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Obstetric and perinatal outcomes of twin pregnancies conceived following IVF/ICSI treatment compared with spontaneously conceived twin pregnancies

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ABSTRACT

Objective: Twin pregnancy is associated with increased obstetric and perinatal risk. There are conflicting reports on whether assisted conception (ART) further increases these risks. The aim of this study is to assess the obstetric and perinatal outcomes of twin pregnancies according to mode of conception.
Study design: A retrospective study of all viable dichorionic-diamniotic (DCDA) twin pregnancies ($n = 539$) delivered at Cork University Maternity Hospital, Ireland between 2009 and 2012, divided according to spontaneous conception (SC) and ART conception, specifically IVF or ICSI.
Results: The ART conceived group were on average 4 years older (36.8 ± 4.23 vs 32.3 ± 4.93 years) and more frequently nulliparous (73.7%; $n = 126$ vs 36.1%; $n = 133$) than their SC counterparts ($p < 0.001$).

There was no significant difference in maternal antenatal complications. ART twins were twice as likely to be delivered by caesarean section (CS) (OR 2.35; 95% CI 1.76–3.14). There was no significant difference in the rates of preterm birth or NICU admission according to mode of conception. ART conceived twins were almost twice as likely to be delivered moderately preterm ($32–33^{+6}$) (OR 1.98, 95% CI 1.21–3.23) and were more likely to have RDS and neonatal hypoglycaemia
Conclusions: Twin pregnancy, irrespective of mode of conception, carries an increased risk of morbidity and mortality for both mother and babies and therefore couples should be counselled regarding the increased risk of iatrogenic twinning associated with double embryo transfer. However, for those that do conceive twins, they can be advised that assisted conception conveys no significant disadvantage over naturally conceived twin pregnancies.

Introduction

Since the introduction of assisted conception, in particular in-vitro fertilisation (IVF) and intra-cytoplasmic sperm injection (ICSI), there has been a steady increase in the number of multiple pregnancies. Coupled with the rise of assisted-conception multiple pregnancies, is the trend for women to delay childbearing until later in the third decade when the risk of naturally conceiving a twin pregnancy is higher. In Ireland, over the last decade (2002–2011), there has been an increase of 52.7% in the number of live born twins delivered and a similar trend has been noted in other countries [1–3].

Twin pregnancy is associated with increased perinatal risk, in particular low birth weight, prematurity and associated perinatal morbidity and mortality and for the mother, an increased risk of gestational hypertensive disorders [4]. There are conflicting reports on whether assisted conception further increases these risks when compared to spontaneously conceived pregnancies with some studies reporting an increased risk of low birth weight, preterm birth [5–9] whereas other studies report no increased maternal nor perinatal risk conferred by mode of conception [10–13]. Indeed in a systematic review by Helmerhorst et al. [14] perinatal mortality in twins conceived using ART was 40% lower compared with spontaneously conceived twins. We aimed to assess the obstetric and perinatal outcomes of twin pregnancies

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delivered in our unit and compare the outcomes according to mode of conception. Our study population had antenatal, intrapartum and postpartum care at a single tertiary maternity hospital where there are standard management protocols in place for twin pregnancy. In Ireland, all women are entitled to state-funded obstetric care and those women who have a private health insurance policy, may choose to attend an obstetrician for private care delivered solely by that obstetrician. The state-funded twin clinic in the maternity hospital is led by a Maternal–Fetal Medicine (MFM) specialist together with a registrar and a dedicated midwife sonographer. Of the 10 consultants who offer private obstetric care, six are MFM specialists.

Materials and methods

This was a retrospective study of twin pregnancies delivered at Cork University Maternity Hospital, Ireland over a 4-year period (2009–2012). All viable dichorionic-diamniotic (DCDA) twin pregnancies (based on ultrasound-assigned chorionicity at approximately 12 weeks' gestation and confirmed by pathological examination of the placenta following delivery) were included in the study. None of the twin pairs resulted from higher-order multiple gestation fetal reduction. The twin pregnancies were divided according to mode of conception; spontaneously conceived (SC) and those who conceived using assisted reproduction techniques (ART), specifically IVF or ICSI. The following exclusion criteria were used: twin pregnancies complicated by early fetal loss (less than 12 weeks' gestation) or second trimester loss of both twins and women who conceived using intrauterine insemination (IUI) or ovulation induction techniques. Monochorionic twin pregnancies were excluded from the study as they are more frequently associated with spontaneous conception and have an increased risk of adverse perinatal outcome when compared with DCDA twins.

Maternal and obstetric outcomes were recorded from birth records, maternal obstetric charts and laboratory data. Specific maternal outcome measures were gestational hypertensive disorders; either pre-eclampsia (defined as persistent blood pressure measurements of $\geq$140/90 mmHg after 20 weeks' gestation with associated proteinuria $>$300 mg/24 h) or pregnancy-induced hypertension (persistent blood pressure readings $\geq$140/90 mmHg, without associated proteinuria, occurring after 20 weeks' gestation), gestational diabetes mellitus (diagnosed by oral glucose tolerance test at approximately 28 weeks' gestation) and obstetric cholestasis (pruritus and deranged liver transaminases with elevated serum bile acids). The gestation at delivery, mode of delivery and onset of labour (i.e. spontaneous or induced labour) were recorded.

Perinatal outcomes were recorded from birth records, maternal obstetric charts and neonatal intensive care (NICU) database. Perinatal outcome measures included second trimester spontaneous reduction, intrauterine fetal demise or stillbirth of one twin ($\geq$24 weeks' gestation and/or weighing 500 g or more), intrauterine growth restriction (IUGR; defined as estimated fetal weight less than tenth percentile for gestational age), prematurity (defined as birth occurring at less than 37 weeks' gestation), degree of prematurity; extremely preterm ($<$28 weeks' gestation), very preterm (28–31^{+6} weeks' gestation), moderately preterm (32–33^{+6} weeks' gestation) and late preterm (34–36^{+6} weeks' gestation), birth weight, low Apgar score (defined as $<$5 at 1 min and/or $<$7 at 5 min), NICU admission and mean length of stay (days) in the NICU. A composite measure of perinatal morbidity included any of the following: hypoxic ischaemic encephalopathy (HIE), necrotising enterocolitis (NEC) or sepsis.

Results

Five hundred and forty-four women were identified as have an on-going DCDA twin pregnancy at approximately 12 weeks' gestation. Five of these women were further excluded from the study as they had a second trimester miscarriage of both twins, resulting in 539 women being included in the study.

Mode of conception

One hundred and seventy-one women (31.7%) had conceived using ART and 368 women (68.3%) had spontaneously conceived (SC) twins. Of the ART group, 109 (63.7%) conceived following IVF treatment, 20.5% (n = 35) following ICSI treatment and 15.8% (n = 27) had IVF/ICSI using donor oocyte (Table 1).

Maternal demographics

The mean maternal age of the study group was 33.7 $\pm$ 5.17 years. Amongst the group who conceived spontaneously the mean age was 32.3 $\pm$ 4.93 years, compared with a mean age of 36.8 $\pm$ 4.23

Table 1
Maternal characteristics and antenatal complications according to mode of conception.

Maternal characteristics	Total population (n = 539)[a]	Spontaneous conception (n = 368)[a]	ART conception (n = 171)[a]	Unadjusted OR (95% CI)[b]	Adjusted OR (95% CI)[b]	p-Value
Mean age (yr, SD)	33.69 ± 5.17	32.25 ± 4.93	36.81 ± 4.23	–	–	–
Age range (yr)	17–51	17–46	26–51	–	–	–
Antenatal care						<0.001
Public	368 (68.3)	285 (77.4)	83 (48.5)	–	–	
Private	171 (31.7)	83 (22.6)	88 (51.5)	–	–	
Parity						
Nulliparous	259 (48.1)	133 (36.1)	126 (73.7)	–	–	<0.001
Multiparous	280 (51.9)	235 (63.9)	45 (26.3)	–	–	<0.001
Mode of ART						
IVF	–	–	109 (63.7)	–	–	
ICSI	–	–	35 (20.5)	–	–	
Donor oocyte	–	–	27 (15.8)	–	–	
Antenatal complications						
GDM[c]	22 (4.1)	14 (3.8)	8 (4.7)	1.24 (0.66–2.32)	0.86 (0.41–1.81)	0.709
GHD[d]	100 (18.6)	63 (17.1)	37 (21.6)	1.34 (0.97–1.84)	0.81 (0.55–1.20)	0.128
OC[e]	21 (3.9)	12 (3.3)	9 (5.3)	1.65(0.88–3.08)	1.39 (0.66–2.95)	0.188

[a] Values are shown in n (%) unless otherwise stated.
[b] Adjusted for age, parity and type of antenatal care.
[c] Gestational diabetes mellitus.
[d] Gestational hypertensive disorders; specifically pre-eclampsia or pregnancy-induced hypertension.
[e] Obstetric cholestasis.