Perinatal outcomes in 375 children born after oocyte donation: a Danish national cohort study

Sara S. Malchau, M.D.,[a] Anne Loft, M.D.,[a] Elisabeth C. Larsen, M.D., Ph.D.,[a] Anna-Karina Aaris Henningsen, M.D.,[a] Steen Rasmussen, M.Sc.,[b] Anders Nyboe Andersen, M.D., D.M.Sci.,[a] and Anja Pinborg, M.D., D.M.Sci.[a]

[a] Fertility Clinic, Rigshospitalet, University of Copenhagen; and [b] Department of Health Statistics, Danish National Board of Health, Copenhagen, Denmark

Objective: To describe perinatal outcomes in children born after oocyte donation (OD) compared with in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), and spontaneous conception (SC).
Design: National cohort study.
Setting: Fertility clinics.
Patient(s): Three hundred seventy-five children born after OD during the period 1995–2010.
Intervention(s): None.
Main Outcome Measure(s): Mean birth weight, mean gestational age, risks of low birth weight (LBW), preterm birth (PTB), congenital malformations, cesarean delivery, preeclampsia, and admittance to neonatal intensive care unit.
Result(s): We found an increased risk of PTB in OD pregnancies. The adjusted odds ratio (AOR) of PTB in OD singletons was 1.8 (95% CI, 1.2–2.69), 2.5 (95% CI, 1.7–3.6), and 3.4 (95% CI, 2.3–4.9) compared with IVF, ICSI, and SC, respectively. The risk of LBW was also increased. The AOR of LBW was 1.4 (95% CI, 0.9–2.2), 1.8 (95% CI, 1.2–2.8), and 2.6 (95% CI, 1.7–4.0) compared with IVF, ICSI, and SC. The risk of preeclampsia was increased in OD pregnancies with an AOR of 2.9 (95% CI, 1.8–4.6), 2.8 (95% CI, 1.7–4.5), and 3.1 (95% CI, 1.9–4.9) compared with IVF, ICSI, and SC. After additional adjustment for preeclampsia, perinatal outcome improved. Among the twins, the difference between the groups was less pronounced.
Conclusion(s): Pregnancies after OD have a poorer perinatal outcome than those after standard IVF and ICSI mainly because of the high prevalence of preeclampsia. (Fertil Steril® 2013;99: 1637–43. ©2013 by American Society for Reproductive Medicine.)
Key Words: Assisted reproduction, egg donation, low birth weight, obstetric outcome, oocyte donation, perinatal outcome, preeclampsia, preterm birth

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/malchaus-perinatal-outcome-oocyte-donation-art/

Use your smartphone to scan this QR code and connect to the discussion forum for this article now.*

* Download a free QR code scanner by searching for "QR scanner" in your smartphone's app store or app marketplace.

In 2010, roughly 5.8% of all Danish children born were conceived via assisted reproductive techniques (ART), including in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), frozen embryo transfer (FET), and oocyte donation (OD) (1, 2). Oocyte donation comprises a small proportion of all ART treatments used in Denmark, with only 225 treatments and 54 children born in 2010 (1). Until January 2007, only women undergoing ART treatment for infertility were allowed to donate oocytes, and donations were limited to egg sharing. Obviously, these women donated a limited number of eggs. Since January 1, 2007, anonymous egg donation from fertile donors has been allowed in Denmark but without any economical compensation to the donors. This liberalization of the law has increased the egg supply, but Danish women in need of donor eggs still must wait for several years before undergoing treatment; thus, many use cross-border reproductive care (3, 4). In Denmark, oocyte donation is only allowed for women younger than 45 years.

In previous studies, the OD population was characterized by advanced maternal age and multiple gestations (5–9). It is well known that ART increases the risk of obstetric and perinatal complications, primarily due

Received June 21, 2012; revised and accepted January 17, 2013; published online March 7, 2013.
S.S.M. has nothing to disclose. A.L. has nothing to disclose. E.C.L. has nothing to disclose. A-K.A.H. has nothing to disclose. S.R. has nothing to disclose. A.N.A. has received consultancies, grants, and payment for lectures from Merck Serono, Ferring Pharmaceutical, and MSD (all outside of this work). A.P. has nothing to disclose.
Reprint requests: Sara S. Malchau, M.D., Fertility Clinic, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, DK–2100 Copenhagen, Denmark (E-mail: smalchau@hotmail.com).

Fertility and Sterility® Vol. 99, No. 6, May 2013 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2013.01.128

to the higher multiple birth rates, but slightly increased risks are also found in singletons (10–12). An increased risk of obstetric complications, such as first trimester vaginal bleeding, preeclampsia, pregnancy-induced hypertension, preterm birth, and cesarean delivery, has been reported after OD (5–8, 13–14). Of these, the increased risk of pregnancy-induced hypertension has been well documented (5–7, 13–14). With regard to neonatal outcomes such as intrauterine growth restriction and malformations, the reports are few, and most studies have concluded that no differences exist between OD and standard IVF (8, 14). However, a large study by Gibbons et al. (15) indicated that lower mean birth weights and gestational ages characterized children born after OD compared with IVF. Our study clarified the obstetric and neonatal outcomes of children born after OD compared with those conceived by standard IVF, ICSI, or spontaneous pregnancies.

MATERIALS AND METHODS

All children born after OD in Denmark from 1995–2010 were identified in the Danish IVF register: n = 375 (251 singletons, and 124 twins). Two control cohorts of children born in 1995–2009 after either IVF (11,060 singletons, and 6,532 twins) or ICSI (5,866 singletons, and 3,101 twins) were identified. The third control group, spontaneously conceived (SC) singletons (n = 33,852), were matched by date and year of birth; this group was twofold the size of the IVF plus the ICSI group. Further, all SC twins born during the same period were identified (n = 30,002). Data on perinatal outcomes were extracted from the Medical Birth Register and were available for the total study period from 1994 to 2010. Diagnoses were obtained from the Hospital Discharge Register (HDR); records for hypertensive disorders of pregnancy, cesarean delivery, admittance to neonatal intensive care unit (NICU), and congenital malformations were available for the years 1997 to 2010. Women who delivered in Denmark after an OD procedure performed in another country could not be identified and were not included in the study.

Statistics

The differences between study and control populations were analyzed in SPSS, version 15.0 (SPSS, Inc.) and SAS version 9.1.3 (SAS Institute). $P<.05$ was considered statistically significant. Differences of the mean of continuous parametric data were analyzed with the use of Student's t test. For nonparametric data, the medians and ranges were reported, and the differences were analyzed in SPSS with the Wilcoxon-Mann-Whitney test. The chi-square test was used to compare the distributions between two groups.

Multivariate logistic regression analyses were performed to estimate the risks of preterm birth (PTB, gestational age <37 weeks), low birth weight (LBW, birth weight <2,500 g), hypertensive disorders of pregnancy (chronic hypertension, pregnancy-induced hypertension, and preeclampsia), and cesarean delivery in children conceived after OD. The analyses were adjusted for maternal age, parity, child sex, and year of birth. Additional analyses adjusted for preeclampsia. All stillbirths and children with missing information on gestational age or birth weight as well as children with a gestational age of <140 days or >307 days and children with a birth weight <200 g or >9,900 g were excluded from the analyses of birth weight, gestational age, LBW, PTB, and small for gestational age (SGA).

For singletons of primiparous women, the age-stratified analyses were performed for birth weight and gestational age. The risk of being SGA and large for gestational age (LGA) was calculated according to the 10th percentile by Marsal's formula with the use of birth weight, child gender, and standard intrauterine growth curves for Scandinavia (16).

According to Danish legislation, studies based solely on register data and with no personal involvement of the participants do not require approval from an ethics committee. The study was approved by the Danish Data Protection Agency (CVR no. 11-88-37-29) and the National Board of Health. The authors have no conflicts of interest.

RESULTS

Background Characteristics

Mean maternal age was statistically significantly higher in the OD group compared with IVF, ICSI, and SC for both singletons and twins (Table 1). The proportion of first-time mothers was statistically significantly higher in the OD group than the SC group for both singletons and twins, but not compared with IVF and ICSI (see Table 1).

Perinatal Outcomes

Singletons. The mean and median birth weight and gestational age were statistically significantly lower in OD pregnancies in IVF, ICSI, and SC pregnancies. The OD singletons had a statistically significantly higher percentage of both PTB and LBW than children in all three control groups (Table 2). Adjusted odds ratios of LBW were statistically significantly increased in the OD group when compared with the ICSI and SC groups (Table 3). The risks of PTB were also increased compared with IVF, ICSI, and SC. When adjusting for preeclampsia in addition to maternal age, parity, child sex, and year of birth, the risk of LBW for OD singletons was only statistically significantly increased when compared with the SC group (see Table 3). For PTB, adjusted odds ratios for preeclampsia showed statistically significantly increased risks compared with ICSI and SC.

The incidence of very preterm birth (VPTB, gestational age <32 weeks) in OD pregnancies exceeds the incidence for children born after both ICSI and SC (see Table 2). The percentage of very low birth weight (VLBW, birth weight <1,500 g) only statistically significantly differed between the OD and SC singletons. The frequencies of SGA in OD singletons were statistically significantly higher compared with the ICSI and SC groups. However, in the adjusted analysis there was no increased risk of being born SGA when compared with the three control groups. There was no increased risk of being LGA in OD singletons.

A maternal age stratified analysis (<35, 35–40, >40 years) for mean birth weight and gestational age that includes