

Obstetric outcome after single embryo transfer

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien vid Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Göteborg, fredagen den 12 april 2013 kl.9.00

av

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Avhandlingen baseras på följande arbeten:

- I. Sazonova A, Källen K, Thurin-Kjellberg A, Wennerholm UB, Bergh C.
Obstetric outcome after *in-vitro* fertilization with single or double embryo transfer.
Human Reproduction 2011;26:442-450.
- II. Sazonova A, Källen K, Thurin-Kjellberg A, Wennerholm UB, Bergh C.
Factors affecting obstetric outcome of singletons born after IVF.
Human Reproduction 2011;26:2878-2886.
- III. Sazonova A, Källen K, Thurin-Kjellberg A, Wennerholm UB, Bergh C.
Obstetric outcome in singletons after *in vitro* fertilization with cryopreserved/thawed embryos.
Human Reproduction 2012;27:1343-1350.
- IV. Sazonova A, Källen K, Thurin-Kjellberg A, Wennerholm UB, Bergh C.
Neonatal and maternal outcomes comparing women undergoing two *in vitro* fertilization (IVF) singleton pregnancies and women undergoing one IVF twin pregnancy.
Fertility & Sterility 2013;99:731-737.

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ABSTRACT

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Obstetric outcome after single embryo transfer

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Background: Children born after IVF have a poorer neonatal outcome than children born after spontaneous conception, even after adjustment for confounders. In Sweden, since 2003 an increasing amount of IVF cycles are single embryo transfers (SET). This gives the opportunity to investigate and compare the outcome after SET and double embryo transfers (DET).

Aim: To assess the neonatal and maternal outcomes after IVF, particularly after SET.

Methods: *Paper I:* All IVF children born in Sweden after IVF treatment during the years 2002-2006 and their mothers were included (n=13 544 children) and compared with all children in the general population born during the same time period and their mothers (n=587 009 children) concerning neonatal and maternal outcomes. *Paper II:* All IVF singletons born after fresh IVF cycles and own oocytes were included (n=8941) and cross-linked with the Swedish Medical Birth Registry. Four major outcomes were investigated: very preterm birth (<32 weeks), small for gestational age (SGA), placenta previa and placental abruption. Maternal characteristics (age, parity, BMI, smoking and years of infertility) and treatment-related variables (number of oocytes retrieved, number of embryo culture days, number of transferred and cryopreserved embryos and “vanishing twin”) were investigated for independent association with the four selected outcomes. *Paper III:* All singletons after cryopreserved (n=2348) and fresh IVF cycles (n=8944) were included and compared with all singletons born after spontaneous conception (n=571914). *Paper IV:* Outcomes for women (n=921) undergoing two IVF pregnancies with singletons (n=1842) were compared with women (n=991) undergoing one IVF pregnancy with twins (n=1982).

Results: *Paper I:* Children born after IVF had a poorer neonatal outcome than children in the general population. Comparing IVF singletons, irrespective of the number of embryos transferred, with singletons in the general population, significantly higher rates of preterm birth (<28 w, <37 w), low birth weight (LBW) and very low birth weight (VLBW) were found. *Paper II:* Age, primiparity, smoking, BMI, years of infertility and ‘vanishing twin’ were associated with an increased risk of one or both of the two selected outcomes very preterm birth and SGA. Maternal age and blastocyst transfer were associated with an increased risk of placenta previa. Smoking was significantly associated with placental abruption. *Paper III:* Singletons from cryopreserved cycles had increased rates of extreme preterm birth (<28 w) as compared with singletons from the general population. A lower rate of LBW was found for singletons after cryopreservation cycles than for singletons from fresh cycles. The rates of large for gestational age (LGA) and macrosomia (>4500g) were higher for singletons after cryopreservation cycles than for singletons in the general population and for singletons after fresh cycles. Higher rates of preeclampsia were noted for pregnancies after cryopreservation cycles versus general population and fresh cycles. *Paper IV:* Preterm birth, very preterm birth, LBW, VLBW and SGA were dramatically increased for IVF twins as compared with two IVF singletons with the same mother with adjusted odds ratios between 4 and 16. Significantly higher rates of respiratory complications, sepsis and jaundice were detected among the IVF twins. Significantly higher rates of preeclampsia, preterm premature rupture of the membranes and Cesarean section were observed for IVF twin pregnancies.

Conclusions: Children born after IVF, also singletons and irrespective of the number of embryos transferred, had a poorer neonatal outcome than singletons in the general population. In singletons born after fresh IVF, certain maternal characteristics and the number of embryos transferred, when there was a ‘vanishing twin’, affected the neonatal outcome negatively. Singletons born after cryopreservation as compared with fresh IVF cycles had a better neonatal outcome as regards LBW. An increased rate of placenta previa was observed after blastocyst transfer. Maternal and neonatal outcomes were dramatically better for women who had two IVF singleton pregnancies than for those with one IVF twin pregnancy. The finding of an increased rate of LGA and macrosomia after cryopreservation needs further studies. The results support SET as the main transfer strategy.

Keywords: *in-vitro fertilization/ single embryo transfer/ neonatal outcome/ maternal outcome*

ISBN: 978-91-628-8634-9