

# In vitro fertilization outcomes after fresh and frozen blastocyst transfer in South Asian compared with Caucasian women

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**Objective:** To study pregnancy outcomes between South Asian and Caucasian women undergoing frozen blastocyst transfer cycles. **Design:** Retrospective cohort study.

#### **Setting:** Not applicable.

**Patient(s):** Caucasian and South Asian patients undergoing frozen blastocyst transfer between January 2011 and December 2014. **Intervention(s):** Not applicable.

Main Outcome Measure(s): Live birth rate.

**Result(s):** A total of 196 Caucasian and 117 South Asian women were included in our study. Indians were on average 2.2 years younger than Caucasian women (34.9 vs. 37.1 years), and were more likely to be nulliparous (59% vs. 43%). All other baseline characteristics were similar. In women undergoing their first frozen ET cycle, implantation rate (49% vs. 47%), clinical pregnancy rate (PR; 54% vs. 49%), and live birth rate (43% vs. 43%) were similar between South Asians and Caucasians, respectively. In patients who underwent a prior fresh blastocyst transfer, the live birth rate was significantly lower in South Asian versus Caucasian women (21% vs. 37%). **Conclusion(s):** Our data demonstrate that IVF outcomes are better in frozen versus fresh cycles

among South Asian women. The IVF clinics may wish to consider these findings when counseling South Asian patients about the timing of ET. (Fertil Steril® 2016;105:1484–7. ©2016 by American Society for Reproductive Medicine.) **Key Words:** Ethnicity, disparity, IVF, frozen embryo transfer



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**S** tudies demonstrating ethnic differences in reproductive outcomes have highlighted the importance of reporting these disparities; however, few studies have adequately assessed potential etiologies for these differences (1). The available literature suggests women with South Asian ethnicity carry a worse prognosis compared with their Caucasian coun-

terparts. Although the etiology for these differences has not been clearly elucidated, oligo-ovulation and polycystic ovarian syndrome (PCOS) are higher in this population (2).

Assisted reproductive technology (ART) outcomes among different ethnic groups were examined in two British studies. The first study found a nonsignificant reduction in live birth rate

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Fertility and Sterility® Vol. 105, No. 6, June 2016 0015-0282/\$36.00 Copyright ©2016 American Society for Reproductive Medicine, Published by Elsevier Inc. http://dx.doi.org/10.1016/j.fertnstert.2016.02.027 (LBR; 16% vs. 22.6%) in South Asian versus Caucasian women (3). The second study demonstrated higher cancellation rates (22.7% vs. 9.1%) and lower LBRs (9.1% vs. 22.7%) in South Asian versus Caucasian women (4). These studies also suggested poor embryo quality, which may contribute to lower pregnancy rates (PRs) among South Asian women.

Our center previously reported lower implantation rates (28% vs. 39%) and LBRs (24% vs. 41%) in fresh transfer cycles with similar quality blastocysts among South Asian versus Caucasian women (5). The results of this study suggested that there may be an endometrial component to the differences observed in this cohort. To control for possible differences in endometrial receptivity associated with fresh stimulated IVF cycles, we compared IVF outcomes among South Asian and Caucasian women in exclusively frozen ET cycles at Stanford University IVF Center.

### **MATERIALS AND METHODS**

We conducted a retrospective cohort analysis of all our nondonor, nongestational carrier cycles undergoing frozen blastocyst transfer between January 2011 and December 2014 at Stanford University IVF Center. Approval was obtained from Stanford University Institutional Review Board to conduct this study.

A total of 196 Caucasian and 117 South Asian women were included. For patients undergoing multiple frozen ETs, only the first cycle was included to maintain independent sampling. Ethnicity data were gathered from patient selfreporting questionnaires. Those who indicated Caucasian or white were considered Caucasian. Patients who reported South Asian or Indian were included in the South Asian category. Patients who self-reported other or unknown were not included in this review.

Data collected included age, obstetric history, body mass index (BMI), cycle day 3 FSH, number of previous fresh cycles, and indication for IVF. Cycle characteristics included endometrial thickness, medicated or natural cycle, and number and quality of blastocysts transferred.

Blastocysts were required to be 3BB quality or better at the time of cryopreservation on day 5 or 6 by Gardner grading scale (6). There were no significant differences in cryopreservation technique during the study period. All embryos were cryopreserved using our institutional vitrification protocol using the SAGE vitrification kit (Origio).

Patients underwent a standardized frozen ET protocol either using a natural or programmed cycle. The natural cycle was conducted as described by Lathi et al. (7). In brief, hCG was administered when a lead follicle measured  $\geq$  17 mm and the patient reported a negative home ovulation test. The frozen ET was performed 7 days later, unless the patient had a positive LH surge, in which case the ET was performed 6 days later. The programmed cycle was conducted as described by Lathi et al. (7) from 2011–2012, then simplified in 2012 to a protocol using oral  $E_2$  (6 mg), vaginal P, and no GnRH agonist.

The primary outcome measured was LBR, and secondary outcomes included positive pregnancy test ( $\beta$ -hCG >5 mIU/ mL 9–10 days after transfer), implantation rate (number of gestational sacs seen at 6.5 weeks per number of embryos transferred), clinical PR (gestational sac seen at 6.5 weeks), and spontaneous pregnancy loss (loss of pregnancy after gestational sac seen on transvaginal ultrasound).

Statistical analysis was performed using SAS software, version 9.4. The  $\chi^2$  analysis and Student's *t* test were used for dichotomous and continuous variables, respectively. All tests were two-tailed with an alpha of 0.05. Univariate analysis was used to compare all baseline characteristics. A multivariate regression model was used to estimate the independent contribution of South Asian ethnicity on treatment outcomes, adjusting for baseline characteristics that approached statistical significance (*P*<.1).

#### RESULTS

A total of 196 Caucasian and 117 South Asian women were included in our study. South Asians were on average 2.2 years younger than Caucasian women (34.9 vs. 37.1 years; P=.01), and were more likely to be nulliparous (59% vs. 43%; P=.02). All other baseline characteristics were similar, including BMI, day 3 FSH, and indication for IVF (Table 1). A higher percentage of South Asian patients had PCOS compared with Caucasian women (20.5% vs. 11.8%); however, this did not reach statistical significance.

Table 2 includes cycle characteristics in each group. Of all transfers, 79% used a natural cycle (vs. programmed) and were not different between groups. The number of embryos were comparable (1.37 in South Asian vs. 1.34 in Caucasian women). All other parameters were similar between groups, including endometrial thickness, percentage of cycles in which all the embryos obtained during the fresh cycle were cryopreserved ("freeze-all"), and percentage of high quality embryos, defined as 4AB or better.

A similar number of South Asian and Caucasian patients underwent a "freeze-all" cycle before their first frozen ET (25% vs. 23%). The indications for "freeze-all" were similar between groups, and were mostly due to the use of preimplantation genetic screening either for aneuploidy screening or single gene disorders. Only four patients (2 Caucasian and 2 South Asian women) were converted to "freeze-all" cycles during their stimulation due to the risk of developing ovarian hyperstimulation syndrome (OHSS). In patients who underwent a fresh transfer (151/196 Caucasian and 88/117 South Asian women), the LBR from the fresh transfer was 21% versus 37% (P<.01) in South Asian versus Caucasian women. The LBR were not statistically different between fresh and frozen cycles in Caucasian women (37% vs. 43%; P=.48); however, were significantly lower in fresh cycles versus frozen cycles in South Asian women (21% vs. 43%; P=.03).

A similar number of South Asian and Caucasian patients underwent their first frozen ET due to a failed fresh transfer

### TABLE 1

Baseline characteristics of women undergoing frozen blastocyst embryo transfer.

Variable	South Asian (n = 117)	Caucasian (n = 196)	P value
Age, y	34.9	37.1	.01
BMI, kg/m <sup>2</sup>	24.5	24.5	.77
Nulliparous, %	59	43	.02
Day 3 FSH	$6.06 \pm 1.30$	$7.04 \pm 1.84$	.13
No. of prior fresh IVF cycles, mean $\pm$ SD	1.5 ± 0.95	1.43 ± 0.94	.29
Diminished ovarian reserve	6.9	15.1	.08
Endometriosis	11.0	6.5	.26
Male factor	27.4	38.1	.11
PCOS	20.5	11.8	.08
Tubal	8.2	8.6	.94
Other/unexplained	26.0	19.7	.28
Note: Values are presented as percentages, unless stated otherwise. BMI = body mass index;			

PCOS = polycystic ovarian syndrome.

Shah. IVF outcomes after FET in South Asians. Fertil Steril 2016.

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