Donor oocytes are associated with preterm birth when compared to fresh autologous in vitro fertilization cycles in singleton pregnancies

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Objective: To use a national registry to examine the role of oocyte donation on pregnancy outcomes in singleton pregnancies.
Design: Retrospective cohort.
Setting: Not applicable.
Patient(s): Women undergoing autologous cycles and donor oocyte recipients in the United States from 2008–2010.
Intervention(s): None.
Main Outcome Measure(s): Preterm delivery, birth weight <2,500 g, small for gestational age birthweight, perinatal death.
Result(s): The rates of preterm delivery and low birthweight for all members of this cohort were higher than the US national average. Pregnancies resulting from oocyte donation were significantly more likely to end before 34 weeks' and 37 weeks' gestation (adjusted odds ratio [OR] = 1.30, 95% confidence interval [CI] = 1.03–1.64 for 34 weeks' gestation, adjusted OR = 1.28, 95% CI = 1.12–1.46 for 37 weeks' gestation), and to result in infants weighing <2,500 g (adjusted OR = 1.21, 95% CI = 1.02–1.44). However, once gestational age at delivery is accounted for, these infants are actually at decreased risk of having a small for gestational age birthweight (adjusted OR = 0.72, 95% CI = 0.58–0.89) and of perinatal death (adjusted OR = 0.29, 95% CI = 0.09–0.94).
Conclusion(s): Data from a national cohort indicate that donor oocyte recipients are more likely to deliver preterm when compared with autologous patients. The effect of donor oocyte donation on birthweight is likely a function of an increased rate of preterm delivery among this population. (Fertil Steril® 2016;106:660–5. ©2016 by American Society for Reproductive Medicine.)
Key Words: Donor oocytes, preterm birth, low birth weight, perinatal death

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Infants conceived using assisted reproductive technology (ART) represent 0.7%–1.4% of all births in the United States (1). The use of donor oocytes for IVF, first reported in 1983 (2), has increased over time (3), representing approximately 12% of all IVF cycles in 2011 (4). Donor oocytes are most often used for age-related infertility, in women with poor ovarian reserve, and in women who carry genetic abnormalities (5).

Previous studies on pregnancy complications when using IVF have largely used data from autologous cycles (6–9). Infants conceived using autologous IVF cycles are more likely to be born preterm when compared with spontaneously conceived infants of mothers of similar maternal age. Many of these studies also found increased risk of low birthweight among infants conceived by IVF. When compared with subfertile women who spontaneously conceived, Declercq et al. (10) found that offspring of women undergoing autologous IVF were more likely to be born preterm, with lower birthweights, and that the risk of poor outcomes in both groups was higher than among women who conceived spontaneously without signs of subfertility. One cohort even showed an increased risk of neonatal death associated with IVF (11).

Little information is available regarding perinatal outcomes when using donor oocytes for IVF compared with autologous cycles. Most studies

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have used small datasets from single institutions, and have yielded conflicting results. One study (12) showed no difference in donor oocyte pregnancies with a wide range of outcomes, including gestational age at delivery and birthweight. Other studies showed increased risk of preterm labor (13) and preterm delivery (14). A small cohort from Denmark (15) showed increased risk of preterm delivery and low birthweight when compared with autologous IVF pregnancies. A Swedish study (16) showed an increased risk of induction of labor as well as cesarean delivery in donor oocyte recipients. In one study (17) of >550,000 pregnancies, donor oocytes were no more likely to result in an ectopic pregnancy (EP) than autologous oocytes, but information regarding other birth outcomes from larger cohorts remains scarce. In the present study we used data from a large national database to determine whether pregnancy complications, including preterm delivery, low birthweight, small for gestational age (SGA) birthweight, and perinatal death, occur more frequently in pregnancies in donor oocyte recipients compared with a similar group of autologous recipients.

MATERIALS AND METHODS

This study is a retrospective analysis comparing fresh autologous to fresh donor oocyte IVF cycles reported to the Society for Assisted Reproductive Technology's Clinical Outcome Reporting Systems (SART CORS) database between 2008 and 2010. Collected through voluntary submission, the SART registry is deidentified and represents data collected from 90%–97% of ART clinics in the United States during 2008–2010 (18).

Outcomes examined include preterm birth, defined as live birth before 37 weeks 0 days' gestation; low birthweight, defined as birthweight <2,500 g; and perinatal death, defined as a pregnancy ending either in a stillbirth or in a live birth, but with a neonatal death occurring within 28 days of birth. To determine whether a neonate was born SGA, birthweight was compared to a standardized table of US birthweights generated by Oken et al. (19, 20). Infants were coded as SGA if their birthweights were <10th percentile for gestational age. We also examined whether deliveries occurred before 28 weeks 0 days' gestation and 34 weeks 0 days' gestation.

The sample for this project was restricted to pregnancies ending in a singleton infant born after at least 23 weeks 0 days' gestation, but at <42 weeks 6 days' gestation, with higher order births excluded given more frequent adverse pregnancy outcomes seen with multiple gestations. Pregnancies were excluded if birthweights were >4 standard deviations more or less than the mean weight for gestational age. Pregnancies were also excluded if reported birthweights were ≤100 g, as well as >6,500 g. Finally, a number of individual women appear in the dataset more than once, as the basis of observation is the pregnancy, not the patient. Thus, if more than one pregnancy for a woman was in the database, only the first pregnancy with complete data on all outcome and control variables was retained.

The independent t test (for continuous variables) and χ^2 test (for categorical variables) were used to compare outcomes between the donor and autologous groups in bivariable analyses. Logistic regression was used for multivariable analyses, which controlled for factors that might influence perinatal outcomes, including oocyte age, whether intracytoplasmic sperm injection (ICSI) was used, recipient age for donor oocyte cycles, patient age for autologous cycles, number of oocytes retrieved, number of embryos transferred, and day of transfer (day 3 vs. day 5). The maximum number of fetal heartbeats ever seen on ultrasound during the pregnancy was also included to account for the effects of vanishing twins/higher order multiples. These control variables were drawn from preexisting literature on this topic (21, 22). Data were analyzed using STATA version 14.0 (StataSoft Corp.).

The Institutional Review Board at the University of Illinois at Chicago deemed this study exempt from review as it involves a secondary data analysis of a deidentified dataset. The Society for Assisted Reproductive Technology also granted permission to use the SART CORS registry data for this study.

RESULTS

A total of 68,762 cycles met the sample criteria. Of these, 111 were missing data on perinatal death, 2,380 were missing data on transfer timing (day 3 vs. day 5), 48 were missing information on how many embryos were transferred, 70 were missing information on ICSI, and 234 were missing data on the maximum number of fetal heartbeats seen. A further 114 observations were excluded as birthweights were >4 standard deviations from the mean birthweight for gestational age. After these observations were eliminated, a further 1,827 observations were dropped as these represented multiple pregnancies for the same patient. The final sample included 63,978 cycles with complete data on outcomes and control variables, representing 8,852 donor cycles (13.8% of the sample) and 55,126 autologous cycles (Table 1). The overall preterm delivery rate in this cohort is 18.1%; the rate among the oocyte donation group is significantly higher than that among the autologous group (22.4% vs. 17.4%; $P<.001$). Pregnancies using donor oocytes were also more likely to end before 34 weeks' gestation (5.8% vs. 4.2%; $P<.001$) but not before 28 weeks' gestation. Of this sample, 9.6% of cycles resulted in an infant with a birthweight <2,500 g, with a higher rate found among the donor oocyte cohort (10.8% vs. 9.4%; $P\leq.001$). However, infants born using donor oocytes were actually less likely to be SGA (6.9% vs. 8.3%; $P<.001$). Overall, 0.3% of cycles ended in either a stillbirth (5 deliveries) or neonatal death (209 deliveries), but there was no difference between the oocyte donation and autologous groups ($P=.47$). The 2,853 cycles excluded from the final analysis sample due to missing data were significantly less likely to use donor oocytes than cycles with complete data (10.8% vs. 13.7%; $P<.001$), but when these cycles were included in the bivariable comparisons shown in Table 1, neither the magnitude nor the significance of these conclusions changed (data not shown).

Results in Table 2 confirm that women using donor oocytes are more likely to deliver before 37 weeks' and 34 weeks' gestation, even when controlling for other factors (adjusted odds ratio [OR] = 1.28, 95% confidence interval [CI] = 1.12–1.46 for 37 weeks, adjusted OR = 1.30, 95% CI 1.03–1.64 for 34 weeks). Table 3, column 1, indicates that donor oocyte pregnancies