92/1329)	5.3 (206/3837)	6.2 (1241988)	6.5 (40/610)	5.0 (66/1299)	< 0.0001*

Data presented as percentages, mean and ± standard deviations, unless stated otherwise

PGT-A, preimplantation genetic testing for aneuploidy

[a] $p < .0001$ compared to White group

[b] $p < .01$ compared to White group

*Statistical significance is defined as $p < .05$

age, BMI, infertility etiology, cumulative dose of gonadotropins, surge progesterone levels, number of oocytes retrieved, mature oocyte count, rate of biopsied embryos, and embryo quality, there was no statistically significant association between race and the odds of achieving a euploid embryo (aOR 1.31; 95% CI 0.63–2.17, $p = 0.42$) (Supplementary Table I).

A sub-analysis was performed to examine differences in IVF outcomes (CPR, LBR, and CPL rate) in patients who underwent autologous SEET following a synthetically prepared endometrium. A total of 4949 women underwent SEET. Of these, 3067 self-reported as White (62%), 257 as Black (5%), 844 as Asian (17%), 427 as Hispanic (8.7%), 115 as other (2.3%), and 239 did not specify their race (5%). Demographic characteristics and embryo quality are described in Table 3. Black patients were older in stimulation cycles ($p < 0.0001$), SEET cycles ($p \leq 0.0001$), and had a higher BMI (27.5 ± 4.9 kg/m^2, $p < 0.0001$) than their counterparts. Endometrial thickness, estradiol, progesterone levels, day of biopsy, and good quality embryos at the time of transfer were similar among all groups (Table 3). Pregnancy outcomes following SEET are shown in Table 4. CPR, LBR, and CPL did not differ among women of varying self-reported races. In a multivariable logistic controlling for oocyte age and age at transfer, BMI, infertility etiology, and embryo quality, race had no association with lower odds of achieving a clinical pregnancy, live birth, or clinical pregnancy loss after SEET (Supplementary Table II).

Table 3 Demographic and cycle characteristics of patients that underwent a single euploid embryo transfer by self-reported racial background

	White (*n*=3067)	Black (*n*=257)	Asian (*n*=844)	Hispanic (*n*=427)	Other (*n*=115)	Not specified (*n*=239)	*P* value
Age at retrieval (years)	35.3 ± 3.7	37.4 ± 3.5[a]	36.1 ± 3.2	35.9 ± 3.7	37.1 ± 4.1[a]	35.3 ± 4	< 0.0001*
Age at transfer (years)	35.9 ± 3.7	37.8 ± 3.4[b]	36.6 ± 3.2[c]	36.3 ± 3.7[c]	37.6 ± 4.1[b]	35.9 ± 4.1	< 0.0001*
BMI (Kg/m^2)	23.9 ± 4.4	27.5 ± 4.9[a]	23.2 ± 3.7	25.7 ± 4.42	25.1 ± 3.3	25.2 ± 3.3	< 0.0001*
Gravidity	1.8 ± 2.3	1.8 ± 2	1.9 ± 1.1	1.0 ± 1.9	1.0 ± 1.7	1.0 ± 1.1	0.46
AMH	3.6 ± 3.9	3.3 ± 3.7	3.6 ± 3.3	3.3 ± 3.4	3.5 ± 3.8	3.4 ± 2.6	0.61
Baseline day 3 FSH (IU/mL)	6.6 ± 2.7	6.2 ± 3	6.6 ± 2.1	6.2 ± 3	6.6 ± 3.51	6.3 ± 2.8	0.24
Baseline antral follicle count	12.7 ± 8.8	12.3 ± 9	12.5 ± 8.4	13.1 ± 9	11.9 ± 9	12.2 ± 8.2	0.59
E2 at transfer (pg/mL)	248 ± 98.2	275 ± 100.4	234 ± 88.2	288 ± 101.8	284 ± 105.4	255 ± 96.4	0.34
P4 at transfer (ng/mL)	26.1 ± 10.6	26.8 ± 11.3	25.8 ± 9.1	27.0 ± 10.3	26.7 ± 9.8	27.2 ± 10.4	0.08
Endometrial thickness at time of transfer (mm)	9.6 ± 2.1	9.5 ± 1.8	9.5 ± 1.5	9.6 ± 1.8	9.6 ± 1.5	9.6 ± 1.9	0.6
SEET embryo quality %[α]							
Good (≥ 4BB)	64.4 (1963/3067)	61.9 (159/257)	62.9 (532/844)	64.5 (274/427)	62.3 (71/115)	64.1 (154/239)	0.89
Moderate (4 BC or 4 CB)	27 (828/3067)	25.1 (64/257)	24.7 (211/844)	26.7 (115/427)	24.7 (29/115)	24.1 (57/239)[c]	0.43
Fair (4 CC)	8.5 (276/3067)	12.9 (34/257)[a]	12.3 (101/844)[a]	8.7 (38/427)	12.9 (15/115)[a]	11.7 (28/239)[a]	< 0.001*
Average embryo biopsy day	5.3 ± 1.6	5.4 ± 1.6	5.5 ± 1.5	5.4 ± 1.8	5.3 ± 1.6	5.4 ± 1.9	0.68

Data presented as mean and ± standard deviations, unless stated otherwise. *BMI*, body mass index; *AMH*, anti Mullerian hormone; *FSH*, follicle stimulating hormone; *E2*, estradiol; *P4*, progesterone

[α]Modified Gardner Scoring system (Expansion; Inner Cell Mass; Trophectoderm)[12]

*Statistical significance is defined as $p < .05$

[a]$p < .0001$ compared to white group

[b]$p < .01$ compared to white group

[c]$p < .05$ compared to white group

Table 4 Pregnancy outcomes based on self-reported racial background

	White (*n*=3067)	Black (*n*=257)	Asian (*n*=844)	Hispanic (*n*=427)	Other (*n*=115)	None specified (*n*=239)	*P* value
Clinical pregnancy rate	1930 (62.9)	162 (63)	528 (62.5)	261 (61.1)	72 (62.6)	149 (62.3)	0.62
Live birth rate	1502 (48.9)	129 (50.1)	410 (48.5)	208 (48.7)	57 (49.5)	116 (48.5)	0.74
Clinical pregnancy loss rate	428 (13.9)	33 (12.8)	118 (13.9)	53 (12.4)	15 (13)	33 (13.8)	0.42

Data presented as percentages

Discussion

The results of this analysis suggest that race is neither associated with rate of embryonic euploidy nor compromised pregnancy outcomes following SEET. Whereas prior studies have investigated reproductive outcomes after fresh transfer of unscreened embryos and the relationship between genetic ancestry and embryonic aneuploidy, this study is the first to solely focus on the influence of race on embryo euploidy status.

It has been theorized that certain conditions may play a role in poor IVF outcomes among different races. Some studies reported that Black women undergoing IVF had significantly higher BMI when compared to other races [18, 19]. This is consistent with our data, as Black patients had the highest BMI of all the groups studied. Potential explanations for worse prognosis in obese women include abnormal secretion of hormones (such as total and free testosterone, androstenedione and SHBG, and growth hormone) [20], insulin resistance, and direct effects on oocyte and embryo quality, although the mechanisms are largely unknown [20]. Contrary to previous studies that reported lower levels of AMH in Black and Hispanic women, we found no differences in AMH levels among cohorts [8, 9]. However, our study also demonstrated that Black women required higher doses of gonadotropins, which may be the result of higher BMI in this group. Similar to our analysis, Sharara and McClamrock found that Black patients required more aggressive ovarian

stimulation compared to White patients [21]. Additionally, in our study, Black women presented at an older age than their counterparts and represent a minority in our study population (5%). This group of patients is at a fundamental disadvantage since they have higher risks for aneuploidy and are more likely to have medical comorbidities [19, 22–24]. This is consistent with previous studies that reported that Black women tend to delay seeking care for infertility [2, 21] and are less likely to undergo IVF with PGT compared to White women [25]. Although the specific impact of age and BMI was notable in euploidy rates in the unadjusted analysis, after controlling for these variables, race did not have an impact on our primary and secondary outcomes.

When analyzing the etiology of infertility, we found that tubal and uterine factors were more prevalent in Black patients. Both have been associated with significantly reduced implantation, clinical pregnancy, and live birth rates after IVF, as well as increased risk of miscarriage [5, 19, 26]. Nevertheless, Black woman had comparable clinical outcomes despite their infertility etiology, especially, uterine factor, after SEET.

While several studies have identified disparities in ART cycles, few have evaluated embryonic development from COH [5, 27]. One study by Jayaprakasan et al. found that Asian and White women had a similar oocyte yield, fertilization rate, and blastulation rate [27]. Dhillon et al. reported a higher oocyte yield and fertilization rate in Black and Asian women compared to White women [28]. McQueen et al. noted that Black women had fewer mature oocytes, fertilized oocytes, day 5 transfers, and blastocysts for cryopreservation compared with White women [5]. Shahine et al. similarly found no difference in fertilization and blastulation rate, or embryo quality between Asian and White patients [29]. Finally, our study showed that although the number of oocytes retrieved following COH was higher among Black patients, the oocyte maturity rate was the lowest among the same group. Conversely, the blastulation rate was significantly higher for Black patients and lower for Asian and patients that self-reported as other. These findings contradict previous research by Seifer et al., where Black women had lower blastulation rates when compared to White women [4], suggesting that ART outcomes of Black women could benefit if they had earlier access to care. With a rise in PGT cycles, the generalizability of these studies is restricted. Moreover, despite the increasing clinical use of PGT-A, there is paucity of data regarding the relationship between race and euploidy. Franasiak et al. evaluated the relationship between genetic ancestry and embryonic aneuploidy and found that genetic ancestry does not have an impact on embryonic aneuploidy [30]. However, it is important to distinguish that race and ancestry are not equivalent. Whereas ancestry is based on the genetic lineage and geographical origin, race is a social construct and does not reflect the complex genetic diversity within human populations. Factors proposed to affect ART outcomes are more likely related to access to care, individual habits, and underlying causes of subfertility, rather than being driven by genetic lineage. Therefore, it becomes imperative to examine the relationship between race and the status of euploidy in embryos. Understanding this association can shed light on any potential disparities or effects that race might have in this context. The results of our analysis show no significant differences in euploidy rates among women of different racial backgrounds, providing valuable insights into this important aspect of reproductive health.

The majority of the literature has established lower pregnancy rates and LBR among Black women compared to White women undergoing fresh IVF cycles. US registry-based studies demonstrate that ethnic minorities have lower CPR and/or LBR after IVF, compared with White women, although previous analyses have been limited by heterogeneity, missing data, and inadequate power [19, 31]. Only one study has looked into pregnancy outcomes followed by euploid embryo transfers among different races [29]. Their findings revealed lower IR among Black women in comparison to other racial groups. However, it is important to note that their research did not explore the potential link between race and euploidy rates and the resulting suboptimal outcomes after IVF. In contrast to their study, our research seeks to address this gap by evaluating euploidy rates in diverse racial backgrounds as a potential contributing factor to the disparities in ART outcomes. By doing so, we aim to gain a comprehensive understanding of the underlying factors that may influence ART success in different racial groups. By capitalizing on SEET on a medically primed endometrium model to control for embryonic and implantation factors, we found no differences in LBR among the different races and represented.

To our knowledge, this study is the first to show no difference in euploidy rates in embryos from patients of different self-reported racial backgrounds. Additionally, it is the first to exclusively evaluate outcomes following SEET among patients of the most common racial backgrounds in the United States of America.

Our study distinguishes itself as it was performed at a single, high-volume academic center with a team of embryologists all uniformly trained, thereby reducing the inherent variability that may arise from multicenter studies. Patients with recognizable risk factors for failed embryo implantation or poor embryonic development, such as parental chromosomal rearrangements, were excluded from the analysis, thus making our findings more generalizable. Additionally, by including only euploid embryos, we controlled for one of the most common causes of implantation failure and early pregnancy loss, aneuploidy. Furthermore, our study was appropriately powered for the main outcome of interest, and the total number of embryos analyzed met the required sample size based on our power analysis.

Notwithstanding our best efforts to avoid biases, some shortcomings and limitations exist in the analysis. The most notable limitation is its retrospective design, which increases the chance of selection bias. In addition, the study relies on self-reported racial background, which has been shown that people self-identify differently over time [31–33], which makes this data susceptible to confounding and misclassification. Furthermore, the study classification system did not allow for mixed racial/ethnic representation, and, when stratifying by groups, patients that self-reported as other and did not specify their race constitute an important portion of the subjects (8 and 3%, respectively) having a potential influence on the results. However, after performing a sensitivity analysis to address this limitation, our findings were similar to our initial analysis. Another potential limitation is that specific socioeconomic data were not available for analyses within this dataset. And although the single center nature of the analysis signifies that patients have equal availability of services and physicians, affordability and access may be different among patients and could contribute to ART and obstetrical outcome differences in minority populations. Finally, information regarding personal habits such as illicit drug use and cigarette smoking were not available; therefore, we could not assess whether these practices impacted our outcomes.

Conclusion

While differences in patient response to ART by race were observed, euploidy rates and pregnancy outcomes were comparable among patients of different racial backgrounds who underwent a SEET. Thus, providers can reassure patients that race neither interferes with the ability to achieve a euploid embryo nor the opportunity to achieve favorable pregnancy outcomes following ART treatment using PGT-A and SEET. Further research is needed to confirm these findings and to better understand the underlying mechanisms associated with racial disparity so that strategies can be developed to improve access to care and treatment outcomes in non-white populations.

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Declarations

Ethics approval This retrospective study was approved by the Icahn School of Medicine at Mount Sinai Institutional Review Board, Inc. Date 6/2/2022–6/1/2023. Study-18–00441-CR002.

Conflict of interest Dr. AC is an advisor and/or board member of Progyny. The remaining authors declare no competing interests.

References

1. Feinberg EC, Larsen FW, Catherino WH, Zhang J, Armstrong AY. Comparison of assisted reproductive technology utilization and outcomes between Caucasian and African American patients in an equal-access-to-care setting. Fertil Steril. 2006;85(4):888–94.
2. Jain T. Socioeconomic and racial disparities among infertility patients seeking care. Fertil Steril. 2006;85(4):876–81.
3. Chandra, Anjani, Casey E. Copen, and Elizabeth H. Stephen. Infertility and impaired fecundity in the United States, 1982-2010: Data from the National Survey of Family Growth. No. 2013. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, 2013.
4. Seifer DB, Zackula R, Grainger DA. Trends of racial disparities in assisted reproductive technology outcomes in black women compared with white women: Society for Assisted Reproductive Technology 1999 and 2000 vs. 2004-2006. Fertil Steril. 2010;93(2):626–35.
5. McQueen DB, Schufreider A, Lee SM, Feinberg EC, Uhler ML. Racial disparities in in vitro fertilization outcomes. Fertil Steril. 2015;104(2):398-402.e1.
6. Chan M, Mita C, Bellavia A, Parker M, James-Todd T. Racial/ethnic disparities in pregnancy and prenatal exposure to endocrine-disrupting chemicals commonly used in personal care products. Curr Environ Health Rep. 2021;8(2):98–112.
7. Land KL, Miller FG, Fugate AC, Hannon PR. The effects of endocrine-disrupting chemicals on ovarian- and ovulation-related fertility outcomes. Mol Reprod Dev. 2022;89(12):608–31.
8. Kotlyar AM, Seifer DB. Ethnicity/race and age-specific variations of serum AMH in women-A review. Front Endocrinol (Lausanne). 2021;9(11):593216.
9. Seifer DB, Golub ET, Lambert-Messerlian G, Benning L, Anastos K, Watts DH, Cohen MH, Karim R, Young MA, Minkoff H, Greenblatt RM. Variations in serum Müllerian inhibiting substance between white, black, and Hispanic women. Fertil Steril. 2009;92(5):1674–8.
10. Li HJ, Seifer DB, Tal R. AMH independently predicts aneuploidy but not live birth per transfer in IVF PGT-A cycles. Reprod Biol Endocrinol. 2023;21(1):19.
11. Jiang X, Yan J, Sheng Y, Sun M, Cui L, Chen ZJ. Low anti-Müllerian hormone concentration is associated with increased risk of embryonic aneuploidy in women of advanced age. Reprod Biomed Online. 2018;37(2):178–83.
12. Engmann L, Jin S, Sun F, Legro RS, Polotsky AJ, Hansen KR, Coutifaris C, Diamond MP, Eisenberg E, Zhang H, Santoro N. Racial and ethnic differences in the polycystic ovary syndrome metabolic phenotype. Am J Obstet Gynecol. 2017;216(5):493.e1-493.e13.
13. Sengoku K, Tamate K, Takuma N, Yoshida T, Goishi K, Ishikawa M. The chromosomal normality of unfertilized oocytes from patients with polycystic ovarian syndrome. Hum Reprod. 1997;12(3):474–7.
14. Hernandez-Nieto C, Lee JA, Slifkin R, Sandler B, Copperman AB, Flisser E. What is the reproductive potential of day 7 euploid embryos? Hum Reprod. 2019;34(9):1697–706.
15. Sekhon L, Shaia K, Santistevan A, Cohn KH, Lee JA, Beim PY, Copperman AB. The cumulative dose of gonadotropins used for controlled ovarian stimulation does not influence the odds of embryonic aneuploidy in patients with normal ovarian response. J Assist Reprod Genet. 2017;34(6):749–58.
16. Veeck L, Bodine R, Clarke RN, Berrios R, Libraro J, Moschini R, Zaninovic N, Rosenwaks Z. High pregnancy rates can be achieved after freezing and thawing human blastocysts. Fertil Steril. 2004;82:1418–27.

17. Zegers-Hochschild F, Adamson GD, Dyer S, Racowsky C, de Mouzon J, Sokol R, Rienzi L, Sunde A, Schmidt L, Cooke ID, et al. The international glossary on infertility and fertility care, 2017. Hum Reprod. 2017;32:1786–2180.
18. Luke B, Brown MB, Stern JE, Missmer SA, Fujimoto VY, Leach R. Racial and ethnic disparities in assisted reproductive technology pregnancy and live birth rates within body mass index categories. Fertil Steril. 2011;95(5):1661–6.
19. Seifer DB, Frazier LM, Grainger DA. Disparity in assisted reproductive technologies outcomes in black women compared with white women. Fertil Steril. 2008;90(5):1701–10.
20. Lashen H, Afnan M, Sharif K. A controlled comparison of ovarian response to controlled stimulation in first generation Asian women compared with white Caucasians undergoing in vitro fertilisation. Br J Obstet Gynaecol. 1999;106:407–9.
21. Sharara FI, McClamrock HD. Differences in in vitro fertilization (IVF) outcome between white and black women in an inner-city, university-based IVF program. Fertil Steril. 2000;73(6):1170–3.
22. Scott RT Jr, Ferry K, Su J, Tao X, Scott K, Treff NR. Comprehensive chromosome screening is highly predictive of the reproductive potential of human embryos: A prospective, blinded, nonselection study. Fertil Steril. 2012;97:870–5.
23. Bleil ME, Gregorich SE, Adler NE, Sternfeld B, Rosen MP, Cedars MI. Race/ethnic disparities in reproductive age: An examination of ovarian reserve estimates across four race/ethnic groups of healthy, regularly cycling women. Fertil Steril. 2014;101(1):199–207.
24. Schuh-Huerta SM, Johnson NA, Rosen MP, Sternfeld B, Cedars MI, Reijo Pera RA. Genetic variants and environmental factors associated with hormonal markers of ovarian reserve in Caucasian and African American women. Hum Reprod. 2012;27(2):594–608.
25. Makhijani R, Godiwala P, Grady J, Christy A, Thornton K, Grow D, Engmann L. Black race associated with lower live birth rate in frozen-thawed blastocyst transfer cycles: An analysis of 7,002 Society for Assisted Reproductive Technology frozen-thawed blastocyst transfer cycles. Fertil Steril. 2022;117(2):360–7.
26. Stewart EA, Cookson CL, Gandolfo RA, Schulze-Rath R. Epidemiology of uterine fibroids: A systematic review. BJOG. 2017;124(10):1501–12.
27. Jayaprakasan K, Pandian D, Hopkisson J, Campbell BK, Maalouf WE. Effect of ethnicity on live birth rates after in vitro fertilisation or intracytoplasmic sperm injection treatment. BJOG. 2014;121(3):300–6.
28. Dhillon RK, Smith PP, Malhas R, Harb HM, Gallos ID, Dowell K, et al. Investigating the effect of ethnicity on IVF outcome. Reprod Biomed Online. 2015;31(3):356–63.
29. Shahine LK, Lamb JD, Lathi RB, Milki AA, Langen E, Westphal LM. Poor prognosis with in vitro fertilization in Indian women compared to Caucasian women despite similar embryo quality. PLoS One. 2009;4(10):e7599.
30. Franasiak JM, Olcha M, Shastri S, Molinaro TA, Congdon H, Treff NR, Scott RT Jr. Embryonic aneuploidy does not differ among genetic ancestry according to continental origin as determined by ancestry informative markers. Hum Reprod. 2016;31(10):2391–5.
31. Mersha TB, Abebe T. Self-reported race/ethnicity in the age of genomic research: Its potential impact on understanding health disparities. Hum Genomics. 2015;9(1):1.
32 Hitlin S, Scott Brown J, Elder GH Jr. Racial self-categorization in adolescence: Multiracial development and social pathways. Child Dev. 2006;77(5):1298–308.
33. Seifer DB, Sharara FI, Jain T. The disparities in ART (DART) hypothesis of racial and ethnic disparities in access and outcomes of IVF treatment in the USA. Reprod Sci. 2022;29(7):2084–8.