Antenatal factors associated with significant birth weight discordancy in twin gestations

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OBJECTIVE: The purpose of this study was to evaluate factors that are associated with significant birth weight discordancy.

STUDY DESIGN: As a part of an ongoing collaborative study of twins, maternal and fetal data were obtained from the medical records of twin gestations at eight medical centers. The study population was divided into groups by difference in birth weight discordancy (≥20%, ≥25%, and ≥30%)

RESULTS: Severe birth weight discordancy was associated with fetal growth deceleration by 20 to 28 weeks (adjusted odds ratio, 4.90; 95% CI, 3.15-7.64) and between 28 weeks to birth (adjusted odds ratio, 3.48; 95% CI, 1.72-7.06). Antenatal bleeding (adjusted odds ratio, 1.86; 95% CI, 1.08-3.21), preeclampsia (adjusted odds ratio, 1.70, 95% CI, 1.21-2.41), and monochorionicity (adjusted odds ratio, 2.35, 95% CI, 11.71-3.23) were also associated with birth weight discordancy.

CONCLUSION: These data demonstrate the importance of the early diagnosis of placental chorionicity, because monochorionicity is associated with a 2-fold increase in birth weight discordancy in twin gestations. (Am J Obstet Gynecol 2003;189:813-7.)

Key words: Twin gestation, monochorionicity, birth weight discordancy

The number of multiple births in the United States has increased at an unprecedented rate over the past two decades. In 2001, there were 128,717 multiple births, twins comprising most of these births.[1] Because of their higher frequency of growth restriction and prematurity, infants of multiple gestations are at greater risk for neonatal morbidity and fetal, neonatal, and infant death. Discordancy in growth among twin gestations is probably related to the process of twinning and the incapacity of the uterine-placental environment to provide for the increased nutritional requirement of two fetuses. Severe discordancy in birth weight has been associated with adverse perinatal outcomes. Many studies have reported an increased perinatal death rate in twin pregnancies in which there has been ≥25% discordancy in weight at birth.[2-5] But the definition of severe discordancy has varied throughout the medical literature. Lanni et al[6] advocate the use of the 90th and the 95th percentile, 23.9% and 29.2%, respectively, as cutoff values for the definition of severe birth weight discordancy. The management of these pregnancies, including antenatal surveillance and early delivery, continue to be the topic of much argument. It would be clinically important to identify antenatal factors that are associated with severe birth weight discordancy early enough to improve outcomes. The purpose of this study was to evaluate factors that are associated with significant birth weight discordancy.

Methods

As part of an ongoing collaborative study of twins, maternal and fetal data were obtained from the medical records of twin pregnancies at eight medical centers in Miami, Fla, Baltimore, Md, Ann Arbor, Mich, Charleston, SC, Galveston, Tex, New York, NY, Wichita, Kan, and Philadelphia, Pa. The study population was divided into groups by difference in birth weight discordancy: ≥20% was defined as mild; ≥25% was defined as moderate, and ≥30% was defined as severe. The study sample was limited to pregnancies that met the following inclusion criteria: (1) both twins born alive; (2) 28 weeks of gestation by last

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Received for publication February 27, 2003; revised May 12, 2003; accepted May 14, 2003.

Presented at the Twenty-Third Annual Meeting of the Society for Maternal-Fetal Medicine, San Francisco, Calif, February 3-8, 2003.

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0002-9378/2003 $30.00 + 0

doi:10.1067/S0002-9378(03)00658-6

Table I. Description of study population

	<20% (n = 2474)	*≥20% (n = 536)*	*≥25% (n = 328)*	*≥30% (n = 200)*
Maternal age (y)*	27.4 ± 6.3	28.1 ± 6.6	27.9 ± 6.6	28.2 ± 6.5
Parity*	1.4 ± 1.3	1.1 ± 1.4	1.03 ± 1.4	1.1 ± 1.3†
Height (cm)*	64.4 ± 2.7	64.3 ± 2.7	64.4 ± 2.8	64.5 ± 2.8
Pregravid weight pounds*	150.1 ± 2.7	153 ± 42	151 ± 41	151 ± 41.4
BMI (%)				
<18.5 kg/m^2	14	12	14	13.2
18.5-24.9 kg/m^2	54	50	50	48.3
25-29.9 kg/m^2	11	14	15	17.2
>30 kg/m^2	21	24	21	21.3
Race and ethnicity (%)				
White	39	44‡	46	52.3§
Black	40	34‡	33.3	28.2§
Hispanic	19	18‡	16.5	14.4§
Other	2	4‡	4.2	4.1§
Monochorionic (%)	16	23§	28§	31§
Smoking (%)	11	11	12	11

*Data are given as mean ± SD.
†$P < .05$, probability value denotes statistical significance with respect to the <20th percentile group.
‡$P < .01$, probability value denotes statistical significance with respect to the <20th percentile group.
§$P < .0001$, probability value denotes statistical significance with respect to the <20th percentile group.

menstrual period, first-trimester ultrasonography, or best obstetric estimate (a combination of clinical and ultrasonographic estimates); (3) documented sex and birth weight of both infants in the pair; and (4) the absence of major congenital anomalies, as documented by normal findings in the newborn infant medical record. All data were abstracted from hospital charts. The institutional review boards at the respective institutions approved this study.

Study variables. The abstracted data included maternal age, race (black non-Hispanic, white non-Hispanic, Hispanic, Asian, and others), parity, maternal size variables (height, pregravid weight, pregravid body mass index [weight/height^2]), and history of smoking. Rates of maternal weight gain were calculated in pounds per week and divided into <20 weeks, 20 to 28 weeks, and 28 weeks to birth; the rates of average fetal growth in grams per week were divided similarly in subgroups of gestational weeks. Variables on maternal medical and obstetric complications included chronic hypertension, pregestational diabetes, hypothyroidism, bleeding during pregnancy, gestational diabetes mellitus, preterm premature rupture of membranes, preterm labor, <37 weeks, <32 weeks, preeclampsia, monochorionicity, rates of twin-to-twin transfusion, and velamentous cord insertion. On the basis of serial ultrasonographic estimates of fetal weight with the use of Hadlock tables,[7] growth deceleration was characterized at the <10th percentile (for singletons) by 20 weeks (<14 g/wk), 20 to 28 weeks (<90 g/wk), and after 28 weeks to birth (<168 g/wk). Chorionicity was determined by early ultrasound and confirmed by pathologic evaluation.

Statistical analysis. Statistical analyses were performed with SPSS (SPSS Inc, Chicago, Ill). Descriptive statistics were obtained for all variables. Continuous variables were analyzed by with two-sample *t* tests; dichotomous variables were analyzed by χ^2 tests. Outcomes were modeled with multivariate and logistic regression and controlled for confounding factors, such as parity and placental membranes.

Results

The study population included 3910 twin gestations, including 520 pregnancies ≥20% discordancy, 328 pregnancies with ≥25% discordancy, and 200 pregnancies with ≥30% discordancy. Table I shows the characteristics of the study population by discordancy groups. The groups did not differ significantly in maternal age, pregravid weight, height, body mass index, or a history of smoking but differ with respect to race and ethnicity. Monochorionicity was more prevalent in all groups of discordancy, particularly in the severely discordant group (31% vs 16%, $P < .0001$). The rate of average fetal growth in grams per week was found to be significantly lower in each group as early as 20 weeks but becoming more pronounced as the pregnancy progressed (Table II). An association was found between inadequate early maternal weight gain (<20 weeks) and fetal growth <10th percentile, significant for mid and late fetal growth (adjusted odds ratio, 1.82; 95% CI, 1.34-2.45) and for 28 weeks to birth (adjusted odds ratio, 1.66; 95% CI, 1.25-2.2).

Table III shows the models that were associated with severe discordancy, adjusted for maternal parity and placental membranes. Bleeding before 20 weeks of gestation, preeclampsia, and monochorionic placentation were associated significantly with birth weight discordancy. Table III also includes models of factors that were associated with fetal growth <10th percentile by period of

Table II. Maternal complications, pregnancy characteristics and outcomes

	<20% (n = 2474)	*≥20% (n = 536)*	*≥25% (n = 328)*	*≥30% (n = 200)*
Chronic hypertension (%)	2	3	2	2
Diabetes mellitus (%)	1	2	1	1
Hypthyroidism (%)	5	2	2	0*
Bleeding (%)	5	6	8†	8†
Cerclage (%)	3	3	3	4
Gestational diabetes mellitus (%)	5	6	5	6
Preterm premature rupture of membranes (%)	20	15†	12*	10*
Preeclampsia (%)	5	21*	23*	24‡
Preterm labor (%)	33	28	28†	27
<32 Weeks (%)	14	17	21‡	23‡
Twin-to-twin transfusion (%)	2	9*	12*	16*
Velamentous insertion (%)	3	7*	7*	7*
Rates of maternal weight gain (lb/wk)§				
<20 Weeks	0.79 ± 0.47	0.76 ± 0.45	0.77 ± 0.45	0.73 ± 0.63
20-28 Weeks	1.5 ± 0.63	1.5 ± 0.59	1.5 ± 0.60	1.5 ± 0.60
28 Weeks to birth	1.7 ± 1.8	2.1 ± 3.1†	2.3 ± 3.8†	2.4 ± 2.4†
Rates of average fetal growth (g/wk)§				
<20 Weeks	16 ± 5.1	15.3 ± 4.8†	15.2 ± 4.7†	14 ± 4.2‡
20-28 Weeks	92 ± 36	84.4 ± 33.5‡	81.3 ± 33*	88 ± 33‡
28 Weeks to birth	155 ± 24	139 ± 27*	134 ± 25*	130 ± 25*

*$P < .0001$, probability value denotes statistical significance with respect to the <20th percentile group.
†$P < .05$, probability value denotes statistical significance with respect to the <20th percentile group.
‡$P < .01$, probability value denotes statistical significance with respect to the <20th percentile group.
§Data are given as mean ± SD.

gestation. A significant association was found between fetal growth and birth weight discordancy in twin pregnancies even before 20 weeks, which increased as the gestation progressed. Among monochorionic pregnancies, several complications were associated with severe birth weight discordancy (Table III), which included twin-twin transfusion, oligohydramnios and polyhydramnios sequence, velamentous cord insertion, and vascular communications in the placenta. Even after twin-twin transfusion cases were excluded, the association of velamentous cord insertion and significant birth weight was still present.

Comment

This study is one of the largest to date to address antenatal factors that are associated with the serious complication of birth weight discordancy in twin gestations. Similar to previous reports, we found monochorionicity to carry a 2-fold increase in significant discordancy after adjusting for parity.[8,9] Similarly, we reported a significant increase in birth weight discordancy in monochorionic pregnancies that is associated with velamentous insertion of the cord. Hanley et al[9] reported a 13-fold risk of this complication with this cord complication. Their dramatic results may be attributed to their lower cutoff value of 20% for defining discordancy. Other abnormalities in placentas have been reported recently to be associated with significant birth weight discordancy. Almog et al[10] found placental apoptosis to be increased in the smaller fetus and concluded that these findings might play a role in discordancy among twins. Redline et al[11] found avascular villi to be involved in this condition. Other factors in our study that were associated with birth weight discordancy include obstetric complications such as preeclampsia and bleeding at <20 weeks of gestation.

The factors strongly correlated with birth weight in concordant twin gestations are maternal height, pregravid or early pregnancy body weight, maternal fat deposition, and gestational weight gain.[12] Although we did not find a significant difference in both groups with maternal height, pregravid weight, and body mass index, we found a significant association with maternal weight gain and fetal growth of <10th percentile. Several studies on twin gestation have established clearly the importance of maternal weight gain before 20 weeks of gestation on twin birth weight.[13-15] Luke et al[15] have shown in a previous report that early maternal weight gains, by 28 weeks of gestation, have the greatest effect on the intrauterine growth and birth weight of twins. Prenatal nutrition programs, which recommend an increase in caloric intake early in twin gestation, have shown a significant increase in birth weights and in the reduction in preterm births.[16,17] A recent publication recommends body mass index–specific maternal weight gains to achieve optimal rates of fetal growth and birth weights in twin gestations.[18] Improved maternal nutrition may facilitate growth, even in the presence of discordancy.

We found an association between fetal growth deceleration and birth weight discordancy as early as 20

Table III. Adjusted odds ratios of risks that are associated with twin birth weight discordancy

	≥20%			≥25%			≥30%		
	Adjusted odds ratio	*95% CI*	*P value*	*Adjusted odds ratio*	*95% CI*	*P value*	*Adjusted odds ratio*	*95% CI*	*P value*
Variables									
Bleeding*	1.39	0.93-2.08	.110	1.77	1.13-2.78	.010	1.86	1.08-3.21	.030
Preeclampsia*	1.63	1.28-2.06	<.0001	1.68	1.27-2.23	<.0001	1.70	1.21-2.41	.003
Preterm premature rupture of membrane*	0.76	0.59-0.98	.040	0.57	0.40-0.80	.001	0.48	0.30-0.77	.002
Monochorionicity†	1.63	1.30-2.05	<.0001	2.05	1.57-2.67	<.0001	2.35	1.71-3.23	<.0001
Fetal growth<10th percentile									
0-20 Weeks	1.04	0.77-1.41	.780	1.05	0.73-1.51	.790	1.36	0.88-2.10	.170
20-28 Weeks*	2.90	2.13-3.93	<.0001	3.76	2.64-5.36	<.0001	4.90	3.15-7.64	.0001
28 Weeks to birth‡	2.01	1.41-2.86	<.0001	3.21	1.93-5.34	<.0001	3.48	1.72-7.06	.0001
Monochorionic pregnancies only									
Twin-to-twin transfusion†	3.97	2.42-6.53	<.0001	4.14	2.44-7.04	<.0001	5.81	3.25-10.39	<.0001
Oligohydramnios/polyhydramnios†	3.05	1.53-6.07	.002	2.60	1.24-5.46	.01	3.35	1.56-7.18	.002
Velamentous cord insertion	2.95	1.49-5.86	.002	2.58	1.25-5.30	.010	2.32	1.03-5.22	.040
	3.28	1.54-7.00	.002§	3.09	1.38-6.92	.006§	2.77	1.05-7.31	.040‡
Vascular communications	2.48	1.5-4.08	<.0001	2.73	1.60-4.65	<.0001	2.95	1.62-5.37	<.0001
	1.33	0.47-3.76	.590§	1.84	0.65-5.20	.250§	1.21	0.27-5.43	.810

*Models adjusted for parity and placental membranes.
†Models adjusted for parity only.
‡Models adjusted for parity, membranes, and previous fetal growth.
§Model excluding those pregnancies complicated by twin-to-twin transfusion syndrome.

weeks, which increased with advancing gestation. Most studies have shown decreased fetal growth in the third trimester among normal twin gestations.[19-21] Smith et al[22] have shown that suboptimal first-trimester growth may be associated with low birth weight, low birth weight percentile, and premature delivery in singleton pregnancies. Our study suggests that, in twin gestations that are complicated with birth weight discordancy, the "insult" occurs as early as 20 to 28 weeks. Rodis et al[23] reported similar findings in their study by concluding that twins who ultimately become discordant exhibit demonstrable differences as early as 23 to 24 weeks. Monochorionic twins warrant more intense serial sonography surveillance in gestation.

In summary, monochorionicity, inadequate maternal weight gain, and early fetal growth deceleration are the most important antenatal factors that are associated with significant birth weight discordancy. Maternal nutritional intervention in twin gestations early in pregnancy acts as a primary prevention; serial sonography acts as a secondary prevention by identifying those twins who are at risk for significant birth weight discordancy, which allows for appropriate surveillance and intervention.

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Correction

The table was omitted from the article by Tocci et al (Tocci A, Roberts IR, Kumar S, Bennett P, Fisk NM. $CD34^+$ cells from first-trimester fetal blood are enriched in primitive hemopoietic progenitors. Am J Obstet Gynecol 2003;188:1002-10). It is reprinted below in its entirety.

Table. Limiting dilution analysis on M210B4 of 5-week LTC-IC frequency in first-trimester fetal blood and term cord blood $CD34^+$ cells

			LTC-IC Frequency	
Experiment No.	*Cell source*	*Gestational age (wk)*	*Based on CAFC*	*Based on HPC*
1	Fetal	10	2.2	ND
2	Fetal	9	0.8	0.6
3	Fetal	10	0.9	0.7
4	Cord	40	0.4	ND
5	Cord	40	0.9	0.6

Data expressed as 5-week LTC-IC per 100 $CD34^+$ cells. *ND*, Not done.