ORIGINAL ARTICLE: ASSISTED REPRODUCTION

# Impact of oocyte donation on perinatal outcome in twin pregnancies

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**Objective:** To compare perinatal outcomes of twin pregnancies after oocyte donation (OD), in vitro fertilization (IVF) with autologous oocyte (AO), and non-IVF conception.
**Design:** Five-year retrospective cohort study.
**Setting:** Tertiary university medical center.
**Patient(s):** All patients with twin pregnancies who gave birth after 24 weeks of gestation. The outcomes of 102 OD twin pregnancies were compared with those of 201 AO and 369 non-IVF twin pregnancies.
**Intervention(s):** None.
**Main Outcome Measure(s):** Obstetrical complications (pregnancy-induced hypertensive disorders, gestational diabetes, cholestasis, preterm rupture of membranes, mode of delivery, and postpartum hemorrhage) and neonatal outcome (preterm birth, low birth weight, neonatal hospitalization, and perinatal mortality).
**Result(s):** There was an increased incidence of preeclampsia (OD 26.5%, AO 7.0%, non-IVF 8.7%) and postpartum hemorrhage (OD 23.5%, AO 12.4%, non-IVF 7.6%) in the OD group compared with the AO and non-IVF groups. After adjustment for confounding factors, including maternal age and chorionicity, the risk of preeclampsia remained higher in the OD group, as did the risk of postpartum hemorrhage. The OD group was not at higher risk than the AO and non-IVF groups for other complications, particularly for preterm birth or low birth weight.
**Conclusion(s):** OD twin pregnancies are associated with a higher risk of preeclampsia and postpartum hemorrhage than AO and non-IVF twin pregnancies. (Fertil Steril® 2017;■:■–■. ©2017 by American Society for Reproductive Medicine.)
**Key Words:** Oocyte donation, twin gestation, assisted reproduction technology, preeclampsia, postpartum hemorrhage

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Until several years ago, oocyte donation (OD) was indicated only for women with premature ovarian insufficiency (1). Demand has increased since then, because indications for this treatment have been extended to women with multiple failures of in vitro fertilization (IVF) with the use of autologous oocytes (AO) (2). In France, the number of IVF attempts with the use of OD doubled from 2005 to 2013, increasing from 506 to 1,099 (3). But we know that these figures are far from an exhaustive count of the number of pregnancies from OD managed and delivered in France, because most couples using this assisted reproductive technology (ART) initially undergo IVF abroad, owing to both the legislation and waiting times in France (4, 5).

The literature strongly suggests that women using OD are at higher risk of obstetrical complications than women using their own oocytes. Studies consistently find a higher risk of pregnancy-induced hypertension and preeclampsia in this population (6–16). On the other hand, inconsistent results are reported for the risks of postpartum hemorrhage (PPH) and neonatal complications, particularly preterm delivery and fetal growth restriction (FGR) (8, 10, 13, 15–17).

Because of the significant proportion of twin pregnancies among women using OD, it is important to know the consequences of OD in this population. However, most studies of obstetrical outcomes of OD pregnancies include only singleton pregnancies (6, 8–12). Furthermore, twinning is an

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independent risk factor for pregnancy-induced hypertension (PIH), preeclampsia, preterm delivery, and FGR (18, 19). Comparing only twin populations would make it possible to distinguish the separate roles of OD conception and twinning in perinatal complications. A few authors have done so, but generally with small sample sizes (14, 16, 17).

The objective of the present study was to compare perinatal outcomes of twin pregnancies after IVF with the use of OD, IVF with the use of AO, and non-IVF conception in a retrospective cohort of twin pregnancies including a substantial number of OD pregnancies.

## MATERIALS AND METHODS

### Patients

This observational single-center retrospective study took place at a French tertiary university maternal-fetal medicine center with 5,200 births per year. It included all women with twin pregnancies who gave birth after 24 weeks of gestation from January 1, 2010, to October 31, 2014. Women transferred during pregnancy from another maternity unit because of maternal disease or fetal disease and women with monochorionic monoamniotic pregnancies were excluded.

### Ethical Statement

This study was approved by the National Data Protection Authority (Commission Nationale de l'Informatique et des Libertés, CNIL no. 1755849). Under French regulations, this study was exempt from Institutional Review Board approval 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 Ile-de-France Institutional Review Board.

### Data Collection

We reviewed each woman's complete obstetrical medical file. The mode of conception was the principal factor studied. Women were classified into three groups: IVF with OD (OD), IVF with AO (AO); and pregnancies achieved without IVF (non-IVF). We collected from the obstetrical records the mothers' social and demographic characteristics, medical, surgical, and obstetrical histories, obstetrical complications, gestational age at birth, mode of labor onset, mode of delivery, birth weight, and neonatal complications. Except for oocyte origin, which is usually asked about, we had no access to data related to the IVF procedure, which was performed elsewhere, sometimes abroad.

### Study Outcomes

The perinatal outcomes studied were: PIH, preeclampsia, HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count), abruptio placentae, gestational diabetes, cholestasis of pregnancy, premature rupture of the membranes (PROM), cesarean delivery, PPH, preterm birth, FGR defined by a birth weight below the 5th percentile (20), and perinatal mortality rate. PIH was defined as systolic blood pressure $\geq$140 mm Hg and/or diastolic blood pressure $\geq$90 mm Hg after 20 weeks' gestation. Preeclampsia was defined by hypertension associated with proteinuria $\geq$300 mg/24 h.

Social and demographic characteristics and medical history were compared according to the mode of conception (OD, AO, non-IVF). We then compared the following outcomes among the three groups: maternal complications during pregnancy, mode of delivery, postpartum complications, and neonatal complications.

### Statistical Analysis

A univariate analysis enabled us to compare the complication rates in all three groups. For qualitative variables, the groups were compared with the use of chi-square test or Fisher exact test, as appropriate. For quantitative variables, we used analysis of variance or Kruskal-Wallis test, as appropriate. Then for the complications significantly associated with the mode of conception in the univariate analysis, we conducted a multivariate analysis with logistic regression models that allowed us to adjust for the women's demographic characteristics and for chorionicity. To take maternal age into account, we used fractional polynomials, which enabled us to integrate maternal age as a continuous variable to optimize our modeling of the role of this variable in the onset of complications. The multivariate models included all variables associated with the complication we studied in the univariate analysis ($P<.1$). Clinically pertinent interactions were tested, and an interaction variable for mode of labor onset $\times$ mode of delivery was created. The statistical analyses were performed with the use of Stata software, version 11.0.

## RESULTS

During the study period, 805 women with twin pregnancies gave birth after 24 weeks' gestation in our maternity hospital. After exclusion of 13 women with monochorionic monoamniotic pregnancies and 120 referred to our tertiary unit who had transferred during pregnancy from another maternity unit because of maternal or fetal disorders during pregnancy, the study included 672 women: 102 pregnancies (15.1%) resulted from IVF with OD, 201 (30.0%) from IVF with AO, and 369 (54.9%) from non-IVF conception. The outcomes of the 1,344 newborns were compared according to mode of conception (Supplemental Fig. 1).

### Patient Population

The women's social and demographic characteristics and their medical and obstetrical histories were analyzed according to mode of conception (Table 1). Women in the OD group were significantly older than those in the other two groups (mean 43.1 years compared with 34.6 years in the AO group and 32.7 years in the non-IVF group; $P<.001$). We also found higher rates of nulliparas and white race in the OD group. The groups did not differ significantly in preconception body mass index, smoking, history of hypertension, diabetes,