ORIGINAL ARTICLE: ASSISTED REPRODUCTION

Outcome of monochorionic twins conceived by assisted reproduction

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Objective: To evaluate monochorionic twins conceived by assisted reproductive technology (ART).
Design: We compared perinatal outcomes of monochorionic twins conceived by ART with their dichorionic counterparts and with spontaneous monochorionic twins.
Setting: Referral center.
Patient(s): Mothers to monochorionic and dichorionic twins conceived by ART and spontaneous monochorionic twins.
Intervention(s): None.
Main Outcome Measure(s): Maternal characteristics, pregnancy complications, and perinatal outcomes.
Result(s): Monochorionic twin pregnancies (n = 25) comprise 7.2% of all ART twins and 4.9% of all monochorionic twins in this data set. Monochorionic pairs have a significantly worse outcome compared with dichorionic sets in terms of lower gestational age and birth weight. ART appears to increase the already high risk of monochorionicity compared with spontaneous conception: odds ratio (OR), 2.9 (1.1–7.3) for preterm birth at <32 weeks and OR, 5.9 (2.5–1.49) for birth weight <1,500 g.
Conclusion(s): Monochorionic twins after ART are at increased risk of adverse perinatal outcomes compared with spontaneous monochorionic twins and with dichorionic twins conceived by ART. (Fertil Steril® 2015;■:■–■. ©2015 by American Society for Reproductive Medicine.)
Key Words: Monochorionic twins, assisted reproduction, pregnancy complications

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The monozygotic twinning rate increases after all methods of infertility treatment (1–3). In contrast to ovulation induction techniques, where the number of resulting embryos is practically uncontrolled, assisted reproductive technology (ART, i.e., all methods of IVF and ET) offers a reduced risk of multiple pregnancies with single ETs. Yet the potential risk of zygotic splitting after ART has become clear. In a recent study from the United States, Gee et al. found that in 0.5% of twin, 29% of triplet, and in 64% of quadruplet births there were fewer fresh embryos transferred than the number of births, indicating that monozygotic twinning might be related to iatrogenic plurality (4). This method, like many others, does not count the frequency of monochorionic twins—the subset of monozygotic twins with the highest risk of fetal morbidity and mortality (5).

The outcomes of monochorionic twins conceived by ART have not been extensively studied, and the two available studies yield conflicting results. Mascarenhas et al. (6) evaluated monochorionic twins conceived by ART and concluded that these pregnancies have increased fetal loss when compared with dichorionic pregnancies. In contrast, Ghalili et al. (7) did not find significant differences between spontaneous and ART monochorionic pregnancies. In light of this ambiguity we sought to compare the perinatal outcomes of monochorionic twins conceived by ART with their dichorionic counterparts and with spontaneous monochorionic twins.

MATERIAL AND METHODS

We evaluated twin pregnancies, followed and delivered ≥24 weeks' gestation at the Maternity Hospital Dr. Alfredo da Costa, Lisbon, Portugal, during the period September 1, 1994, through December 31, 2014. Our hospital is a tertiary perinatal center that cares for the Lisbon area and serves as a referral center for the south of Portugal. Information about pregnancy and delivery was registered prospectively on a preset form and subsequently entered into a computerized system. We excluded twin

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gestations that were delivered only and were not followed at our service.

Monochorionicity was established by standard ultrasound criteria confirmed by postpartum placental clinical and pathological examination; gestational age was calculated from the last menstrual period confirmed by first trimester sonography. In this study there were no monoamniotic sets after ART, hence we excluded monoamniotic sets from the controls as well. Indicated preterm deliveries were carried out on the basis of maternal and/or fetal conditions. We offered weekly to twice weekly follow-up including sonographic fetal biophysical profile and nonstress fetal heart rate testing, biweekly fetal growth assessment, and Doppler velocimetry of the umbilical and middle cerebral arteries as indicated.

In otherwise normally progressing gestations, we offered, after detailed counseling, elective deliveries at 36–37 completed weeks of gestation. We compared the perinatal outcomes of monochorionic-diamniotic twins conceived by ART (all methods of IVF and ET) with their dichorionic counterparts and with spontaneous (no treatment) monochorionic twins. Because of the rarity of the condition, we did not subdivide cases by the nature of embryo (fresh or thawed). We considered the following variables: maternal age and parity; maternal complications such as premature contractions (<34 weeks of gestation); hypertensive disorders (preeclampsia, pregnancy-induced hypertension, and chronic hypertension); gestational diabetes; preterm rupture of membranes at <34 weeks of gestation; mode of delivery; gestational age at birth; birth weight; frequency of births at less than 32, 32–35, and 36 or more weeks (reason for preterm birth was not specified); birth weight less than 1,500 g, 1,500–2,499, and 2,500 g or more and birth weight discordance of >25% (intertwin birth weight difference expressed as percentage of the heavier twin, calculated per total number of pregnancies); frequency of twin-twin transfusion syndrome (TTTS); frequency of Apgar scores <7 at 5 minutes; major malformations (excluding stillbirths, calculated per total number of fetuses); and early (<7 days of life) neonatal death (calculated per total number of fetuses).

We compared continuous data by using two-tailed Student's t test, and categorical data by two-tailed χ^2 or Fisher's exact tests. We used SPSS, version 17, for statistical analyses. $P<.05$ was considered statistically significant for continuous data. We calculated the odds ratio (OR) and 95% confidence interval (CI) for categorical data. Because of anonymous data collection, the study was exempt from approval by the local Institutional Review Board.

RESULTS

The data included 25 monochorionic twin pregnancies (50 twins) and 320 dichorionic twin pregnancies (640 twins) conceived by ART as well as 483 (966 twins) spontaneous monochorionic twins. Thus monochorionic twins comprise 7.2% of all ART twins, and monochorionic twins after ART comprise 4.9% of all monochorionic twins. Table 1 shows the comparison between monochorionic twins conceived by ART and spontaneous monochorionic twins. The data indicate that ART mothers were significantly older

TABLE 1

Comparison between monochorionic twins conceived by ART and spontaneous monochorionic twins.

	Monochorionic twins		
Variable	**ART, n = 25**	**Spontaneous, n = 483**	**Statistic**
Maternal age, y	33.9 ± 5.4	29.9 ± 5.3	<.001
Nulliparas	21 (84)	259 (53.6)	4.5 (1.6, 15.6)
Premature contractions	14 (56)	264 (54.7)	1.0 (0.4, 2.4)
Hypertensive disorders	4 (16)	89 (18.4)	1.0 (0.4, 2.4)
Premature rupture of membranes ≤34 wk	4 (16)	46 (9.5)	1.8 (0.5, 5.2)
Diabetes	3 (12)	56 (11.6)	1.0 (0.2, 3.2)
Vaginal birth	5 (20)	148 (30.6)	0.6 (0.2, 1.5)
Cesarean in labor	6 (24)	88 (18.2)	1.4 (0.5, 3.5)
Elective cesarean	14 (56)	247 (51.1)	1.2 (0.5, 2.8)
Gestational age (wk)	33.1 ± 3.7	34.5 ± 2.7	.07
<32	7 (28)	56 (12)	2.9 (1.1–7.3)
32–35	10 (40)	188 (38.9)	1.0 (0.4–2.4)
≥36	8 (32)	239 (49)	0.3 (0.1–0.7)
Birth weight, g	1,754 ± 591	2,088 ± 537	<.001
<1,500	17 (34)	127 (13.4)	5.9 (2.5–1.49)
1,500–2,499	29 (58)	616 (65)	0.7 (0.4, 1.3)
≥2,500	4 (8)	204 (24.5)	0.3 (0.1, 0.8)
Birth weight discordance >25%[a]	5 (20)	60 (12.4)	1.8 (0.6, 4.8)
Major malformations[a]	5 (10)	50 (5.2)	2.0 (0.7, 5.7)
TTTS	2 (8)	47 (9.7)	0.8 (0.1, 3.1)
Intrauterine fetal death	0	8 (0.8)	–
5-min Apgar score <7	0	16 (1.7)	–
Early neonatal deaths[a]	4 (8)	11 (1.2)	7.4 (1.9, 23.4)

Note: Data are shown as mean ± standard deviation or n (%). Statistics are shown as *P* values or odds ratio (95% confidence interval).

[a] Numbers per pregnancy or fetuses, as appropriate.

Simões. Monochorionic twins following ART. Fertil Steril 2015.