Are there ethnic differences in pregnancy rates in African-American versus white women undergoing frozen blastocyst transfers?

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Objective: To determine whether frozen-thawed blastocyst transfer pregnancy rates (PR) are lower in African-American compared with white women.
Design: Retrospective review of frozen blastocyst cycles.
Setting: University-based assisted reproductive technology (ART) program.
Patient(s): All patients who underwent a frozen blastocyst transfer between 2003 and 2008.
Intervention: None.
Main Outcome Measure(s): Live birth rate.
Result(s): One hundred sixty-nine patients underwent transfer of a frozen-thawed blastocyst. African-American women had a higher incidence of leiomyoma (40% vs. 10%) and tubal and uterine factor infertility. There was no difference in the live birth rate for African-American patients (28.0%) compared with white patients (30.2%). Of the patients who underwent a frozen-thawed blastocyst transfer, 58% (n = 98) had their fresh, autologous IVF cycle, which produced the cryopreserved blastocyst, at Walter Reed Medical Center. A higher peak serum E_2 level was noted in African-American patients (5,355 pg/mL) compared with white patients (4,541 pg/mL). During the fresh cycle, the live birth rates between African-American and white patients were significantly different at 16.7% versus 39.7%, respectively.
Conclusion(s): Live birth rates after frozen blastocyst transfer are not different between African-American and white women despite a fourfold higher incidence of leiomyomas in African-American women. (Fertil Steril® 2011;95:89–93. ©2011 by American Society for Reproductive Medicine.)

Key Words: Ethnicity, racial, disparities, live birth rate, infertility, IVF, ART

Since the advent of IVF clinicians have sought to optimize cycles and identify factors that impact pregnancy success. More recently ethnicity has been identified as an inherent, nonmodifiable factor that affects pregnancy outcomes. The reason for ethnic differences in IVF outcomes remains an enigma. The first US studies on ethnic differences in IVF emerged in 2000 and compared African-American women with white women (1–3). Sharara and McClamrock (3) demonstrated a lower African-American pregnancy rate (PR) in an inner city clinic, whereas subsequent studies revealed inconsistent results (1, 2, 4, 5). Although limited by small sample sizes these early studies established precedence for future investigation of racial and ethnic disparities in IVF outcomes.

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One confounder in examining ethnic differences in IVF pregnancy outcomes is the underutilization of services by certain ethnicities. In an equal access to care facility, Feinberg and colleagues (6) found an approximate 20% reduction in live birth rates in an African-American cohort when compared with a white cohort. Since that time, more than 100,000 cycles have been examined by three large retrospective analyses, demonstrating significant reductions (25%–38%) in African-American live birth rates after IVF when compared with white cohorts (7–9). The reason for this ethnic disparity remains unknown, but increased prevalence of leiomyoma, tubal disease, and obesity in the African-American infertile population are possible explanations (1, 2, 4–6, 8–11).

Recent work suggests that endometrial receptivity in response to gonadotropin stimulation may explain ethnic differences in PRs in Asian women versus white women, as the quality of embryos at cleavage stage and blastocyst stage appear to be similar between both ethnic groups (12–14). In fresh nondonor IVF cycles, the PRs of Asian women were lower than that of white women (12–14). Interestingly, PRs with controlled hormonal replacement for endometrial preparation are similar using the oocyte donation model between Asian and white women (15).

At present numerous studies have confirmed the finding of decreased PRs and increased miscarriage rates in African-American women during fresh IVF/ intracytoplasmic sperm injection (ICSI) cycles (3, 6–9, 16). We hypothesize that tubal and uterine factors are responsible for the ethnic disparity in pregnancy outcomes in fresh

cycles, and the same disparity would be seen in frozen embryo cycles. The objective of this study was to determine whether an ethnic disparity exists in live birth rates between African-American and white women after frozen-thawed blastocyst ETs.

MATERIALS AND METHODS

Study Design

A retrospective cohort analysis of all patients undergoing frozen blastocyst ETs was performed. Institutional Review Board approval was obtained from the Walter Reed Army Medical Center (WRAMC) Division of Clinical Investigation. The main outcome analyzed was live birth rate. Other outcome measures included clinical PRs and spontaneous abortion rates.

Patients

Electronic records were evaluated for all patients who underwent a frozen blastocyst ET cycle between January 2003 and December 2008. One hundred eighty-six patients were identified who underwent transfer of at least one frozen-thawed blastocyst. No frozen donor embryo cycles were performed. For patients who underwent multiple frozen ET cycles, only their first cycle was included in the analysis to maintain independent sampling. Demographic and IVF cycle characteristic data were recorded. Ethnicity was documented as reported by the patient on intake evaluation.

Blastocysts selected for cryopreservation met requirements as established by the embryology laboratory at WRAMC. No cleavage stage embryos were frozen. Blastocysts were required to be grade BB or better by modified Gardner grading scale. Due to the strict criteria, historically only 10% of the patients had embryos that met the cryopreservation requirements of our laboratory. As a result, the successful thaw/survival rate for frozen blastocysts within the laboratory exceeded 95%. There were no significant changes in cryopreservation techniques during the study period.

Patient Treatment Protocol

Patients were given SC leuprolide acetate (LA), 1 mg/d, starting in the midluteal phase of the preceding menstrual cycle or after 2–4 weeks of taking oral contraceptives (OC) (with a 5-day overlap). At baseline all patients had suppressed serum E_2 levels and a transvaginal ultrasound examination demonstrating an early proliferative pattern. If leiomyomas were present on ultrasound, their size and location were documented. Before the cycle start, all patients had saline sonohysterographic testing to ensure a normal uterine cavity. No patients included in the analysis had evidence of cavity distortion at cycle start.

The patients began sequentially increasing doses of oral micronized 17β-E_2, starting at 2 mg once a day and increasing to a maximum dose of 2 mg three times a day. Serial serum E_2 measurements and transvaginal ultrasound evaluation of the endometrium were performed. Once E_2 levels exceeded 200 pg/mL and an appropriate trilaminar endometrial pattern was obtained, the GnRH agonist treatment was discontinued and P in oil, 50 mg/d IM, was initiated. The blastocyst transfer occurred 5 days after the start of P supplementation.

Blastocysts selected for transfer were based on morphological assessment. Each patient was placed in the dorsal lithotomy position without sedation. The blastocyst transfer was performed under ultrasound guidance. Serum quantitative hCG testing was performed 9 and 11 days after blastocyst transfer and transvaginal ultrasound was performed approximately 4 weeks later to confirm an intrauterine pregnancy. Pregnancy outcome data were collected.

Subgroup Analysis

For all study patients who underwent frozen-thawed blastocyst transfer, electronic medical records were reviewed to ascertain data for an antecedent fresh IVF or ICSI cycle that produced the cryopreserved blastocysts used in the frozen-thawed cycle. Ninety-eight patients had complete data for fresh, autologous IVF/ICSI stimulation (leading to a cryopreserved blastocyst) through WRAMC. Demographic, cycle, and pregnancy outcome data of this subset of patients were recorded. Similar to the frozen cycles, before the cycle start all patients had a saline sonohysterogram to ensure a normal uterine cavity without distortion. All fresh ETs were performed under ultrasound guidance.

TABLE 1

Baseline characteristics and cycle parameters between African-American and white women undergoing frozen-thawed blastocyst ET.

Characteristic	African-American women (n = 50)	White women (n = 119)	*P* value
Age (y)	34.1 ± 3.6	34.7 ± 4.2	.31
Gravidity	1.8 ± 2.2	1.5 ± 1.9	.54
Parity	0.6 ± 1.1	0.8 ± 0.8	.2
Leiomyoma present	20/50 (40%)	11/119 (10%)	<.001[a]
Leiomyoma >3 cm present	6/50 (12%)	1/119 (1%)	.002[a]
Peak E_2 (pg/mL)	891 ± 792	909 ± 723	.89
Endometrial stripe (mm)[b]	10.4 ± 2.5	9.4 ± 1.9	.01[a]
Embryos transferred	2.1 ± 0.6	2.1 ± 0.6	.75

[a] $P<.05$, statistically significant difference.
[b] At the time of frozen-thawed blastocyst ET.

Csokmay. Ethnic disparity in frozen embryo cycles. Fertil Steril 2011.

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (version 16.0.1, 2008; SPSS, Inc., Chicago, IL). For normally distributed data, a *t*-test was used to compare the mean values. For data that were not normally distributed, a Mann-Whitney rank sum test was used to compare the mean values. Differences in outcome rates were analyzed using a χ^2 test or Fisher's exact test when appropriate. An α error of 0.05 was considered significant for all comparisons. All data were reported as mean ± SD.

RESULTS

There were 186 patients identified who underwent transfer of a frozen-thawed blastocyst between 2003 and 2008. Of these, there were 119 white women, 50 African-American women, and 17 women of other ethnicities (Hispanic, Asian, mixed). Only those patients of African-American or white ethnicity were included in this analysis.

The baseline characteristics of the 169 patients undergoing a frozen-thawed blastocyst transfer are seen in Table 1. African-American and white women had similar age (mean 34.1 and 34.7 years, median 35.0 and 35.0 years, respectively), gravidity, and parity. Leiomyomas were more frequently seen on ultrasound in the African-American patients than in white women (40% vs. 10%, $P<.001$). When examining patients with leiomyoma more than 3 cm, 12% of African-American women were affected compared with only 1% of white women ($P=.002$). During the treatment with oral E_2, the African-American and white patients had a maximum endometrial thickness of 10.4 mm and 9.4 mm, respectively, before blastocyst transfer ($P=.01$). Although statistically significant, the 1-mm difference did not likely represent a clinically significant result. The mean number of blastocysts (2.1) transferred per patient was also similar between both groups. In Table 2 are the infertility diagnoses demonstrating that African-American women had a higher likelihood of tubal factor (64% vs. 31%) and uterine factor (40% vs. 10%), and a lower likelihood of anovulation (4% vs. 22%) when compared with white women.

Pregnancy outcome, the primary end point, is shown in Table 3. The overall PR after frozen-thawed blastocyst transfers for African-American women was 62.0% compared with 57.1% for