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Pregnancy outcome of non-anonymous oocyte donation: a case-control study

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ABSTRACT

Objective: To evaluate the maternal and neonatal outcome of non-anonymous oocyte donation compared to *in vitro* fertilization.

Study design We compared 84 oocyte donation pregnancies with a 251 matched *in vitro* fertilization cohort. Maternal and neonatal outcomes were retrieved from a nationwide perinatal registry. Oocyte donation and *in vitro* fertilization pregnancies were matched for maternal age, study center, ZIP code and embryo transfer date. Both maternal and neonatal complications and outcome were compared between oocyte donation and *in vitro* fertilization with univariate and multivariate logistic regression analyses, adjusting for maternal age, donor age, socio-economic status, ethnicity, and parity.

Results: In total, 277 women underwent 541 oocyte donation cycles. The median recipient age was 34.9 years (IQR: 31.5–38.5), while the median donor age was 34.4 years (IQR: 31.7–37.0). Clinical pregnancy rate was 26.6%, which is comparable to standard *in vitro* fertilization treatment. Donor age in years (OR 0.93, 95% CI 0.88–0.99) and a previous pregnancy of the recipient (OR 1.69, 95% CI 1.02–2.78) were significantly associated with clinical pregnancy rate. Both singleton and multiple oocyte donation pregnancies were associated with pregnancy-induced hypertension compared with *in vitro* fertilization singleton and multiple pregnancies (OR 1.99, 95%CI 1.02–3.89, OR 6.43, 95% CI 1.67–24.72, respectively). No significant differences in neonatal outcome were observed.

Conclusion: Oocyte donation pregnancies are associated with an increased incidence of pregnancy-induced hypertension compared with age-matched *in vitro* fertilization controls. However, no significant differences in neonatal outcome were observed between oocyte donation and *in vitro* fertilization.

Introduction

Oocyte donation (OD) has been used as a successful treatment option for infertility since the first ongoing pregnancy in 1984 was reported [1]. One of the most prevalent indications for OD is primary ovarian insufficiency (POI), either idiopathic [2,3], genetic (as in Turner syndrome) [4], or after cancer treatment [5]. Other indications include maternally inherited genetic abnormalities [6] and multiple failed *in vitro* fertilization (IVF) [7].

Although OD gives infertile women the opportunity to conceive, a higher incidence of harmful maternal consequences compared with naturally conceived pregnancies has been reported. Women who conceived by OD have an increased risk of pregnancy-induced hypertension (PIH) [7–14] and an increased rate of caesarean section deliveries [5,7–10,14,15]. OD does not seem to be associated with increased risks for new-borns [9,14–16], although a lower birth weight and lower gestational age in OD pregnancies compared with IVF singletons have recently been reported [17,18].

There are limitations when interpreting the results from most previous studies. One of the issues is the selection of controls. Studies were performed in countries where, in contrast to the

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Dutch policy, anonymous donorship or financial compensation for OD is allowed. In our center, a donor only receives financial compensation for medical costs, and is a relative of the recipient with a completed family. Therefore, our OD donors are generally older compared with (anonymous) donors in previous studies. In addition, in some studies spontaneous pregnancies have been used as controls [13,19], even though IVF pregnancies are associated with more obstetric complications than naturally conceived pregnancies [20]. In others, advanced maternal age IVF pregnancies have also been used as controls instead of age-matched IVF groups [21].

Taking these issues into account, we aimed to evaluate the maternal and neonatal outcome of non-anonymous OD compared to IVF.

Materials and methods

Subjects

We performed a case-control study using non-anonymous OD subjects as cases and matched IVF subjects as controls. The OD cohort included all women who underwent OD treatment in the Erasmus MC Medical Centre between 1992 and 2009. In the Netherlands, anonymous donorship or financial compensation for donation is not allowed. In general, recipients present themselves with a donor who originates from the recipients' close surroundings, being a family member or a close friend. A more distant acquaintance or even donation offered through advertisements is only allowed if it can be demonstrated that any form of coercion (psychological or financial) has been avoided. All donors were proven fertile and had children of their own, in accordance with the Dutch directive regarding OD [22]. Prior to OD, an extended screening of recipient, partner and donor has been performed. If any medical contraindication has been observed, the OD procedure is cancelled.

All donors were counseled by a psycho-social counselor prior to an evaluation of each particular case by the Medical Ethical Committee. Treatment was pursued after positive advice. Of the donors, most (>95%) were relatives or close friends of the recipient, and a small proportion (<5%) had no familial or friendship bond with the recipient and was acquired through internet or discussion fora. In most cases (>95%), recipients had the same donor in following attempts.

Information was retrieved from medical records retrospectively. Cycles without embryo transfers were excluded. Informed consent was obtained from participants according to our Institutional Review Board.

OD and IVF pregnancies were matched by date of embryo transfer (<3 months), maternal age and ZIP code. Pregnancy outcome data was extracted from The Netherlands Perinatal Registry (PRN). This registry contains population-based information of 96% of all pregnancies in the Netherlands. The PRN is a database containing linked and validated data [23,24] from three professional registries: the obstetric database for midwives, the obstetric database for gynaecologists, and the neonatal/paediatric database. The board of the PRN gave us permission to use the registry for this study.

Outcome measures

Clinical pregnancy was defined as a pregnancy diagnosed by ultrasonographic visualization of ≥1 gestational sacs or definitive clinical signs of pregnancy. Similarly, an ectopic pregnancy assessed by ultrasound was considered a clinical pregnancy. Clinical pregnancy rate is defined as the number of clinical pregnancies expressed per 100 embryo transfer cycles [25]. Pregnancy loss was divided in a clinical pregnancy loss <14 weeks gestational age and losses between 14 and 24 weeks.

Pregnancy outcome included maternal and neonatal parameters. Maternal outcome parameters were pregnancy-induced hypertension (PIH), preeclampsia (PE), placental abruption, postpartum haemorrhage, placenta praevia, gestational diabetes mellitus (GD), mode of delivery, and medication during delivery (oxytocin or prostaglandin). GD was defined as a glucose serum level >7 mmol/L after an overnight fast. PIH was defined as at least one measurement of a diastolic blood pressure ≥90 mm Hg. Proteinuria was defined as >300 g of protein in the urine per day. PE was defined as PIH with proteinuria. These cases were included in both PIH and PE rates. Postpartum haemorrhage was defined as >1000 mL blood loss within 24 h after delivery.

Neonatal parameters were gestational age (in weeks), Apgar-score at 5 min postpartum, birth weight (grams), the presence of congenital malformations, and perinatal death (<7 days after delivery). Two combined parameters were used to increase power since complications were rare: 'poor outcome new-born' and 'poor outcome mother'. Poor outcome new-born was defined as having ≥1 of the following complications: prematurity (<37 weeks), perinatal death (<7 days after delivery), Apgar-score <7 at 5 min postpartum, congenital malformations or birth weight $<p_{10}$. Poor outcome mother was defined as having ≥1 of the following maternal complications: PIH, PE, placental abruption, postpartum haemorrhage, placenta praevia or GD.

Statistical analysis

Continuous variables were tested for normality using the *Q*–*Q* plots and Shapiro–Wilk test. Since most variables were not-normally distributed (except for the donor age), baseline characteristics are presented as medians (ranges) or numbers (frequencies).

Wilcoxon tests were used to compare continuous variables. For categorical variables, frequencies were analyzed in contingency tables with Mantel–Haenszel Chi Square tests as our case and control group were matched.

We evaluated maternal and neonatal outcome of non-anonymous oocyte donation compared to IVF with univariate and multivariate logistic regression analyses, adjusting for maternal age, donor age, socio-economic status, ethnicity and parity. Results were expressed as odds ratios (ORs) and 95% confidence intervals (CI). As both fresh and cryopreserved embryos were used, and they may result in different pregnancy rates, we also analyzed the group with first cycle fresh embryos. As no significant differences were observed (data not shown), analyses were not adjusted for fresh *versus* cryopreserved embryos.

Regarding pregnancy outcome, no differences were observed in neonatal outcome between fresh and frozen embryo transfers in donor egg cycles [26]. We did not adjust our results for fresh *versus* cryopreserved for pregnancy outcome.

Statistical significance for all analyses was defined as a two-tailed *p*-value of less than or equal to 0.05. Data analysis was performed using the statistical software package SAS version 9.1 (SAS Institute Inc., Cary, NC, USA) and SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Between 1992 and 2009, 232 women underwent 541 OD cycles (Fig. 1). Of the women with POI ($n = 147$), 109 women were diagnosed with POI without an obvious cause, 12 after cancer treatment, 16 with Turner's syndrome, and 10 with gonadal dysgenesis. Of the women without POI ($n = 85$), 53 women had multiple failed IVF attempts, 19 had maternally inherited genetic