



Maternal and perinatal outcomes in spontaneous versus assisted conception twin pregnancies



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ABSTRACT

Objective: To compare maternal and perinatal outcomes in twin pregnancies conceived via assisted reproductive techniques (ART) compared with spontaneous twin pregnancies.

Study design: This retrospective study examined 345 dichorionic, di-amniotic twin pregnancies (207 conceived spontaneously and 138 conceived via ART), delivered between January 2007 and June 2011 at the San Pietro Fatebenefratelli Hospital, Rome, a tertiary medical centre. Maternal and perinatal outcomes were compared. A multiple logistic regression analysis was performed to calculate risk estimates as odds ratios (OR) adjusted for maternal age, parity and systemic diseases. Patient data were obtained from a computerized database and analyzed using Statistical Package for the Social Sciences Version 17.

Results: Gestational age and birth weight were lower in the ART group, and preterm delivery, gestational diabetes and placental abruption were higher in the ART group compared with the spontaneous conception group. The incidence rates of respiratory complications, patent ductus arteriosus and admission to the neonatal intensive care unit were higher among ART newborns. Length of hospital stay for mothers and newborns was longer in the ART group. No differences in mode of delivery, Apgar score at 5 min, congenital anomalies, perinatal mortality, and other considered pregnancy and neonatal complications were found between the two groups. Multivariate analysis adjusted for maternal age, parity and systemic diseases revealed that only the rates of placental abruption [OR 7.45, 95% confidence interval (CI) 2.05–26.98] and patent ductus arteriosus (OR 3.39, 95% CI 1.01–11.46) were significantly higher for the ART group.

Conclusions: Twin pregnancies conceived via ART are at greater risk of poorer outcomes than spontaneous twin pregnancies. This may be related to the type of conception and specific negative features of subfertile patients undergoing infertility treatment.

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1. Introduction

There has been a dramatic increase in the number of twin pregnancies since the first successful birth following in vitro fertilization in 1978 [1]. Twin gestations increased from 18.9 per 1000 to 32.6 per 1000 between 1980 and 2008 in the USA [2]. The main contributors to this rise are the increasing childbearing age,

due to the trend to postpone motherhood, and the use of assisted reproductive techniques (ART) for infertility treatment [3]. The multiple gestation rate is high in ART pregnancies because of the need to stimulate excess follicles and transfer excess embryos to achieve reasonable pregnancy rates. Approximately 20% of deliveries following ART in Europe are twins [4], compared with a natural incidence of 1–1.5% in spontaneously conceived births [5].

Multiple pregnancies remain the most common complication of infertility treatment. Despite advances in obstetric and neonatal care, twin pregnancies have worse outcomes than singleton pregnancies, including preterm delivery, pregnancy-induced complications, caesarean section, prematurity, low birth weight (LBW), birth defects, long-term sequelae and death [6–8]. These

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conditions not only affect the families involved but also place financial stress on the healthcare system due to extensive lifelong medical bills [9].

Singleton pregnancies after IVF have been reported to be at increased risk for adverse perinatal outcomes, including preterm birth, LBW and perinatal mortality [10]. Data on twin pregnancies, however, are controversial and there has been extensive debate in the literature on whether the risks associated with twin pregnancies following IVF differ from those of spontaneous twin pregnancies [11–13].

The purpose of this study was to compare obstetric and perinatal outcomes of dichorionic twin pregnancies conceived via ART with those of spontaneous twin pregnancies.

2. Materials and methods

Between January 2007 and June 2011, 14,087 singleton pregnancies, 391 twin pregnancies and 21 triplet pregnancies were delivered at the San Pietro Fatebenefratelli Hospital, Rome, a tertiary medical centre with an university-affiliated obstetric unit dealing with high-risk cases. Monochorionic twin pregnancies and twin pregnancies reduced to singleton births were excluded from the study. Only ART pregnancies obtained following conventional IVF and intracytoplasmic sperm injection (ICSI) were analyzed; pregnancies conceived via ovulation induction, intra-uterine insemination or egg donation were excluded from the study. After these exclusions, 345 dichorionic, di-amniotic twin pregnancies were available to the study. We considered pregnancies ending by either second trimester abortion (defined as spontaneous termination of pregnancy after completion of 14 weeks and before 24 weeks of weeks of gestation) or spontaneous delivery after 24 weeks of pregnancy. The gestational age was based on the last known menstrual period, confirmed by first-trimester ultrasound estimate, for spontaneous pregnancies, and by adding 2 weeks to the date of oocyte retrieval for ART pregnancies. Spontaneous pregnancies with discrepancies in menstrual and ultrasonographic gestational age estimates were excluded.

For each pregnancy included in the study, the following data were analyzed from the maternal medical records: age at delivery, mode of conception, type of infertility treatment, gravidity and parity, systemic diseases before pregnancy which are known to be linked with poor pregnancy outcomes (including thrombophilia, endometriosis and hypothyroidism), gynaecological surgery (including laparoscopic or abdominal myomectomy, bilateral or unilateral ovariectomy, bilateral or unilateral salpingectomy, and ovarian cystectomy), smoking during pregnancy, cerclage procedure, gestational age (in weeks) at the time of abortion/delivery, mode of presentation, mode of delivery, antepartum and

postpartum complications, antenatal admission, admission to intensive care unit and length of hospital stay (including antenatal admission). Women with a history of diabetes mellitus or hypertension before pregnancy were excluded from the study. Thrombophilia was defined as an inherited or acquired predisposition to venous thrombo-embolism diagnosed on laboratory testing. A diagnosis of endometriosis was based on the results of a diagnostic or operative laparoscopy. A diagnosis of hypothyroidism was based on the results of thyroid blood tests.

The main perinatal outcomes retrieved from 700 neonatal medical records were birth weight, length, head circumference, Apgar score at 5 min after birth, congenital anomalies, stillbirth rate, neonatal morbidity and mortality, admission to neonatal intensive care unit (NICU) and length of hospital stay. International Classification of Diseases-9-CM was used to identify pregnancy complications and clinical problems in the newborns.

Preterm delivery and very preterm delivery were defined as delivery before 37 and 32 weeks of gestation, respectively. Birth weight of <2500 g and <1500 g was defined as LBW and very low birth weight (VLBW), respectively. Neonates with a birth weight below the 10th percentile for gestational age were defined as small for gestational age (SGA). Perinatal deaths included stillbirths after 24 weeks of gestation with birth weight of >500 g and the liveborns who died within 7 days of delivery.

Data analysis was performed using Statistical Package for the Social Sciences Version 17.0 (SPSS Inc., Chicago, IL, USA). Normally distributed data were analyzed using Student's *t*-test. Mann-Whitney *U*-test was used to test group differences in non-parametric variables. *Z*-test was used for comparison of proportions. Multiple logistic regression was used to assess the association between pregnancy outcomes and the two groups, adjusting for potential confounding variables including maternal age, parity and history of systemic diseases. *p*-Values <0.05 were considered to indicate statistical significance.

This study was approved by the local institutional review board and the hospital ethics committee.

3. Results

The study population included 345 dichorionic, di-amniotic twin pregnancies. The incidence of twins was 2.7% of all births. The ART group encompassed 138 (40%) pregnancies conceived by ART (75 (21.7%) resulting from ICSI and 63 (18.3%) resulting from IVF). The spontaneous conception group consisted of 207 (60%) twin pregnancies conceived spontaneously.

Table 1 shows the maternal and perinatal characteristics for the study population. The women who conceived via ART were older and more often nulliparous than the women who conceived

Table 1
Demographic and clinical characteristics.

Variable	ART twin pregnancies (n=138)	Spontaneous twin pregnancies (n=207)	<i>p</i> -Value
Mean (\pm SD) age at delivery (years)	38.5 \pm 5.5	33.5 \pm 5.1	<0.005
>35	90 (65.2)	86 (41.5)	<0.005
>40	50 (36.2)	13 (6.3)	<0.005
Nulliparous (%)	130 (94.2)	108 (52.2)	<0.005
History of miscarriage (%)	36 (26.1)	51 (24.6)	0.851
History of recurrent miscarriage (%)	8 (5.8)	5 (2.4)	0.097
Systemic diseases (%)	55 (39.9)	36 (17.4)	<0.005
Hypothyroidism (%)	21 (15.2)	14 (6.8)	0.026
Endometriosis (%)	10 (7.2)	3 (1.4)	0.007
Thrombophilia (%)	24 (17.4)	19 (9.2)	0.006
Gynaecological surgery (%)	54 (39.1)	18 (8.7)	<0.005
Smoking during pregnancy (%)	13 (9.4)	31 (15.0)	0.173
Caesarean section (%)	132 (95.7)	192 (92.8)	0.380
Emergency caesarean section (%)	62 (44.9)	90 (43.5)	0.884
Vertex presentation of first twin (%)	101 (73.2)	159 (76.8)	0.473

ART, assisted reproductive techniques; SD, standard deviation.

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