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Maternal and neonatal health outcomes following assisted reproduction

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Abstract This study assessed the risk for maternal complications in women and neonatal outcomes in children conceived following assisted reproductive treatment as compared with spontaneously conception and also separately evaluated conventional IVF and intracytoplasmic sperm injection (ICSI). The prospective cohort included 1161 women with singleton pregnancies: 561 who conceived following assisted reproduction (223 following IVF and 338 following ICSI) and 600 who conceived spontaneously. No differences were observed in pregnancy complications (including spontaneous abortion, pregnancy-induced hypertension, gestational diabetes and Caesarean delivery) except for significantly increased risk for excess vaginal bleeding in assisted reproduction pregnancies (21.4% versus 12.9%; OR 1.67, 95% CI 1.18–2.37), which was prominent in women who reported polycystic ovary syndrome. Neonates born following assisted reproduction had increased risk for prematurity (10.6% versus 5.3%; OR 1.72, 95% CI 1.04–2.87), and IVF, but not ICSI, was associated with significantly increased risk for prematurity (OR 2.36, 95% CI 1.28–4.37) and low birthweight (OR 1.89, 95% CI 1.03–3.46). In conclusion, this study observed only an increased risk for excess vaginal bleeding as a pregnancy-associated complication in singleton pregnancies following assisted compared with spontaneous conception. However, singleton neonates born following IVF, but not ICSI, were at increased risk for prematurity.

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Introduction

Despite the widespread use of assisted reproduction treatment, there is still concern regarding the safety of these treatments to both mothers and their neonates. Although the rate of multiple births following assisted reproduction is increased as compared with spontaneously conceived pregnancies and complications following multiple births are well known (McDonald et al., 2005), singleton assisted reproduction pregnancies are also at increased risk for adverse pregnancy outcome compared with spontaneously conceived singleton pregnancies, as reported in two systematic reviews (Helmerhorst et al., 2004; Jackson et al., 2004). These include an increased risk for preterm birth (<37 weeks), low birthweight (<2500 g) and very low birthweight (<1500 g), small-for-gestational-age and Caesarean delivery. In addition, Jackson et al. (2004) reported increased risk for maternal complications including placenta praevia, vaginal bleeding, pre-eclampsia and gestational diabetes mellitus.

Although maternal age and parity were usually adjusted in these analyses, data regarding other potential confounders such as past obstetric outcome, medical history, infertility (type and treatment), smoking, educational level and body mass index (BMI) are limited.

In Israel, assisted reproduction treatment is funded in the framework of the national health insurance for the first two children, with no limitation on the number of treatment cycles for women up to the age of 45. Currently, 4.2% of all live births in Israel are conceived following assisted reproduction and the percentage is rising (Department of Health Information, Ministry of Health, Israel, 2010). Considering recent concerns (Helmerhorst et al., 2004; Jackson et al., 2004; McDonald et al., 2009) and the increasing number of children born following assisted reproduction, this study was designed to evaluate the risks for maternal and neonatal complications following assisted reproduction treatment as compared with spontaneously conceived pregnancies, as well as conventional IVF and intracytoplasmic sperm injection (ICSI) compared with spontaneously conceived pregnancies.

Materials and methods

The prospective cohort was composed of singleton pregnancies following assisted reproduction and spontaneously conceived singleton pregnancies. Women were identified at 6–12 weeks of gestation, during ultrasound examination at the two participating IVF units (Sheba Medical Centre and Assaf Harofeh Medical Centre). Spontaneously conceived pregnancies were recruited at five community women's healthcare centres and at the two participating medical centres. Of these, 133 women were identified during ultrasound examination at 6–12 weeks of gestation. In addition, 467 women with singleton live birth were randomly selected from the delivery room records and recruited by telephone call following delivery hospitalization. Only women demonstrating one gestational sac with a fetal heart pulse were included in the study.

All women were recruited from June 2006 to December 2008. Telephone interviews were conducted 6 weeks following delivery.

Study population

The final cohort was composed of 1161 women with singleton pregnancies. A flow chart of patient participation in the study is presented in Figure 1.

Questionnaire and variables

The telephone interview 6 weeks following delivery included demographic (age, education), medical history (hypertension, diabetes, asthma, malignancy, epilepsy) and obstetric history (number of abortions, number of live births) as well as details regarding the current pregnancy, including spontaneous abortion (defined as loss of

Participants	ART	SC	Total
Eligible	632	746	1378
Refused	31 (4.9%)	75 (10.1%)	106 (7.7%)
Not located	31 (4.9%)	62 (8.3%)	93 (6.7%)
Language problem	9 (1.4%)	9 (1.2%)	18 (1.3%)
Total responded	561[a]	600[b]	1161

Figure 1   Flow chart of the study population.
[a] = 223 women recruited following IVF (40%) treatment and 338 (60%) women following ICSI treatment;
[b] = 133 women with one gestational sac and one heart beat recruited following ultrasound examination at 8–12 gestational weeks together with 467 women with singleton live birth recruited randomly from hospital records post delivery. ART = assisted reproduction treatment; ICSI = intracytoplasmic sperm injection; SC = spontaneous conception.