

# Oocyte donation recipients of very advanced age: perinatal complications for singletons and twins

Elodie Guesdon, M.D.,<sup>a,b</sup> Aurélie Vincent-Rohfritsch, M.D., M.Sc.,<sup>a,b</sup> Sarah Bydlowski, M.D.,<sup>c,d</sup> Pietro Santulli, M.D., Ph.D.,<sup>e,f</sup> François Goffinet, M.D., Ph.D.,<sup>a,b,e</sup> and Camille Le Ray, M.D., Ph.D.<sup>a,b,e</sup>

<sup>a</sup> Port Royal Maternity Unit, Cochin Hospital, Assistance Publique–Hôpitaux de Paris, Paris; <sup>b</sup> DHU Risks in Pregnancy; <sup>c</sup> ASM13, Department of child psychiatry, Paris; <sup>d</sup> Inserm Unit 669, Paris, University of Paris-Sud and Paris Descartes, UMR-50669, Paris; <sup>e</sup> Sorbonne Medical Faculty Paris Descartes, Paris; and <sup>f</sup> Gynecology and Reproductive Medicine Ward, Cochin Hospital, Assistance Publique–Hôpitaux de Paris, Paris, France

**Objective:** To compare maternal, obstetric, and neonatal outcomes between women who underwent oocyte donation at or after age 50 years and from 45 through 49 years.

**Design:** Single-center, retrospective cohort study.

**Setting:** Maternity hospital.

**Patient(s):** Forty women aged 50 years and older (“older group”) and 146 aged 45–49 years (“younger group”).

**Intervention(s):** Comparison between the older and younger groups, globally and after stratification by type of pregnancy (singleton/twin pregnancy).

**Main Outcome Measure(s):** Maternal, obstetric, and neonatal outcomes.

**Result(s):** The rate of multiple-gestation pregnancies was similar in both groups (35% in the older and 37.7% in the younger group). We observed no significant difference globally between the two groups for outcomes, except for the mean duration of postpartum hospitalization, which was significantly longer among the older women (mean  $\pm$  SD, 9.5  $\pm$  7.4 days vs. 6.8  $\pm$  4.4 days). The rates of isolated pregnancy-related hypertension and of fetal growth restriction in singleton pregnancies were statistically higher in the older than in the younger group (19.2% vs. 5.5%, and 30.7% vs. 14.3%, respectively). Complication rates with twin pregnancies were similar between groups and very high compared with singleton pregnancies.

**Conclusion(s):** Complication rates were similar among women aged 50 years and older and those aged 45–49 years. Nonetheless, given the high rate of complication in both groups, especially among twin pregnancies, single embryo transfer needs to be encouraged for oocyte donations after age 45 years. (Fertil Steril® 2017;107:89–96. ©2016 by American Society for Reproductive Medicine.)

**Key Words:** Advanced maternal age, obstetric complications, oocyte donation, twin pregnancy

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Since the mid-1970s, both the mean age of women at delivery and the proportion of women aged 40 years and older at delivery have not stopped rising in industrialized countries. This phenomenon, although multifactorial, is explained especially by advances in

reproductive medicine. Oocyte donation in particular continues to increase (1) and allows women to become mothers at a very advanced age, into their sixth decade and even after menopause. However, these women are at risk of complications because of their age, on the one

hand, and their use of donated oocytes, on the other (2–4); both factors are known to be associated with a high rate of obstetric complications. The literature describes higher risks of maternal and obstetric complications for women at an advanced age who are pregnant via oocyte donation; these include gestational diabetes, hypertension, pre-eclampsia, premature rupture of the membranes, and cesarean delivery (5–7). Neonatal risks are also higher, with more preterm deliveries and more infants with a birth weight <2,500 g (8, 9). However, most of these studies define advanced maternal age as older than

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Reprint requests: Elodie Guesdon, M.D., Maternité Port Royal, Hôpital Cochin, Assistance Publique–Hôpitaux de Paris, 123 Bd de Port-Royal, Paris 75014, France (E-mail: [elodie.guesdon75@gmail.com](mailto:elodie.guesdon75@gmail.com)).

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40 or 45 years, and few have assessed risks among women aged 50 years and older. The several published studies are either descriptive series without a comparison group (10, 11) or comparative studies with either a heterogeneous comparison group (12) or relatively few subjects in the comparison group (13).

Moreover, in older women, oocyte donation is often required and associated with a high rate of multiple pregnancies, well known to be high-risk pregnancies (10, 12–14).

Our aim was to assess the risks of maternal, obstetric, and neonatal complications, according to maternal age (before 50 years or afterward) and type of pregnancy (singleton or twin) among women aged 45 years and older.

## MATERIALS AND METHODS

This retrospective, single-center cohort study reviewed the records of patients giving birth at the Port Royal Maternity Hospital in Paris (France), a level 3 facility with approximately 5,400 deliveries per year, during the period from January 1, 2006, to January 30, 2015.

This study was approved by the National Data Protection Authority (Commission Nationale de l'Informatique et des Libertés, CNIL n° 1755849). Under French regulations, this study was exempt from institutional review board review because it was an observational study using anonymized data from medical records. Women were informed that their records could be used for the evaluation of medical practices and were allowed to opt out of these studies. The study's exempt status was confirmed by the institutional review board Ile-de-France.

### Study Population

We included all oocyte donation recipients aged 45 years and older who gave birth after 22 weeks of gestation during the study period. The study group comprised women aged 50 years or more at delivery ("older"), and the comparison group all those aged 45–49 years at delivery ("younger"). We identified the women from the department's computerized database and then reviewed each woman's complete medical files, one by one. The study included only the women who received prenatal care at our maternity ward from early in pregnancy. Women referred from another hospital during pregnancy because of either a maternal or fetal disorder during pregnancy were excluded.

Our maternity ward's protocols for management—prenatal care, type of delivery, induction, and labor—are the same as those applied to women who are either younger or did not have assisted reproductive technology (ART).

Because the use of donated oocytes is restricted in France to women younger than 43 years, all the women in our study underwent ART with oocyte donation in a facility abroad.

### Study Outcomes

The following maternal and obstetric criteria were studied: pregnancy-related hypertension, defined by systolic blood pressure  $\geq 140$  mm Hg and/or diastolic blood pressure  $\geq 90$  mm Hg; pre-eclampsia, combining hypertension with

proteinuria  $>0.3$  g/24 h; severe pre-eclampsia, defined by at least one of the following criteria: severe hypertension (systolic blood pressure  $>160$  mm Hg and/or diastolic blood pressure  $>110$  mm Hg), renal damage with oliguria  $<500$  mL/24 h, creatinine  $>135$   $\mu\text{mol/L}$  or proteinuria  $>5$  g/d, acute pulmonary edema, persistent severe epigastric pain (Chaussier sign), HELLP syndrome, eclampsia, intractable neurologic disorders (visual disorders, abnormal deep tendon reflexes, headaches), thrombocytopenia  $<100$   $\mu\text{L}$ , abruptio placentae, or fetal distress; gestational diabetes (characterized by fasting blood glucose  $>0.92$  g/L, blood glucose 2 hours postprandial  $>1.20$  g/L, or blood glucose on ingestion of 75 g glucose greater than the thresholds defined by the French College of Gynecologists and Obstetricians and the French-speaking Diabetes Society in 2010 [15]); premature rupture of the membranes (PPROM); cesarean delivery; postpartum hemorrhage (PPH), defined by blood loss  $>500$  mL; hospitalization for more than 24 hours during pregnancy; transfer to the intensive care unit (ICU); mean duration of hospitalization including delivery; and difficulties in mother–child bonding. The latter must have been mentioned in the medical file by the pediatrician caring for the child or a departmental psychologist and have resulted in prolongation of the hospitalization for observation of this bonding and/or hospitalization in a mother–baby psychiatric unit.

The perinatal complications studied were fetal growth restriction (FGR), defined by a birth weight below the 10th percentile (according to the French Audipog curves [16]), preterm delivery before 37 weeks (global preterm birth), before 32 weeks (severe preterm birth), or before 28 weeks (extreme preterm birth), in utero fetal death, 5-minute Apgar score  $\leq 7$ , umbilical cord pH  $\leq 7.10$ , transfer to the neonatal ICU (NICU), and neonatal death.

We compared the maternal and perinatal complications for the two age groups, globally and after stratification by type of pregnancy (singleton or twin). Triplet pregnancies were excluded from the stratified analyses.

The following population characteristics were compared between the groups: women's mean age at delivery, geographic origin, presence of a partner/spouse, parity, any uterine scar, hypertension, obesity, or diabetes, as well as the specific type of oocyte donation (e.g., oocyte donation only or dual gamete donation), as well as the country where the donation took place.

### Statistical Analysis

The statistical analysis compared the numbers of individuals with the  $\chi^2$  test or Fisher's exact test ( $n < 5$ ), and compared means with Student's *t* test. We used STATA version 11.0 software (StataCorp) for the analyses.

## RESULTS

The study included 40 women (26 with singleton pregnancy and 14 with twin pregnancy) aged 50 years and older and 146 women (91 with singleton pregnancy, 53 with twin pregnancy, and 2 with triplet pregnancy) aged 45–49 years who gave birth at Port Royal, after becoming pregnant via oocyte donation during the study period. Two women aged 50 years and older

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