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Does oocyte donation compared with autologous oocyte IVF pregnancies have a higher risk of preeclampsia?

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KEY MESSAGE

Singleton pregnancies after oocyte donation are associated with a significantly higher risk of preeclampsia, pregnancy-induced hypertension and caesarean section compared with pregnancies using autologous oocytes. Fertility practitioners and obstetricians should take this information into consideration when counselling patients interested in receiving donated oocytes and during the follow-up of their pregnancies.

A B S T R A C T

The aim of this study was to evaluate whether pregnancies resulting from oocyte donation have a higher risk of preeclampsia compared with pregnancies after IVF using autologous oocytes. Propensity score matching on maternal age and parity was carried out on a one to one basis, and a total of 144 singleton pregnancies resulting in delivery beyond 22 gestational weeks, achieved by oocyte donation, were compared with 144 pregnancies achieved through IVF and intracytoplasmic sperm injection with the use of autologous oocytes. All pregnancies were achieved after fresh embryo transfer. Obstetric and neonatal outcomes were compared for each pregnancy. Singleton pregnancies after oocyte donation were associated with a significantly higher risk for preeclampsia (OR 2.4, CI 1.02 to 5.8; $P = 0.046$), as well as for pregnancy-induced hypertension (OR 5.3, CI 1.1 to 25.2; $P = 0.036$), and caesarean delivery (OR 2.3, CI 1.4 to 3.7; $P = 0.001$) compared with pregnancies using autologous oocytes.

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Introduction

Oocyte donation constitutes an integral part of modern assisted reproductive care. The first human pregnancy after the transfer of a donated oocyte fertilized *in vitro* to a cyclic recipient was reported by an Australian group in 1983 (Trounson et al., 1983). Although oocyte donation was initially carried out in patients with premature ovarian failure, indications have more recently expanded to older patients with ovarian insufficiency or patients with recurrent failures in IVF (Antinori et al., 1993; Barri et al., 1992; Borini et al., 1995; Pados et al., 1994; Sauer, 1995).

Since the first clinical application of oocyte donation, several studies have evaluated the obstetric and neonatal outcomes of this procedure. One of the first studies that assessed the evolution and outcome of pregnancies from oocyte donation reported a high incidence of obstetric and neonatal complications, such as first-trimester bleeding (34.6%), preeclampsia (32.7%), intrauterine growth restriction (IUGR) (11.5%) and caesarean section (63.5%) (Pados et al., 1994).

Results of subsequent studies, however, have varied between investigators. In studies focusing on the outcome of singleton pregnancies after oocyte donation, the incidence of preeclampsia ranges from 9.8 to 12% (Le Ray et al., 2012; Malchau et al., 2013; Stoop et al., 2012). In studies focusing on pregnancy-induced hypertension (PIH), the incidence of preeclampsia ranges from 13 to 30% (Keegan et al., 2007; Söderström-Anttila et al., 1998; Stoop et al., 2012; Wiggins and Main, 2005; Wolff et al., 1997). It should be emphasized that certain maternal conditions such as Turner syndrome are characterised by a higher incidence of some obstetrical complications such as PIH, preeclampsia and caesarean section (Alvaro Mercadal et al., 2011; Chevalier et al., 2011).

Comparison of complication rates between oocyte donation, and IVF and intracytoplasmic sperm injection (ICSI) pregnancies using autologous oocytes, have produced discrepant results. Studies focusing on differences in preeclampsia rates between oocyte donation pregnancies and IVF–ICSI pregnancies with autologous oocytes have found them to be significantly higher after donated ovum compared with pregnancies after IVF using autologous oocytes (Klatsky et al., 2010; Malchau et al., 2013) whereas others have not (Krieg et al., 2008; Stoop et al., 2012; Wiggins and Main, 2005). Most studies support that singleton pregnancies from oocyte donation present a significantly higher risk of PIH (Keegan et al., 2007; Levron et al., 2014; Söderström-Anttila et al., 1998; Wiggins and Main, 2005), whereas Stoop et al. (2012) found no significant difference. These discrepancies are probably a result of the differences in methodology used, i.e. use of different analysis strategies, small number of participants or problematic matching of participants with the controls. To properly estimate the risk of these complications with oocyte donation, important confounders, such as age, parity and multiplicity (singleton versus multiple pregnancies) must be controlled for when comparing oocyte recipients (who are usually older and nulliparus) with patients undergoing IVF using their own gametes. To date, however, only a small fraction of studies have done this (Klatsky et al., 2010; Stoop et al., 2012). Therefore, it is evident that additional well-matched studies with clear comparisons between case and control groups are needed to provide a conclusive answer to this important clinical question.

The aim of the present study was to assess the occurrence of preeclampsia and other obstetric and neonatal outcomes after oocyte donation and after IVF with autologous oocytes.

Materials and methods

Study design

This retrospective study was conducted at the Fertility Clinic of the Erasme Hospital of the French-speaking Free University of Brussels. The study group consisted of all women with singleton pregnancies achieved after oocyte donation who gave birth to a baby of more than 22 weeks of gestation, between 1991 and 2013. The control group was extracted from women with singleton pregnancies achieved after IVF–ICSI who gave birth to babies of more than 22 weeks' gestation with a delivery at the Erasme Hospital during the same period.

Selection methods and inclusion criteria

During this period, data for 239 singleton pregnancies achieved after oocyte donation and 799 singleton pregnancies achieved after IVF–ICSI with autologous oocytes were available and were included for analysis in this study.

Patients who underwent IVF and ICSI techniques were included in the same group, as no significant differences in the incidence of obstetric or neonatal complications in singleton pregnancies resulting from these techniques have been reported (Bonduelle et al., 2002; Nouri et al., 2013).

All patients in the control group delivered at the maternity ward of the Erasme Hospital, and data about their assisted reproduction technique cycles, pregnancies and deliveries were extracted from the electronic database *Gyneco2000*. Some patients in the study group were followed and delivered in the same unit or elsewhere. When patients delivered in other units, a questionnaire was sent to their gynaecologist and their responses were scanned into the Medical Viewer programme of the Erasme Hospital. In some cases, the files were incomplete, so patients, their physicians, or both, were contacted to retrieve the missing information; however, the dataset remained incomplete.

Exclusion criteria

Exclusion criteria were multiple pregnancies, the application of testicular sperm extraction (TESE) and cycles with preimplantation genetic diagnosis. Patients undergoing cycles of preimplantation genetic diagnosis were heterogeneous, and included mothers with genetic diseases that could interfere with obstetric outcomes. They also included patients with normal fertility and therefore comparison with infertile IVF couples could not be made. Similarly, pregnancies achieved with the use of TESE may not have similar obstetric outcomes compared with pregnancies in which no TESE was needed. Therefore, the rate of caesarean section has been previously shown to be lower in pregnancies with TESE compared with pregnancies from ejaculated sperm (Fedder et al., 2013). As differences in obstetric and neonatal outcomes between pregnancies after fresh and frozen embryo transfer have been reported (Maheshwari et al., 2012; Wennerholm et al., 2013), pregnancies achieved after the use of cryopreserved embryos were excluded. As the incidence of PIH and preeclampsia seems to be higher in patients with Turner's syndrome compared with pregnant women who have undergone oocyte donation who do not have Turner syndrome, patients with this syndrome were excluded (Alvaro Mercadal et al., 2011; Chevalier *et al*, 2011).

Outcomes

Several obstetric and neonatal outcomes have been studied. The primary outcome was the occurrence of preeclampsia. Additional outcomes were first-trimester bleeding, gestational diabetes, IUGR, PIH, weeks of gestation at delivery, mode of delivery, birth weight and Apgar score.

Endometrial preparation of recipients

Recipients with ovarian function

To synchronize the endometrium of the recipient with the stimulated cycle of the donor, a GnRH agonist (Decapeptyl®, Ipsen Pharma Biotech S.A.S., France) was administrated to both donor and recipient on the first day of their cycle and, when pituitary down-regulation was achieved in both donor and recipent, the recipient commenced oral-oestradiol valerate (Progynova®, Bayer Pharma AG, Germany or Provames®, Sanofi Winthrop Industrie, France) (usually 6 mg/day) and the donor started ovarian stimulation. The luteal phase of the recipient was achieved with the vaginal administration of micronized progesterone (Utrogestan®, Besins Manufacturing Belgium SA, Belgium or Laboratoires Besins International, France) (600 mg/day), which was administered until the 12th week of gestation in case of pregnancy.

Recipients with non-functional ovaries

Recipients with non-functional ovaries received oral-oestradiol valerate (Progynova®, Bayer Pharma AG, Germany or Provames®, Sanofi Winthrop Industrie, France) (usually 6 mg/day) and additionally, during the luteal phase, vaginal micronized progesterone (Utrogestan®, Besins Manufacturing Belgium SA, Belgium or Laboratoires Besins International, France) (600 mg/day) up to the pregnancy test or throughout the first gestational trimester in case of pregnancy.

Definitions

The definitions used in the study are presented in **Table 1.**

Statistical analysis and matching procedure

Considering the observational nature of this study, baseline differences in important covariates may confound the association between the use of donated or own oocytes and the evaluated outcomes. To remove the effect of potential confounders, the patients from the two groups were matched for age and nulliparity (yes/no). The investigators were blinded to the obstetric and neonatal outcomes of the women during selection of the participants, whereas automated statistical routine based on propensity scores and by using the nearest neighbour method (Austin, 2008, 2011a; Rubin and Thomas, 1996) was used for matching. A one-to-one method was applied without any replacement using the 'psmatch2' module in STATA 12.1. Following this automated procedure,144 paired patients (with one patient from the group with donated oocytes and one from the group with autologous oocytes) were identified and subsequently analysed.

To evaluate the baseline differences between the two matched samples in the various continuous and the categorical variables, the standardized difference was calculated (Cohen's *d*) (Austin, 2008, 2011b). The standardized difference compares the differences in means in units of the pooled standard deviation. Usually a value ranging from –0.1 to 0.1 indicates negligible differences between the two groups (Normand et al., 2001), although there is no universal agreement.

The analyses of outcomes in the matched samples were conducted with the use of generalized estimating equations models to account for the matched nature of the data (Austin, 2008, 2011b), and robust standard errors were calculated. All statistical tests were two-sided and $P \leq 0.05$ was considered statistically significant. No adjustment for multiple statistical testing was applied. Stata 12.1 for Mac (Stata Corp., College Station, Texas, USA) was used for all analyses.

Ethical approval

The present study was approved from the Ethics committee of the Erasme hospital (Clinical study P2014/054) on 4 February 2014.

Results

After the matching procedure, 144 patients were included in each one of the comparison groups. The mean age of patients in both groups was 35.64 years (22–43 years) and 20 out of 144 in each group were nulliparus. Although patients were matched for maternal age, parity and gravidity, recipients of donated oocytes had a lower body mass index (BMI) and were more frequently smokers compared with women who achieved an IVF–ICSI pregnancy using autologous oocytes (**Table 2**).

In the group with donated ooctyes, 81 out of 144 patients had functional and 63 had non-functional ovaries. Of these, 63 had a premature ovarian failure, nine had ovum donation related to a genetic cause, seven had advanced age and 65 experienced repeated failures in assisted reproduction techniques using their own oocytes (poor

Table 1 – Definitions used in the study.

Gestational age	Calculated by taking the day of oocyte aspiration as day 14 of the cycle
Stillbirth	Intrauterine or intrapartum death of a child with gestational age of ≥22 weeks or with a birth weight of ≥500 g
Pregnancy-induced hypertension	Blood pressure levels ≥140/90 mm Hg, without proteinuria, after 20 weeks of gestation
Preeclampsia	Blood pressure levels ≥140/90 mm Hg on two measurements at least 6 h apart with proteinuria ≥0.3g/day after 20 weeks of gestation (Milne et al., 2005)
Preterm delivery	Delivery before 37 completed weeks of gestation
Very preterm delivery	Delivery before 34 completed weeks of gestation
Extremely preterm delivery	Delivery before 28 completed weeks of gestation
Low birth weight	<2500 g at birth
Intrauterine growth restriction	Estimated fetal weight <10th centile

Table 2 – Patient characteristics.

	Donated oocyte group (n = 144)		Autologous oocyte group (n = 144)		
	Mean ± SD/ count	n	Mean ± SD/ count	n	Cohen's d
Maternal age (years)	35.64 ± 4.54	144	35.64 ± 4.54	144	0.00
Number of previous deliveries	0.187 ± 0.59	144	0.194 ± 0.62	144	–0.01
Number of previous pregnancies	0.653 ± 1.16	144	0.653 ± 1.07	144	0.00
Nullipara (n)	20	144	20	144	0.00
Body mass index (kg/m2)	23.8 ± 5.04	79	25.6 ± 5.04	140	–0.36
Smoking (n)	33	114	19	123	0.39

responders, decreased ovarian reserve, poor oocyte or embryo quality, severe endometriosis).

Obstetric outcomes

Obstetric outcomes are presented in **Table 3**. The rate of preeclampsia was found to be significantly higher in the group with donated oocytes than in the group with autologous oocytes (12.5% versus 5.6%; OR 2.4, CI 1.02 to 5.8; $P = 0.046$). The rate of PIH was also significantly higher (6.9% versus 1.4%; OR 5.3, CI 1.1- to 5.2; $P = 0.036$) in the same group. No significant difference was found between the study and the control group in first-trimester bleeding (6.3 versus 1.4%; OR 4.7, CI 0.98 to 22.9), gestational diabetes (11/144 versus 12/144; OR 0.91, CI 0.40 to 2.05), or IUGR (3/144 versus 1/144; OR 3.0, CI 0.3 to 30.2).

The caesarean section rate of patients who received donated oocytes (48.6%) was higher than in patients with autologous oocytes (29.2%), and the difference was statistically significant (OR 2.3, CI 1.4 to 3.7; $P = 0.001$).

Gestational age at delivery was comparable between the study and the control group. With preterm deliveries, 18% of women from the donated oocytes group and 13.9% from the control group delivered before 37 weeks of gestation. This difference was not statistically significant (OR 1.4, CI 0.7 to 2.9). Preterm deliveries of less than 34 or less than 28 weeks of gestation were also not found to be statistically different between the donated oocytes group and the autologous oocytes group (OR 0.8, CI 0.3 to 2.2 and OR 0.3, CI 0.03 to 3.3, respectively).

The incidence of live birth rates was comparable between the study and the control group (99.3% versus 97.2%, respectively). The only woman of the study group who had a stillbirth, delivered at 24 weeks of gestation because she had a rupture of a cerebral aneurysm and passed away. Out of the four women in the control group who had a stillbirth, two of them delivered at 22 weeks of gestation, one after a premature rupture of the membranes and the other one had a premature delivery because of uterine cervical incompetence. The other two women underwent elective termination of pregnancy at 23 and 31 weeks of gestation, because of congenital malformations (one for major cardiopathy and the other for a cerebellar hypoplasia with polymicrogyria). No stillbirth was associated with preeclampsia.

Neonatal outcomes

Neonatal weight or height at birth, head circumference, Apgar score of infants at 1, 5 and 10 min after delivery, or incidence of low birth weight were comparable between the two groups (**Table 4**). Hospitalization in the neonatal intensive care unit occurred in 15 out of 143 live births from the donated oocyte group and in 23 out of 140 from the autologous oocyte group; the difference was non-significant.

Table 3 – Obstetric outcomes.[a]

	Donated oocyte group n (%)	Autologous oocyte group n (%)	OR/ mean difference	Adjusted CI 95%	*P*-value
First-trimester bleeding	9/144 (6.25)	2/144 (1.38)	4.73	0.98 to 22.85	NS
Gestational diabetes	11/144 (7.64)	12/144 (8.33)	0.91	0.40 to 2.05	NS
IUGR	3/144 (2.08)	1/144 (0.69)	3.04	0.31 to 30.2	NS
PIH	10/144 (6.94)	2/144 (1.38)	5.30	1.11 to 25.23	0.036
Preeclampsia	18/144 (12.5)	8/144 (5.56)	2.43	1.02 to 5.8	0.046
Prenatal hospitalization	15/144 (10.42)	19/144 (13.19)	0.76	0.34 to 1.61	NS
Live birth	143/144 (99.3)	140/144 (97.2)	4.09	0.31 to 30.2	NS
Caesarean delivery	70/144 (48.6)	42/144 (29.17)	2.30	1.43 to 3.69	0.001
Gestational age at delivery (weeks)	38.61 ± 2.61	38.57 ± 3.14	0.04	–0.67 to 0.75	NS
Delivery <37weeks	26/144 (18.06)	20/144 (13.89)	1.38	0.73 to 2.88	NS
Delivery <34weeks	7/144 (4.86)	9/144 (6.25)	0.77	0.27 to 2.19	NS
Delivery <28weeks	1/144 (0.69)	4/144 (2.78)	0.25	0.03 to 3.26	NS

[a] The analysis includes five stillbirths (one in the donated oocyte group and four in the autologous oocyte group, among which two elective terminations of pregnancies took place).

CI, confidence interval; adjusted CI, adjusted for the matching and for women who delivered more than once; IUGR, intrauterine growth restriction; NS, not statistically significant; OR, odds ratio; PIH, pregnancy-induced hypertension.

Table 4 – Neonatal outcomes.[a]

	Oocyte donation (n)	Autologous oocytes (n)	Mean difference OR	CI 95%
Low birth weight	22/143 (15.38%)	21/144 (14.58%)	1.06	0.54 to 2.09
Infants weight (g)	3134 ± 650 (143)	3081.4 ± 675 (144)	52.6	−104.6 to 209.9
Infants height (cm)	49.2 ± 3.4 (87)	49.1 ± 3.2 (129)	−0.02	−0.97 to 0.93
Head circumfrence (cm)	34.3 ± 2.5 (61)	34.2 ± 1.94 (128)	0.11	−0.55 to 0.76
Apgar 1'	8.64 ± 1.86 (113)	8.14 ± 2.11 (141)	0.49	−0.01 to 0.98
Apgar 5'	9.51 ± 1.07 (113)	9.3 ± 1.31 (141)	0.23	−0.07 to 0.54
Apgar 10'	9.64 ± 0.82 (47)	9.68 ± 0.85 (138)	−0.06	−0.33 to 0.21

[a] The analysis includes five stillbirths (one in the donated oocyte group and four in the autologous oocyte group, among which two elective terminations of pregnancies took place).
No statistically significant differences were found between the two groups.
CI, confidence interval; LBW, low birth weight; OR, odds ratio.

Discussion

The present study has shown that singleton oocyte donation pregnancies are associated with an increased risk for preeclampsia, PIH and caesarean delivery compared with IVF–ICSI pregnancies using autologous oocytes. Moreover, oocyte recipients seem to have a higher risk for first-trimester bleeding, although this difference did not reach statistical significance. Pregnancies after oocyte donation were not found to have a higher incidence of preterm delivery (<37 weeks of gestation), extreme (<34 weeks of gestation) or very extreme (<28 weeks of gestation) premature deliveries. Infants conceived either with donor or with own oocytes were comparable in neonatal weight or Apgar score at 5 min after delivery.

One of the strengths of this study is that patients comprising both groups were selected to have only singleton deliveries after fresh embryo transfer and, in addition, patients were matched for age and parity, to minimize possible confounding effects. For the same reason, this study excluded patients with Turner syndrome. Moreover, this study used propensity score analysis during the matching procedure (Austin, 2008). This method has been shown to be advantageous compared with regression-based methods and produces more precise estimates (Austin, 2011a). Furthermore, as an automated algorithm was used to match the two groups, the risk of selection bias during the matching procedure is greatly reduced.

On the other hand, the present study has certain limitations that need to be discussed. First, any type of matching inevitably leads to decreased power compared with regression-based methods (Cepeda et al., 2003), and this should be taken into account when interpreting the results obtained. This is one of the main reasons why matching in this study was limited to age of the mother and nulliparity. Increasing the number of variables on which the samples are matched would cause an even greater decrease in the sample size and that might lead to type II errors.

Furthermore, in this study the two groups were not matched for BMI and smoking habits as in previously published studies (Klatsky et al., 2010; Stoop et al., 2012). Being overweight or obese has been confirmed as a significant risk factor for preeclampsia (English et al., 2015; Paré et al., 2014). The observed baseline difference in BMI, however, is more likely to have led to an underestimation of the true effect size rather than a type I error as women receiving donated oocytes had a lower BMI than women with a pregnancy after IVF–ICSI using autologous oocytes. On the other hand, more women who had a pregnancy using donated oocytes were smokers. It has been shown, however, that smoking is more likely to be associated with a reduced incidence of preeclampsia (Lindqvist and Marsál, 1999; North et al., 2011; Odegard et al., 2000); therefore, this imbalance is more likely to lead to an underestimation of the observed effect size. Hence, the main conclusion of this study, i.e. that the incidence of preeclampsia is increased in women using donated oocytes, would be valid and most likely reinforced even if BMI and smoking matching could be achieved using this dataset.

Nevertheless, other baseline differences might also be present and confound the association between the origin of oocytes during IVF–ICSI and the incidence of preeclampsia in the resulting pregnancy. For example, ethnicity has been shown to be associated with the incidence of preeclampsia (Breathett et al., 2014; Paré et al., 2014), but this information was not available in this dataset and therefore no matching could be carried out.

Moreover, as previously mentioned, patients of the study group were followed and delivered in different hospitals and this could lead to lack of homogeneity in reports of obstetric and neonatal outcomes. All relevant obstetric items, however, were completed in a questionnaire built in accordance with the local database.

Pregnancies achieved after oocyte donation have resulted from donor gametes that are immunologically foreign to the mother (Salha et al., 1999), and this could explain different obstetric outcomes compared with pregnancies with autologous oocytes. The causes of gestational hypertensive disorders are not yet completely understood. Preeclampsia and PIH are probably the consequence of an inadequate immune response between the mother and the fetus, leading to reduced trophoblastic invasion of the spiral arteries, which is the earliest and most obvious histopathological change seen in preeclampsia, and release of factors into the maternal circulation (Vinatier and Monnier, 1995).

Early ovarian dysfunction has been associated with maternal antibodies against the zona pellucida and against granulosa cells (Kelkar et al., 2005). It has been suggested that the maternal antibodies could lead to disrupted trophoblast invasion as occurs in preeclampsia (Keegan et al., 2007). According to this hypothesis, the incidence of preeclampsia would be expected to be higher among patients with premature ovarian insufficiency (POI), compared with patients with functional ovaries. Pados et al. (1994) showed a significant increase of preeclampsia in the POI group compared with patients with functional ovaries; however, other studies (Sheffer-Mimouni et al., 2002; Wiggins and Main, 2005) showed that adverse perinatal outcomes were not significantly associated with ovarian failure. In the present study, 63 out of 144 recipients had POI. Of these 63 patients, nine

developed preeclampsia (14.29%). No significant difference was found between patients with functional and non-functional ovaries in rates of preeclampsia (data not shown). Hence, owing to the small number of cases with preeclampsia, conclusions cannot be drawn about the potential association of POI with preeclampsia.

In the present study, a significant difference in the incidence of preeclampsia was found in the group with donated oocytes compared with the group with autologous oocytes. This association between preeclampsia and oocyte donation has previously been reported but has not always been statistically significant. Klatsky et al. (2010) and Malchau et al. (2013) agree with our findings, showing a difference that was statistically significant for singletons, as well as for twins, when compared separately. Conversely, both Wiggins et al. (Wiggins and Main, 2005) and Stoop et al. (2012) described an increased risk for preeclampsia in pregnancies after oocyte donation, which was not statistically significant. Furthermore, Krieg et al. (2008) found no difference in the incidence of preeclampsia between donor oocyte and autologous oocyte pregnancies. Limitations of this study, such as including patients older than 38 years, and singleton and twin pregnancies together in the autologous oocyte group, could possibly explain the different results.

The results of the present study are in accordance with the findings of several previous studies that have shown a significantly increased risk for PIH in pregnancies with donated oocytes (Klatsky et al., 2010; Levron et al., 2014; Malchau et al., 2013; Söderström-Anttila et al., 1998; Wiggins and Main, 2005) compared with IVF–ICSI pregnancies with autologous oocytes. This has also been confirmed by a recently published meta-analysis (Pecks et al., 2011), in which an increased relative risk for hypertensive disorders in pregnancies after oocyte donation has been found.

As mentioned previously, the overall reported PIH incidence in pregnancies after oocyte donation ranges from 13–30% (Keegan et al., 2007; Söderström-Anttila et al., 1998; Stoop et al., 2012; Wiggins and Main, 2005; Wolff et al., 1997). We did not confirm such a high incidence of PIH in this study. We could hypothesize that, in our cohort, the rates are lower because patients with Turner syndrome were exluded, because of baseline differences in the population evaluated, e.g. percentage of nulliparas or mean age of population, or because of the design of the studies. Clearly, a critical systematic review of the published literature is warranted to assess the true incidence of PIH disorders in these pregnancies while adjusting for other known risk factors such as age and nulliparity.

In the present study, the clearest significant difference was the very high incidence of caesarean section in the donated oocyte group compared with the autologous oocyte group (48.6% versus 29.2%, respectively; $P = 0.001$). Several investigators agree with these findings (Keegan et al., 2007; Krieg et al., 2008; Le Ray et al., 2012; Levron et al., 2014; Söderström-Anttila et al., 1998), whereas Stoop et al. (2012) found no significant difference when analysing singletons alone. It is possible that patients' anxiety or fear to deliver could contribute to a higher level of caesarean section. On the other hand, increased concomitant obstetric pathologies, such as preeclampsia, can cause an increase in the caesarean section rate. When it comes to first-trimester bleeding, in the present study, where only singleton pregnancies were studied, the incidence of first-trimester bleeding was 6.25% in the donated oocyte group, which was not significantly higher than the 1.38% found in the autologous occyte group. This finding seems to agree with the study by Stoop et al. (2012).

In order to evaluate the incidence of preterm delivery, we compared donated oocyte with autologous oocyte groups for deliveries before 37 weeks of gestation and separately for deliveries before 34 and 28 weeks. Neither of these comparisons revealed a significant difference. Published findings on this issue have been controversial. For preterm deliveries before 37 weeks of gestation in singletons, several studies agree with our findings (Keegan et al., 2007; Krieg et al., 2008; Söderström-Anttila et al., 1998), whereas others do not (Malchau et al., 2013; Stoop et al., 2012). The reasons for these differences are not yet clear.

Concerning the neonatal outcome assessed at birth, in the present study no statistically significant difference in the Apgar score was found between infants born form donated ooocytes and those from autologous oocytes. Similar results in the Apgar scores have also been reported (Krieg et al., 2008; Söderström-Anttila et al., 1998; Stoop et al., 2012), Hence, it seems that overall neonatal morbidity is not affected in pregnancies after oocyte donation, although it is a high risk factor for preeclampsia.

In conclusion, the present study shows a significant increase in preeclampsia among oocyte donation singleton pregnancies compared with pregnancies matched for maternal age and parity autologous oocyte IVF–ICSI pregnancies after fresh embryo transfer. Caesarean deliveries and PIH were also higher in this group of pregnancies compared with pregnancies after IVF–ICSI using autologous oocytes. Despite this increased risk of oocyte donation pregnancies for hypertensive disorders and use of caesarean section, overall neonatal outcomes, such as gestational age at delivery, birth weight and Apgar score, can be regarded as comparable with pregnancies after IVF–ICSI using autologous oocytes. This information could help fertility doctors to better inform their patients interested in becoming oocyte recipients about the risks involved. Furthermore, these findings could also be useful for obstetricians who look after pregnancies after oocyte donation.

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