Increased risk of pregnancy-induced hypertension in young recipients of donated oocytes

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Objective: To assess the rates of select obstetric outcomes in oocyte donation (OD) recipients aged <35 years and ≥40 years and compare them to similarly aged IVF patients.
Design: Retrospective anonymous questionnaire study.
Setting: University-based IVF center.
Patient(s): Live-birth outcome was experienced by 199 OD recipients and 488 IVF patients <35 or ≥40 years.
Intervention(s): The OD or IVF cycles.
Main Outcome Measure(s): Response rate, pregnancy outcome, and complications.
Result(s): Response rate was 60%. The OD recipients had significantly higher rates of pregnancy-induced hypertension (PIH) than their IVF counterparts. The OD <35 years had the highest rate (42%), followed by OD ≥40 years (26%), IVF ≥40 years (14%), and IVF patients <35 years (12%). In twin pregnancies, the rates of PIH remained higher in the OD groups: OD <35 years (56%), OD ≥40 years (36%), IVF ≥40 years (25%), and IVF <35 years (22%). Twin pregnancy rate was lowest in IVF patients ≥40 years (19%) and a lower preterm delivery rate (16%) reflected this difference. The cesarean section rates were 50% for singleton and 78% for twin deliveries in the OD patients <35 year; in OD patients ≥40 years, the rates were 75% and 84%, respectively.
Conclusion(s): The OD recipients are at higher risk for untoward obstetric outcomes than their IVF counterparts. Young OD recipients reported the highest rate of PIH, warranting further investigation into an association between early loss of ovarian function and PIH. (Fertil Steril® 2007;87:776–81. ©2007 by American Society for Reproductive Medicine.)

Key Words: Oocyte donation, pregnancy-induced hypertension, obstetric outcome, premature ovarian failure

Oocyte donation (OD) has become a successful means of enabling patients with diminished ovarian reserve to achieve pregnancy. In the United States, the number of treatment cycles in which donated oocytes were used to generate fresh or frozen embryos increased from 5,123 in 1996 to 13,183 in 2000 (1). Although most patients who undergo OD are of advanced maternal age, younger patients with diminished ovarian reserve may also require OD to achieve pregnancy.

Pregnancy outcomes in OD recipients have been characterized in the literature. Recipients achieving live birth are reported to be at increased risk for gestational diabetes, first and second trimester bleeding, cesarean section, preterm delivery (PTD), and pregnancy-induced hypertension (PIH) compared to patients undergoing IVF and the general population (2–8). Many of these studies have focused on women of advanced maternal age, as these patients represent the majority electing OD. To our knowledge, no investigation has specifically focused on young donor egg recipients, although this family-building technique is emerging as a popular option for younger women with premature diminished ovarian reserve.

Pregnancy-induced hypertension is likely due to factors that result in poor placentation (9). It has been shown that patients with premature ovarian failure test positive for the presence of anti-zona pellucida (ZP) antibodies, as well as antibodies against granulosa cells (GC) (10). It is plausible that this interferes with trophoblast–maternal interactions at the endometrial interface. The result may be suboptimal implantation and clinical features of PIH, as well as PTD, low birth weight, and other obstetric outcomes associated with poor placental function.

Our study was undertaken to assess the rates of select obstetric outcomes in OD recipients less than 35 years of age (<35) and recipients greater than or equal to 40 years of age (≥40) and to compare them to similarly aged women who underwent conventional IVF procedures. Based on existing literature and our clinical observations, we hypothesized that the use of donor oocytes to create pregnancy, in-and-of-itself, potentiates obstetric risks. The increased risks observed in donor oocyte cycles could not be explained solely by advanced maternal age. The known risk factors for PIH were then reviewed, and each of these factors was then assessed in the OD <35 recipients who were initially sent questionnaires.

MATERIALS AND METHODS

We conducted a retrospective questionnaire study in women who underwent OD or IVF procedures at our university-based fertility program that resulted in a fresh embryo transfer with a live birth outcome between 1999 and 2003. The

Received February 6, 2006; revised and accepted August 4, 2006.
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0015-0282/07/$32.00
doi:10.1016/j.fertnstert.2006.08.105

study was approved by the NYU Institutional Board of Research Associates (IRB H10877).

Patients <35 years and ≥40 years of age who succeeded with one of these two treatments were identified in our program database. Cycles resulting in triplet pregnancies, of frozen embryo transfer cycles, or cycles monitored at Program satellite offices were not included. Also excluded were cycles in which the patient age was between 35 and 39 years. This exclusion ensured that all patients were of similar ages, given that all donated oocytes were from women <35 years. The final mailing list consisted of 1,224 patients. The data were grouped by age (<35 and ≥40 years) and by treatment type (OD and IVF), with subsequent division of the study population into four groups (OD <35, IVF <35, OD ≥40, IVF ≥40). The age range of women who anonymously donated oocytes for the OD cycles was 21–35 years with a mean age of 25.6 years.

The questionnaire was a one-page, anonymous survey developed to assess the prevalence of select obstetric outcomes based on previous literature reporting untoward events in these patient groups. The questionnaire briefly described the objective of the study. There were two versions of the questionnaire depending on patient age, which differed only in the explanation as to why one's specific age group was relevant to the study. The questionnaire inquired whether the cycle was OD or IVF, the gestational age at time of preterm delivery, if the birth was singleton or twin, and the respective birth weight of the infant. The remaining items were presented in checklist format in laymen's terms including: PTD "less than 37 weeks of gestational age," PIH "high blood pressure during your pregnancy," gestational diabetes mellitus, placenta previa "placenta covering the opening of the uterus," placental abruption "premature separation of the placenta," cerclage placement "a suture about your cervix," uterine infection, antepartum hospitalization, bed rest, blood transfusion, and hysterectomy "removal of your uterus."

Questionnaires were mailed to patients with self-addressed stamped envelopes to facilitate their return. It was stated that by returning the questionnaire, patients would be giving consent for inclusion in the study. The patients were also given the option to identify themselves on the questionnaire if they chose.

The validity of the questionnaire was not evaluated. Categorical data were entered into a Microsoft Excel database (Microsoft, Redmond, WA) and statistical analyses were performed using χ^2, Fischer's exact, Mann-Whitney rank sum, and Student's *t*-tests where appropriate with significance at $P<.05$.

We reviewed the literature for known risk factors for PIH. These included nulliparity, multiple gestation, prior or family history of PIH, chronic medical conditions such as hypertension and diabetes, and extremes of age (9, 11). We then reviewed the charts of the initial patients who were sent questionnaires in the OD <35 (n = 28) group to determine whether they had any preexisting risk factors for the development of PIH. No statistical analysis was conducted on these observations. The inclusion of this information is meant to serve as a descriptor for the study group of interest, namely the young OD recipients.

RESULTS

The overall questionnaire response rate was 60% ranging from 52%–68% by group. There were no differences in the rate of response among the four groups. Patient demographics and outcomes are shown in Table 1. Mean ages of the patients did not differ when young OD versus IVF patients were compared. The IVF ≥40 patients were 2.5 years younger than OD ≥40 patients. The IVF ≥40 patients reported the highest mean birth weight, which was significant when compared to all three other groups. There were significant rate differences reported between the four study groups for the following outcomes: twin gestation, PTD, cesarean section, and PIH. There were no significant differences in rates of elective reduction, gestational diabetes mellitus, placenta previa, placental abruption, blood transfusion, cerclage placement, uterine infection, antepartum hospitalization, bed rest, and hysterectomy. Less than one-third of patients in all groups required antepartum bed rest or hospitalization. The following detail the significant findings.

Twin Gestation Rate

The twin gestation rate was significantly lower in the IVF ≥40 group (19%, $P<.001$) compared to the other three groups (OD <35 [47%], IVF <35 [42%], OD ≥40 [40%]). The twin rates were not statistically different among the OD <35, IVF <35, and OD ≥40 groups (Fig. 1).

Preterm Delivery Rate

The PTD rate reflected the twinning rate such that IVF ≥40 patients with the oldest oocytes and fewest twins also reported the lowest rate of PTD (16%) overall (Table 2). When the groups were compared by order of gestation, there were no significant differences in the rates of PTD for any group, although there was a trend toward higher rates of PTD in the OD groups. There was no difference in the overall PTD rate between the three groups with similarly aged oocytes and same twinning rate (OD <35, IVF <35, OD ≥40).

Cesarean Section Rate

Overall, OD <35 patients reported a 63% cesarean section rate compared to a 47% rate in the IVF <35 group (P = not significant [NS]). However, the cesarean section rates of OD ≥40 patients (78%) and IVF ≥40 patients (55%) were significantly different ($P\leq.001$), and this was largely attributable to the higher cesarean section rate in OD ≥40 singletons (75%). There were no significant differences in rates when comparing the older to younger groups within each type of treatment (Table 3).