Patient and cycle characteristics predicting high pregnancy rates with single embryo transfer: an analysis of the Society for Assisted Reproductive Technology outcomes between 2004 and 2013


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Objective: To analyze factors associated with high live birth rate and low multiple birth rate in fresh and frozen–thawed assisted reproductive technology (ART) cycles.

Design: Retrospective cohort analysis.

Setting: Not applicable.

Patient(s): The study population included 181,523 women undergoing in vitro fertilization with autologous fresh first cycles, 27,033 with fresh first oocyte donor cycles, 37,658 with fresh second cycles, and 35,446 with frozen–thawed second cycles.

Intervention(s): None.

Main Outcome Measure(s): Live birth rate and multiple birth rate after single embryo transfer (SET) and double embryo transfer (DET) were measured, in addition to cycle characteristics.

Result(s): In patients with favorable prognostic factors, including younger maternal age, transfer of a blastocyst, and additional embryos cryopreserved, the gain in the live birth rate from SET to DET was approximately 10%–15%; however, the multiple birth rate increased from approximately 2% to greater than 49% in both autologous and donor fresh and frozen–thawed transfer cycles.

Conclusion(s): This study reports a 10%–15% reduction in live birth rate and a 47% decrement in multiple birth rate with SET compared with DET in the setting of favorable patient prognostic factors. Our findings present an opportunity to increase the rate of SET across the United States and thereby reduce the multiple birth rate and its associated poor perinatal outcomes with assisted reproductive technology pregnancies. (Fertil Steril 2017; –: –: –: –: ©2017 by American Society for Reproductive Medicine.)

Key Words: Double embryo transfer (DET), multiple birth rate (MBR), live birth rate (LBR), SART, single embryo transfer (SET)

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In the United States the multiple birth rate (MBR) and twin birth rate have been rising since 1980, both reaching all-time highs in 2014 of 35.1/1,000 live births and 33.9/1,000 live births, respectively (1). The triplet and higher-order multiple rate has also risen during this period, increasing more than fivefold from 37.0/100,000 live births in 1980 to a peak of 193.5/100,000 live births in 1998, with a relatively steady annual decline to 113.5/100,000 live births in 2014 (1). Half of all twins and 90% of all triplet and higher-order multiples are born either with low birth weight or prematurely, and all

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multiple births are at increased risk of serious maternal and neonatal morbidity (1).

The rise in the MBR has paralleled the widespread use and increasing availability of fertility therapies. In the early years of IVF treatment, in an effort to compensate for low implantation rates, multiple embryos were transferred to improve pregnancy and live birth rates (LBRs) at the risk of resulting in a multiple birth (2). As laboratory and clinical techniques have improved, the contemporary goal of IVF has changed from achieving a pregnancy to narrowing the gap in perinatal outcomes between assisted and spontaneous conceptions (3).

The reversal in the rising trend of triplet and higher-order births coincides with the issuance of national ET guidelines from the American Society for Reproductive Medicine (ASRM)/Society for Assisted Reproductive Technology (SART), first in 1998, with revisions in 1999, 2004, 2006, 2008, 2009, and 2013 (4–11), and the advocacy for elective single embryo transfer (eSET) in clinically appropriate patients (6, 12, 13). Success with IVF today has been defined as a singleton pregnancy resulting in a healthy singleton infant born at term (9, 14–16). Since 2003 eSET has been advocated in Europe to reduce the MBR, and with national insurance coverage for infertility services, several European nations have implemented mandatory eSET policies (17–20).

The recommendation to use eSET in the United States has been inconsistently implemented, likely owing to an absence of financial subsidies for IVF, as well as patient and provider perceptions of reduced LBR (21–23). Analyses of national data in 2004–2012 have shown that eSET is more likely to occur in cases with insurance coverage, retrieval of ≥ 16 oocytes, and the transfer of blastocyst embryos (24). Application of a validated prediction model based on 2006–2012 national data demonstrated that the cumulative LBR is as good as or better with eSET over the course of one fresh and one frozen cycle than with double embryo transfer (DET) in a single cycle, while reducing the MBR by more than tenfold (25).

The objective of this study was to analyze factors associated with high LBR and low MBR in fresh and frozen assisted reproductive technology (ART) cycles. The national SART Clinic Outcome Reporting System (SART CORS) was used to conduct this analysis in efforts to assist the ASRM/SART Practice Committee in updating their current guidelines for number of embryos to transfer.

MATERIALS AND METHODS

All cycles of treatment that started in 2004–2013 were extracted from the SART CORS database. For each woman, cycles were ordered by year of treatment and patient age. The inclusion criterion was female patients who underwent IVF with ET within the queried timeframe. Exclusion criteria for analysis of autologous cycles included history of prior gonadotropin or IVF treatment, freeze-all cycles with subsequent frozen embryo transfer (FET), research cycles, embryo banking cycles, or cycles that used a gestational carrier, including all subsequent cycles for that woman. Donor oocyte cycles had the same exclusion criteria, except that individuals who had had prior autologous cycles were not excluded from analysis. Preimplantation genetic screening/preimplantation genetic diagnosis cycles were excluded, as well as women with a diagnosis labeled as “Other-PGD.” Fresh cycles were limited to cleavage (day 2–3) and blastocyst (day 5–6) ETs, and one or two embryos transferred (single [SET], or double [DET]). The number of supernumerary embryos cryopreserved was categorized as none or one or greater. Thawed embryos in cycle 2 were categorized as cleavage or blastocyst, as coded when entered into the SART CORS database. Maternal age for autologous cycles was categorized as 18–29, 30–34, 35–37, 38–40, and 41–43 years according to the SART age groups. The <35-years-old SART age group was subdivided into 18–29 and 30–34 years to investigate whether these age groups had differing prognoses or outcomes.

Cycles using autologous oocytes were numbered consecutively. By restricting the sample to women without prior treatment, the first autologous cycle always used a fresh oocyte; the second cycle may use either a fresh or thawed embryo. Cycle 2 only included women who did not have a live birth in cycle 1. The first cycle using a donor oocyte was included, even in cases in which that individual had had prior autologous cycles. Donor cycles were excluded if they used frozen oocytes.

A live birth was defined as a birth that was reported as a live birth in the SART database but also that had a gestational duration of at least 22 weeks and a birth weight of at least 300 g. The LBR was computed as a percentage of the number of cycles with the same characteristics. A multiple birth was defined as two or more live births from the same pregnancy. The MBR was computed as a percentage of the total deliveries with live births (not total pregnancies or cycles). Tables consist of observed frequencies in which the denominator is 50 cycles or greater. No standard deviation or confidence intervals are presented because our data represent the full population. The data were analyzed using SAS 9.4 (SAS Institute). The study was approved by the institutional review boards at Michigan State University and University of Michigan.

RESULTS

The study population included 181,523 autologous fresh first cycles and 27,033 fresh first oocyte donor cycles (Table 1), and the mean maternal age was 33.5 and 41.4 years, respectively. For both groups more than 70% were reported as white (after excluding “unknown” ethnicity). In the autologous group, when there was only a single diagnosis, the most frequent was male factor (35.1%), followed by unexplained (19.0%); for all women (including those with either single or multiple diagnoses) the most frequent were male factor (42.8%) and ovulation disorders (15.0%).

Autologous, First Cycle

In autologous first cycles, LBRs were significantly higher for blastocyst embryos compared with cleavage embryos (P ≤ .001), and within day of transfer categories, higher when any vs. no embryos were cryopreserved (P ≤ .001), and declined with advancing maternal age (P ≤ .001) (Table 2). For both cleavage and blastocyst transfers when no embryos were frozen, the LBR was lower and declined with advancing maternal age compared with transfers in which there were
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