Effect of oocyte donation on pregnancy outcomes in in vitro fertilization twin gestations

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Objective: To estimate the effect of oocyte donation on pregnancy outcomes in patients with twin pregnancies conceived via IVF.
Design: Retrospective cohort study.
Setting: Patients with IVF twin pregnancies delivered by one maternal–fetal medicine practice from 2005 to 2013.
Patient(s): Fifty-six patients with IVF twin pregnancies who had oocyte donation and 56 age-matched controls with IVF twin pregnancies who used autologous oocytes. We excluded women aged >50 years because there were no age-matched controls aged >50 years using autologous oocytes.
Intervention(s): None.
Main Outcome Measure(s): Gestational hypertension, pre-eclampsia.
Result(s): The baseline characteristics were similar between the groups, including maternal age, race, parity, chorionicity, and comorbidities. The mean (±SD) age was 43.0 ± 6.0 vs. 41.9 ± 1.7 years. There were no differences in outcomes between the groups in regard to preterm birth, birth weight, or gestational diabetes. There was a greater incidence of gestational hypertension (32.1% vs. 13.0%) and pre-eclampsia (28.3% vs. 13.0%) in the group that underwent IVF with donor oocytes.
Conclusion(s): In patients who conceive twin pregnancies using IVF, oocyte donation increases the risk of gestational hypertension and pre-eclampsia. However, this did not translate into increased rates of preterm birth or low birth weight. Patients who require oocyte donation should be carefully counseled regarding the increased risk for pre-eclampsia and gestational hypertension but should be reassured that oocyte donation does not seem to lead to other adverse outcomes. (Fertil Steril® 2014;101:1326–30. ©2014 by American Society for Reproductive Medicine.)
Key Words: Twins, oocyte donor, hypertension, IVF

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The use of assisted reproduction technology (ART) using donor oocytes has revolutionized the treatment of infertility in women with diminished ovarian reserve, multiple failed previous IVF attempts, or transmittable genetic abnormalities that could affect their offspring (1). As donor oocyte IVF has become more common, the potential obstetric risks resulting from maternal exposure to immunologically foreign fetal antigens have been investigated. Initial reports in IVF cycles in singleton pregnancies using embryos derived from donor oocytes have documented a higher frequency of pre-eclampsia and gestational hypertension, ranging from 23% to 51% (2–5). It was initially thought that the increase risk was due to advanced maternal age, which is associated with oocyte donation. When controlling for maternal age, some studies still demonstrate an increased risk of hypertensive disorders in women who underwent oocyte donation (6–8), whereas others do not (9).

With increasing use of ART there has been a dramatic rise in multiple gestations, with twin pregnancies comprising 1.9% of all US live births in 1980, compared with 3.3% of all US live births in 2009 (10). Twin pregnancy alone has been shown to carry nearly a fourfold increased risk of pre-eclampsia (11), and pre-eclampsia has been reported to occur in anywhere from 6% to 31% of all twin pregnancies

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(12–15). Similar to twin pregnancies, women undergoing donor oocyte IVF are thought to be at an increased risk for adverse perinatal complications, such as preterm delivery, low birth weight, and pre-eclampsia (16, 17). We previously reported that the rate of pre-eclampsia in twin pregnancies was 14.8% overall, and the risk factors independently associated with pre-eclampsia on regression analysis in this population were oocyte donation (adjusted odds ratio [OR] 2.5) and prepregnancy obesity (adjusted OR 2.4) (18). However, this study only examined the relationship between oocyte donation and hypertensive disorders of pregnancy and not other pregnancy complications. In addition, the control group was not age-matched.

The objective of the present study was to test the hypothesis that women with twin pregnancies conceived using embryos derived from donated oocytes are at higher risk for gestational hypertension and pre-eclampsia than age-matched patients with twin pregnancies produced by IVF using autologous oocytes. We also examined whether there are associations between IVF twin pregnancies using donor oocytes and the development of various other adverse obstetric outcomes, using data from a large single-center twin pregnancy experience.

MATERIALS AND METHODS

After Biomedical Research Alliance of New York Institutional Review Board approval was obtained, the charts of all patients with twin pregnancies >24 weeks delivered by a single maternal–fetal medicine practice between June 2005 (when our electronic database was created) and June 2013 were reviewed. We excluded patients with monochorionic–monoamniotic placentation because we typically deliver these patients at 32 weeks, which would most likely be before the onset of pre-eclampsia.

We compared outcomes between patients who underwent IVF with oocyte donation and age-matched controls who underwent IVF using autologous oocytes. Controls were obtained by identifying the next patient with an IVF twin delivery whose age was within 2 years of the age of the case patient. After initial analysis of our data, we excluded women over the age of 50 years because there were no women in this age group who underwent IVF with autologous oocytes. Patients required oocyte donation either for poor response to previous ovarian stimulation, low ovarian reserve, or ovarian failure. In vitro fertilization was provided from several ART centers in the New York area, and patients presented for obstetric care in our practice after an intrauterine twin pregnancy had been documented. Our management of twin pregnancies does not differ according to whether the patient underwent oocyte donation.

The electronic patient database was used to collect detailed information such as demographic characteristics, including obstetric history and pregnancy outcomes, for all patients. Our primary outcome was the presence of gestational hypertension or pre-eclampsia. Standard definitions were used for gestational hypertension and pre-eclampsia (19). Gestational hypertension was defined as a systolic blood pressure level of ≥140 mm Hg or a diastolic blood pressure level of ≥90 mm Hg any time after 20 weeks. Pre-eclampsia was defined as gestational hypertension plus proteinuria (300 mg or more in a 24-hour urine collection). Patients who presented in labor with hypertension and who did not have time to complete a 24-hour urine collection were categorized as having pre-eclampsia only in the following circumstances: [1] proteinuria (1+ or more on random urinalysis) plus severe hypertension (systolic blood pressure level of ≥160 mm Hg or diastolic blood pressure level of ≥110 mm Hg on two occasions 6 hours apart), or [2] proteinuria (1+ or more on random urinalysis) plus hypertension plus laboratory abnormalities (elevated liver function tests or low platelets) (18). For the outcome of gestational hypertension and pre-eclampsia, we excluded patients with a diagnosis of hypertension before pregnancy or before 20 weeks' gestation (20). However, these patients were included for the analysis of other outcomes.

Secondary outcomes included gestational diabetes, gestational age at delivery, preterm birth <37 weeks, <35 weeks, and <32 weeks, birth weight, birth weight discordancy, small for gestational age (defined as birth weight less than the 10th or 5th percentile), and cesarean delivery. To define birth weight percentiles for gestational age we used standard tables for singleton pregnancies (21). We chose singleton tables because they are the standard tables used for twins in the United States in defining growth restriction and determining neonatal outcomes (22–24).

Our power analysis was done post hoc because we planned on searching our entire database. On the basis of the sample size obtained, we had 80% power to show an increase in the rate of gestational hypertension from 15% to 40% with an α error of 5%. Chi-square analysis, Fisher's exact test, and Student's t test were used, when appropriate (SPSS for Windows 16.0). A P value of ≤.05 was considered significant.

RESULTS

After inclusion and exclusion criteria were met, we identified 56 patients who had achieved twin pregnancy by ART with donor oocyte IVF. A second group of 56 age-matched patients who achieved twin pregnancy with IVF using autologous oocytes at our practice was identified.

Baseline demographics are shown in Table 1. There were no differences between the donor oocyte IVF group and the autologous oocyte IVF group. Importantly, maternal age, parity, race, and prepregnancy body mass index (BMI) were similar. They also had similar rates of monochorionic placentation, prepregnancy obesity, prior preterm birth, multifetal reduction, anticoagulation, fibroids, prior cesarean delivery, cervical surgery, and chronic hypertension. Only one patient had pregestational diabetes (in the oocyte donor group).

Pregnancy outcomes are shown in Table 2. There were no differences in outcomes between the groups in regard to gestational age at delivery, preterm birth, birth weight, gestational diabetes, cesarean delivery, and low birth weight percentiles. Regarding the primary outcome, the donor oocyte group had a significantly higher incidence of gestational hypertension (32.1% vs. 13.0%, P=.018) and pre-eclampsia (28.3% vs. 13.0%, P=.05).