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SHORT COMMUNICATION

SZEGED, HUNGARY

Birth Weight Discordance in Spontaneous Versus Induced Twins: Impact on Perinatal Outcome

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***Purpose*:** To compare the rate of birth weight discordance and perinatal outcome of twin pregnancies after assisted reproduction with that of spontaneous twins.
***Method*:** A total of 12,920 deliveries were analyzed retrospectively. Seventy-five twin pregnancies after ART were compared to the 94 spontaneous counterparts. Birth weight discordance was defined as a difference of 20% or more.
***Results*:** Discordance rate was elevated (25.3% vs. 17.0%) among ART twins. SGA was increased and NICU admission was more frequent in discordant group. Unlike-sexed twins were more prevalent (73.7% vs. 37.5%) among discordants after ART.
***Conclusions*:** ART can increase discordance rate which can elevate perinatal risk.

KEY WORDS: ART; discordance; twins.

INTRODUCTION

Perinatal consequences of growth discordance among twin pregnancies is thoroughly evaluated (1,2). Twin birth weight discordance has now clearly been demonstrated to be a risk factor for preterm birth (1) and is associated with increased risk of intrauterine death and malformation-related neonatal deaths (3). Higher perinatal mortality and more frequent neonatal intensive care unit admissions can also be observed among discordant neonates (4). Severely discordant twins (more than 25% difference) have significantly worse perinatal mortality and morbidity if compared to mildly discordant (5–25% difference) or concordant twins (less than 5% difference) (5). Twinning in assisted reproduction is increased and known for its contribution to the high rate of premature deliveries. Obstetric outcome for induced twin pregnancy is less optimal than in spontaneously conceived twin pregnancy (6). Studies in the literature support the hypothesis that discordance rate following IVF-ET is significantly increased (7,8).

Consequently, the elevated birth weight discordance rate among ART neonates can be an independent risk factor partly responsible for pregnancy complications and adverse perinatal outcome. The aim of the study was to test the hypothesis that ART twin pregnancy, especially discordant multiple birth, represents a risk concerning perinatal outcome.

METHODS

We performed a retrospective study from January 1, 1995 to December 31, 2001 at the Department of Obstetrics and Gynecology, University of Szeged. A total of 12,920 deliveries were subjected to analysis. Seventy-five twin pregnancies after assisted reproduction was compared to 94 spontaneous counterparts. Birth weight discordance was defined as a difference of 20% or more. Discordance rate and possible connection of the phenomenon with the prevalence of congenital anomalies, rate of prematurity, Apgar score at 5 min <7, umbilical cord arterial pH <7.20, NICU transfer, and sex ratio were evaluated.

Congenital malformations were diagnosed by the same experienced neonatologist, on the basis of physical examination, chest, abdominal, or skull X-ray, and ultrasonography (cardiac, abdominal, head, etc.) according to International Code of Diagnosis (ICD) criteria.

Statistical analysis was performed with the SPSS for Windows program (SPSS 11.0, Inc. Chicago). Kolmogorov-Smirnov probe was used to test the statistical normality in the surveyed groups. Univariate comparisons were assessed by the Mann-Whitney U probe and by the Wilcoxon test for continuous and categorical variables, respectively. Normality was not proved in our samples due to low number of statistical entries and nonparametric tests were used to test the difference between case and control group. Testing the null-hypothesis, the statistical power at the defined statistical significance level of $P < 0.05$ ranged between 0.8 and 0.68. The Mantel-Haenszel test was used to estimate the correlation of variables between the discordant and nondiscordant twins in the ART and spontaneous pregnancies. The Mantel-Haenszel test was used to estimate the correlation of variables

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Table I. Neonatal Outcome in Spontaneous and Induced Pregnancies

	Spontaneous						ART-group					
	Twin A ($n = 94$)		Twin B ($n = 94$)				Twin A ($n = 75$)		Twin B ($n = 75$)			
	No.	%	No.	%	*P* value	OR (95%CI)	No.	%	No.	%	*P* value	OR (95%CI)
Birth weight (g) (mean ± SD)	2275.57 ± 695.94		2247.20 ± 710.80		<0.05		2387.87 ± 638.63		2336.93 ± 640.80		<0.05	
Small for gestational age	21	22.3	23	24.5	NS[a]	1.12 (0.57–2.21)	15	20.0	13	17.3	NS	0.84 (0.37–1.91)
Apgar score at 5 min <7	10	10.6	12	12.8	NS	1.23 (0.50–3.00)	11	14.7	10	13.3	NS	0.89 (0.36–2.25)
Umbilical cord arterial pH <7.20	86/12	14.0	86/16	18.6	NS	1.41 (0.62–3.19)	69/8	11.6	69/14	20.3	NS	1.94 (0.76–4.98)
NICU admission	51	54.3	50	53.2	NS	0.96 (0.54–1.70)	31	41.3	30	40.0	NS	0.95 (0.49–1.82)
Perinatal mortality[b]	1	1.1	1	1.1			0	0.0	0	0.0		
Male infants	51	54.3	55	58.5	NS	1.19 (0.67–2.12)	42	56.0	43	57.3	NS	1.06 (0.55–2.01)

[a] NS: statistically not significant.
[b] Statistical analysis was not meaningful.

between the discordant and the nondiscordant twin pregnancies relative to the correlation in the case-control group.

RESULTS

The discordance rate was 25.3% in ART group versus 17.0% in the controls. The twin A neonates displayed higher birth weight in both groups. There were no significant differences between the two members of the twins concerning neonatal outcome (Table I).

The difference in prevalence of congenital anomalies was not significant (2.7% vs. 1.1%). The prevalence of SGA was 18.7 vs 23.4 in the ART and in the control group, without any significant difference (Table II). On the contrary SGA among discordants was significantly increased in the case groups (discordant groups: ART – 52.6% and non-ART – 37.5% vs. nondiscordant groups: ART – 7.1% and non-ART – 20.5%) (Table III).

The rate of prematurity was less frequent among the discordant ART neonates (52.6%) than among the spontaneous ones (62.5%), but this difference was not significant between those who were nondiscordants (60.7% vs. 55.1%, respectively). The rate of male infants did not differentiate significantly in the two samples (Table III). The NICU admission was more prevalent among discordant pregnancies (ART: 55.3% and spontaneous: 71.9%) than among nondiscordant twins (ART: 36.6% and spontaneous: 49.4%). Low Apgar score was higher among spontaneous (18.8%) than in ART discordant group (2.6%) whereas the prevalence is higher among nondiscordant ART than spontaneous counterparts (14.3% vs. 11.5%). The umbilical cord arterial pH levels were similar. Unlike-sexed twins could be observed among the discordant ART group in a significantly more prevalent rate (discordant groups: ART – 73.7% and non-ART – 37.5% vs. nondiscordant groups: ART – 37.5% and non-ART – 33.3%). A relevant factor is that the rate of primiparity is significantly higher among ART (61.3% vs. 39.4%, $P < 0.05$ [OR = 2.44;

Table II. Neonatal Outcome of Spontaneous and Induced Pregnancies

	Spontaneus ($n = 188$)		ART ($n = 150$)			
	No.	%	No.	%	*P*	OR (95%CI)
Gestational age (wks) (mean ± SD)	35.34 ± 3.14		35.50 ± 3.00		NS	
Birth weight (g) (mean ± SD)	2273.12 ± 701.99		2362.40 ± 635.93		<0.05	
Congenital anomalies	2	1.1	4	2.7	NS	2.55 (0.46–14.1)
Caesarean section ($n_1 = n/2$)	94/58	61.7	75/49	65.3	NS	1.17 (0.62–2.20)
Premature births	106	58.7	88	56.4	NS	1.10 (0.71–1.70)
SGA	44	23.4	28	18.7	NS	0.75 (0.44–1.28)
Male infants	106	56.4	85	56.7	NS	1.01 (0.66–1.56)
NICU	100	53.2	62	41.3	<0.05	0.62 (0.40–0.96)
Apgar score at 5 min <7	24	12.8	17	11.3	NS	0.87 (0.45–1.69)
Umbilical cord arterial pH <7.20	29/172	16.9	22/141	15.6	NS	0.91 (0.50–1.67)
Perinatal mortality[a]	1	0.5	1	0.7		

[a] Statistical analysis was not meaningful.

Table III. Discordant Versus Nondiscordant Twin Neonates (Mantel-Haenszel Test)

	Discordant ($n = 64$)					Nondiscordant ($n = 274$)					
	Spontaneous ($n = 30$)		ART ($n = 34$)			Spontaneous ($n = 158$)		ART ($n = 116$)			
	No.	%	No.	%	RR[a]	No.	%	No.	%	RR[a]	*P* value
Premature birth	20	62.5	20	52.6	0.84	86	55.1	68	60.7	1.10	<0.05
Gestational age (wks)	33.875 ± 3.90		35.66 ± 2.74		<0.05	35.65 ± 2.88		35.45 ± 3.10			NS[b]
Male infants	16	50	20	52.6	1.05	90	57.7	65	58.0	1.01	NS[b]
Small for gestational age	12	37.5	20	52.6	1.40	32	20.5	8	7.1	0.35	<0.05
Apgar score at 5 min <7	6	18.8	1	2.6	0.14	18	11.5	16	14.3	1.24	<0.05
Umbilical cord arterial pH <7.20	27/6	22.2	34/3	8.8	0.39	145/23	15.9	106/19	17.9	1.13	<0.05
NICU admission	23	71.9	21	55.3	0.77	77	49.4	41	36.6	0.74	NS

[a] RR: relative risk between ART and non-ART groups.
[b] NS: statistically not significant.

95CI = 1.31–4.55]) which also can influence the attitude of the pregnant woman concerning medical counselling modifying the outcome of pregnancy. Also the educational level of pregnant women was higher in the case group (9) improving the cooperation of the mother during pregnancy and determining an optimized lifestyle (i.e. smoking habits).

CONCLUSION

Since 1980, there has been a worldwide dramatic increase in multiple births. This seems to be due to an increase in the age of reproduction, the use of ovulation induction, and the use of in vitro fertilization. Unfortunately, almost a third of these pregnancies involve multiple gestations. Research is currently focusing on methods to improve IVF succes rates while reducing twin and triplet pregnancies and their associated increased morbidity and mortality (10). Though clear ethiology is still unclear resulting in growth discordance of twins exposed to the same maternal enviroment, placental and/or fetal factors should determine the background (11) inducing this phenomenon. Twins who are ultimately discordant at birth may exhibit differences in growth as early as 11–14 weeks of gestation (12). Our study provided further evidence that unlike-sex pairs (13) are significantly more prevalent among discordant ART twins. Data concerning prematurity was controversial in our study. Discordant ART pregnancies represent a high risk for SGA and an increased incidence of NICU admissions.

The observed increased incidence of birth weight discordance following assisted reproduction can be an important risk factor partly responsible for pregnancy complications and adverse perinatal outcome.

The possible differences in the management of pregnancy among ART and non-ART pregnancies cannot influence the pure rate of discordance, but at the same time it can moderate the consequences of this phenomenon.

REFERENCES

1. Cooperstock MS, Tummaru R, Bakewell J, Schramm W: Twin birth weight discordance and risk of preterm birth. Am J Obstet Gynecol 2000;183(1):63–67
2. Redman ME, Blackwell SC, Refuerzo JS, Kruger M, Naccasha N, Hassan SS, Berry SM: The ninety-fifth percentile for growth discordance predicts complications of twin pregnancy. Am J Obstet Gynecol 2002;87(3):667–671
3. Demissie K, Ananth CV, Martin J, Hanley ML, MacDorman MF, Rhoads GG: Fetal and neonatal mortality among twin gestations in the United States: The role of intrapair birth weight discordance. Obstet Gynecol 2002;100(3):474–480
4. Audibert F, Boullier M, Kerbrat V, Vial M, Boithias C, Frydman R: Growth discordance in dichorionic twin pregnancies: Risk factors, diagnosis and management. J Gynecol Obstet Biol Reprod 2002;31(Suppl 1):2S15–2S24
5. Victoria A, Mora G, Arias F: Perinatal outcome, placental pathology, and severity of discordance in monochorionic and dichorionic twins. Obstet Gynecol 2001;97(2):310–315
6. Lambalk CB, van Hoof M: Natural versus induced twinning and pregnancy outcome: a Dutch nationwide survey of primiparous dizygotic twin deliveries. Fertil Steril 2001;75(4):731–736
7. Koudstaal J, Bruinse HW, Helmerhorst FM, Vermeiden JP, Willemsen WN, Visser GH: Obstetric outcome of twin pregnancies after in-vitro fertilization: A matched control study in four Dutch university hospitals. Hum Reprod 2000;15(4):935–940
8. Daniel Y, Ochshorn Y, Fait G, Geva E, Bar-Am A, Lessing JB: Analysis of 104 twin pregnancies conceived with assisted reproductive technologies and 193 spontaneously conceived twin pregnancies. Fertil Steril 2000;74(4):683–689
9. Zádori J, Kozinszky Z, Orvos H, Katona M, Pál A, Kovács L: Dilemma of increased obstetric risk in pregnancies following IVF-ET. J Assist Reprod Genet 2003;20(6):216–221

10. Hardy K, Wright C, Rice S, Tachataki M, Roberts R, Morgan D, Spanos S, Taylor D: Future developments in assisted reproduction in humans. Reproduction 2002;123(2):171–183
11. Westwood M, Gibson JM, Sooranna SR, Ward S, Neilson JP, Bajoria R: Genes and placenta as modulator of fetal growth: Evidence from insulin-like growth factor axis in twins with discordant growth. Mol Hum Reprod 2001;7(4):387–395
12. Kalish RB, Chasen ST, Gupta M, Sharma G, Perni SC, Chervenak FA: First trimester prediction of growth discordance in twin gestations. Am J Obstet Gynecol 2003;189(3):706–709
13. Blumrosen E, Goldman RD, Blickstein I: Growth discordance and the effect of a male twin on birth weight of its female cotwin: A population based study. J Perinat Med 2002;30(6):510–513

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