Twin Pregnancies Complicated by a Single Malformed Fetus: Chorionicity, Outcome and Management

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The objective of this study was to evaluate the impact of one abnormal fetus in a twin pregnancy, to compare impact of chorionicity and clinical outcome of intervention and expectant management. Thirty-seven dichorionic (DC) twins and 18 monochorionic (MC) twins complicated with one malformed fetus were evaluated for gestational age, birthweight and perinatal outcome. Six hundred and forty-two twin pregnancies were evaluated in the database. The control groups consisted of 429 DC and 86 MC twins without anomalous fetus. Mean birthweight and gestational age at birth for DC control group were (n = 429; 2137g and 34.71 weeks), DC study group, n = 37; 2117g (p = .338) and 33.97 weeks (p = .311), and DC study group with major malformations, n = 30; 2019g (p = .289) and 33.3 weeks (p = .01), and showed only significance for gestational age. There was no statistical significance between MC control group, n = 86; 2097g and 34.93 weeks, and MC study group, n = 18; 2237g (p = .338), and 34.42 weeks (p = .502). Because of limited data, the preliminary evaluation for expectant management and intervention, and survival of at least one normal fetus showed no impact. We conclude that, although, all DC twin pregnancies have a risk for preterm delivery, DC twins complicated with major malformation of one twin, have a lower mean gestational age at birth. Preliminary results for intervention does not improve fetal outcome for DC and MC twins and needs further evaluation with greater studies of impact or review.

Keywords: dichorionic, monochorionic, one malformed fetus, expectant management, intervention, outcome

Compared to singleton pregnancies, multiple gestations are at increased risk for preterm delivery, congenital anomalies, and perinatal morbidity and mortality (Botting et al., 1987; Di Renzo et al., 2001). In singleton pregnancies with a congenital anomaly, preterm delivery rates are increased (Iams et al., 2009). In twin gestations, most anomalies are structural malformations and the majority of anomalies involve only one twin (Bryan et al., 1987), which complicates the decision-making procedure for physicians and parents because of the unaffected co-twin.

If the existence of a structural anomaly in one fetus affects the outcome of the pregnancy or has a poor effect on the co-twin, antenatal management options, such as amniodrainage or selective termination may be warranted (Alexander et al., 1997; Leeker & Beinder, 2004; Rustico et al., 2005; Weisz & Rodeck, 2005). Selective feticide (SF) of the anomalous fetus may risk the unaffected fetus and can result in pregnancy loss (Evans et al., 1994; Keith et al., 2002). There are limited reports in the literature regarding the management and perinatal outcomes of twin pregnancies discordant for fetal anomalies (Chang et al., 2004; Gul et al., 2005; Heydanus et al., 1993; Lust et al., 2008; Malone et al., 1996; Malone & D'Alton, 1997; Nassar et al., 2000; Sun et al., 2009; Vandecruys et al., 2006).

The purpose of the current study was to update our clinical results (Gul et al., 2005), and to determine whether or not one abnormal fetus of a twin pregnancy increases the incidence of preterm delivery, to compare the impact of chorionicity, and to compare the clinical outcome of intervention and expectant management (EM).

Material and Methods

Istanbul Bakirkoy Maternal and Children Diseases Hospital is a resident training and referral tertiary center with 18,000 deliveries per annum. All twin pregnancies admitted, followed, and delivered in our maternal-fetal medicine unit between January 2002 and June 2008 were recorded in medical charts and our computer database. A careful ultrasound evaluation was performed to identify or verify fetal

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malformations. Pregnancy details and ultrasonographic findings were also entered into the database. Fetal karyotyping was performed with permission of the parents. Those cases of twin pregnancies with fetal anomalies were reviewed and counseled by the hospital Perinatal-Neonatal Committee.

A major fetal anomaly was defined when it had a significant impact on perinatal morbidity and mortality, or required significant operative intervention to correct. Our study group consisted of cases with fetal abnormalities which were incompatible with life (anencephaly, bilateral renal agenesis, and acardiac-twin reversed arterial perfusion-TRAP), severe disabilities and/or newborns who underwent surgery in the postnatal period (trisomy 21, Turner syndrome, hydrops, infantile polycystic kidney disease, skeletal dysplasia, ventriculomegaly, hydrocephaly, neural tube defects, arachnoid cyst, diaphragmatic hernia, cardiac malformations, omphalocele, and urethral atresia), and finally, mild malformations/ or newborns who underwent surgery after the neonatal period (cleft lip, ureteropelvic junction obstruction, hypospadias, and ambiguous genitalia). The first two groups were assessed as major fetal abnormalities. All monochorionic (MC) twin abnormalities were evaluated as major abnormalities.

In cases of MC twin pregnancies and associated fetal malformations of co-twins, parents were informed about EM and invasive procedures, such as amniodrainage for developing polyhydroamnios or cord occlusion, whereas in dichorionic (DC) placentation, EM or SF were discussed. All twin pregnancies were evaluated for chorionicity in the first trimester by the number of chorionic cavities and in the second and third trimester by the lambda or T-sign, two separately located placentas and/or different fetal sex. Gestational age was based on the last menstrual period and on a first or early second trimester ultrasound.

All abnormalities and placentas were confirmed postnatally or at autopsy. The cases presenting with premature uterine contractions were treated with tocolytics, such as indomethacin or nifedipine, and betamethasone before 34 gestational weeks.

The control group consisted of 429 DC and 86 MC twin gestations delivered during the study period with no sonographically-detected anomalies in either twin. Exclusion criteria were cases with twin-twin transfusion syndrome (TTTS), cases in which both fetuses had a malformation, deliveries before 24 weeks of gestation, and uncompleted data of multiples.

The main outcome measures were gestational age at delivery, birthweight, chorionicity, and perinatal outcome in relation to the fetal anomaly. Statistical analysis was performed using the NCSS 2007 package program (Kaysville, UT, USA). Data were expressed as the mean ± SD or n (%). The Student's t test or Mann–Whitney U-test were used to compare continuous variables and qualitative data were analyzed using the chi-square (χ^2) or Fisher's exact test. A $p < .05$ level was considered statistically significant.

Results

During the study period, our database consisted of 642 twin pregnancies. We had 429 DC normal twins and 37 DC twins with one affected twin. On the other hand, we had 86 regular cases of MC twins and 18 cases of MC twins with one abnormal fetus fulfilling the inclusion criteria. Thirty-four cases were diagnosed as TTTS and 15 cases delivered before 24 weeks gestation were excluded. Three of the 15 cases were complicated because of malformed twins and a decision made for intervention. One case had a misdiagnosis as DC and both twins died after SF (Gul et al., 2005); the second case was a DC twin and had preterm premature rupture of the membranes after SF at 18 weeks and both twins were terminated 2 days after the intervention. The third case was an acardiac twin at 17 weeks gestation and unsuccessful cord occlusion. Three cases were diagnosed because of conjoined twins and another two pregnancies because of hydrocephaly and trisomy 21 in both twins. Eighteen twin pregnancies were excluded because of incomplete data.

The dispersion of fetal anomalies, management, and outcome related to chorionicity are shown in Tables 1 and 2 for DC and MC twins. The mean gestational age at diagnosis was 25.3 weeks (range 12–36 weeks) for DC twins and 25.8 weeks (range 13–36 weeks) for MC twins. The interval from diagnosis to delivery was 8.3 and 8.6 weeks for DC and MC twins, respectively. Delivery before 32 gestational weeks occurred in 65 cases (15.2%) and before 37 weeks in 312 cases (72.7%) in the DC control group.

The study group consisted of 37 DC twins with one affected fetus with malformations. Thirty cases were evaluated as major abnormalities and seven cases as minor abnormalities. In the DC study group, nine cases (24.3%) delivered before 32 gestational weeks and 26 cases (70.2%) before 37 weeks. Five cases of DC twins died spontaneously during pregnancy and eight cases because of SF. Another 10 cases with malformations died after delivery. Two cases died because of prematurity and one case had an intrauterine death at 25 gestational weeks. The remaining 34 normal co-twins survived (91.9%) and were healthy at discharge from the hospital (Table 1). A perinatal mortality rate of 8.1% (3 of 37 cases) for the unaffected fetus in DC twins was calculated.

Delivery occurred before 32 weeks gestation in 12 cases (13.9%) and before 37 weeks in 69 cases (76.5%) in the MC control group. There were three cases (16.7%) that delivered before 32 weeks gestation and 13 cases (72.2%) before 37 weeks in the study group. In the MC study group, all cases were evaluated as major abnormalities with 15 normal co-twins who survived (83.3%) and three cases died during pregnancy or postpartum. The perinatal mor-

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Table 1

Fetal Anomaly, Gestational Age at Delivery and Pregnancy Outcome in Dichorionic Twins With One Fetus With a Malformation

Case	Fetal anomaly	Management	GA at diagnosis	GA at delivery	Outcome	
					Twin with anomaly	Normal co-twin
1	Anencephaly	AD	31	34	IUD	LB
2	Anencephaly	Exp	28	29	NND	NND
3	Lumbosacral meningocele and omphalocele	Exp	26	31	NND	NND
4	Diaphragmatic hernia	Exp	25	36	NND	LB
5	Anencephaly	Exp	29	32	NND	LB
6	Anencephaly	Exp	35	35	NND	LB
7	Anencephaly	Exp	31	37	NND	LB
8	Infantile polycystic kidney disease	Exp	35	37	NND	LB
9	Urethral atresia	Exp	17	28	IUD	LB
10	Trisomy 21	Exp	27	28	NND	LB
11	VSD, PS	Exp	30	31	LB	LB
12	Anencephaly	AD	24	37	IUD	LB
13	Hydrops	Fetocide	18	32	IUD	LB
14	Anencephaly	Fetocide	19	38	IUD	LB
15	Lumbar spina bifida	Fetocide	20	39	IUD	LB
16	Trisomy 21	Exp	12	34	LB	LB
17	Tricuspid atresia	Exp	27	34	LB	LB
18	AVSD, AS, Hydrops	Fetocide	21	38	IUD	LB
19	Lumbar spina bifida	Fetocide	25	32	IUD	LB
20	Omphalocele	Exp	12	29	IUD	LB
21	Hydrops	Exp	24	25	IUD	LB
22	Spina bifida	Fetocide	18	25	IUD	IUD
23	Skeletal dysplasia	Exp	31	34	NND	LB
24	Spina bifida	Fetocide	17	36	IUD	LB
25	Hypoplastic left heart, AVSD	Exp	29	32	NND	LB
26	Encephalomyelocele	Exp	16	31	LB	LB
27	Trisomy 21	Fetocide	16	38	IUD	LB
28	Lumbar spina bifida	Exp	32	33	LB	LB
29	Hydrocephaly	Exp	36	37	LB	LB
30	Ventriculomegaly	AD	31	34	LB	LB
31	Ambiguous genitalia	Exp	34	37	LB	LB
32	Cleft lip	Exp	24	38	LB	LB
33	Unilateral UPJ obstruction	Exp	33	36	LB	LB
34	Bilateral UPJ obstruction	Exp	30	32	LB	LB
35	Bilateral UPJ obstruction	Exp	25	36	LB	LB
36	Hypospadias, bilateral UPJ obstruction	Exp	27	38	LB	LB
37	Hypospadias	Exp	21	34	LB	LB

Note: AD: amniodrainage; AS: aortic stenosis; AVSD: atrio-ventricular septal defect; Exp: expectant management; GA: gestational age in weeks; LB: live birth, IUD: intrauterine death; NND: neonatal death; PS: pulmonary stenosis; UPJ: ureteropelvic junction; VSD: ventricular septal defect.
Cases 1–30: major fetal malformations.
Cases 31–37: mild malformations.

tality rate was 16.7% for the unaffected fetus in MC twin pregnancies. Six cases survived in the abnormal MC group, six cases died because of cord occlusion or alcohol ablation, three cases died during pregnancy, and two cases died after delivery. The last case died after birth at 35 weeks gestation because of anencephaly in which amniodrainage was performed (Table 2).

There was no statistical significance in birth weight and gestational age at delivery between control group twins and normal co-twins (DC or MC twins), including all abnormalities (Table 3). In evaluating major fetal abnormalities and the outcomes of co-twins in these cases (Table 1, cases 1–30 in DC twins, and all cases in Table 2), there was statistical significance in the gestational age at delivery (p = .01), but no signifi-

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Table 2

Fetal Anomaly, Gestational Age at Delivery and Pregnancy Outcome in Monochorionic Twins With One Fetus With a Malformation

Case	Fetal anomaly	Management	GA at diagnosis	GA at delivery	Outcome	
					Twin with anomaly	Normal co-twin
1	Anencephaly	Exp	23	26	IUD	NND
2	Ventriculomegaly	Exp	28	32	NND	LB
3	Acardiac-TRAP	Alcohol	25	37	IUD	LB
4	Anencephaly	Bipolar	13	34	IUD	LB
5	Anencephaly	Exp	27	29	IUD	IUD
6	Arachnoid cyst	Exp	36	38	LB	LB
7	Ventriculomegaly	Exp	34	36	LB	LB
8	Acardiac-TRAP	Bipolar	16	36	IUD	LB
9	Anencephaly	Bipolar	24	34	IUD	LB
10	Ventriculomegaly	Exp	34	35	LB	LB
11	Lumbar spina bifida	Exp	34	36	LB	LB
12	Acardiac-TRAP	Exp	29	33	IUD	IUD
13	Lumbar spina bifida	Bipolar	15	29	IUD	LB
14	Bilateral renal agenesis	Exp	22	38	NND	LB
15	Cystic hygroma, hydrops	Exp	13	36	LB	LB
16	Anencephaly	AD	33	35	NND	LB
17	Acardiac-TRAP	Bipolar	21	38	IUD	LB
18	Ventriculomegaly	Exp	36	38	LB	LB

Note: AD: amniodrainage; alcohol: alcohol ablation; Bipolar: bipolar cord occlusion; Exp: expectant management; GA: gestational age in weeks; LB: live birth, IUD: intrauterine death; NND: neonatal death; TRAP: twin reversed arterial perfusion.
All MC twins with malformation were evaluated as major abnormality.

cance in birth weight. Low birthweight was an expected result for fetuses with malformations, and was a significant finding for all MC and DC twins with malformations, although we excluded fetuses after intervention (n = 29 for DC and n = 12 for MC; p = .0001 for both groups).

There was no statistical significance in birthweight and gestational age at delivery for EM and interventional management for DC and MC twins for the surviving co-twin (Table 4). Perinatal outcome was also insignificant for both treatment options, for at least one surviving normal twin (Table 5).

Discussion

The detection of a malformation in one fetus of a twin gestation poses a dilemma to the parents and the physician. Any intrauterine intervention is associated with an increased risk of premature labor, which in a multiple pregnancy will also involve the co-twin. Three options are available in twin pregnancies with an affected fetus: (1) EM; (2) SF of the anomalous fetus; and (3) termination of the entire pregnancy (Malone & D'Alton, 1997). The last option was not chosen for any of the patients in our study group.

In the literature, the detection rate of anomalies varies as a result of differences in postnatal diagnoses, definition of anomalies, and capability of the perinatologist (Bryan et al., 1987). A supplementary anomaly scan for all types of twins in weeks 19–20 can detect > 80% of structural abnormalities (Sperling et al., 2007). It is a known that chorionicity has a risk of adverse perinatal outcomes, especially for MC twins, mainly because of potential TTTS and intrauterine growth retardation, which also has adverse effects on neonatal outcome (Acosta-Rojas et al., 2007; Hack et al., 2008).

Previous studies have calculated the outcome of one abnormal twin (Chang et al., 2004; Gul et al., 2005; Heydanus et al., 1993; Malone et al., 1996; Malone & D'Alton, 1997; Nassar et al., 2000; Sun et al., 2009) on pregnancies, but none of them have evaluated the additional effect of chorionicity on pregnancy. However, recent studies on anencephaly and prenatal management options have emphasized this issue (Lust et al., 2008; Vandecruys et al., 2006).

In DC twins undergoing EM, there is a high risk of developing polyhydroamnios, which can result in premature contractions and preterm delivery (Lipitz et al., 1995; Nassar et al., 2000; Sebire et al., 1997). In our series we had three cases (3 of 11 cases with EM [27.3%]) that developed polyhydramnios in association with anencephaly or cranial/vertebral pathology. SF is another option, with a main risk of pregnancy loss. The risk involves the technique, the gestational age, and the experience of the perinatologist. Even in the most experienced hands, SF results in pregnancy loss in 3%-16% of cases, with risk increasing with gestational age (Eddleman et al., 2002; Evans et al.,

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Table 3

Birthweights and Gestational Week of Cases at Delivery Based on Study Group

	Birthweight (g, mean ± *SD*)	*p*	Gestational week (weeks, mean ± SD)	*p*
Dichorionic twins — control group (*n* = 858)	2137.58 ± 593.61		34.71 ± 3.14	
Dichorionic twins — normal co-twin (*n* = 37)	2117.02 ± 816.23	0.338	33.97 ± 4.09	0.311
Dichorionic twins — abnormal twin (*n* = 29) §	1462.13 ± 675.96	**0.0001**		
Dichorionic twins with major abnormality — normal co-twin (*n* = 30) ψ	2019.33 ± 765.45	0.289	33.30 ± 4.14	**0.01**
Monochorionic twins — control group (*n* = 172)	2097.33 ± 574.13		34.93 ± 2.78	
Monochorionic twins — normal twin (*n* = 18)	2237.77 ± 734.65	0.338	34.42 ± 3.62	**0.502**
Monochorionic twins — abnormal twin (*n* = 12) ¥	1246.87 ± 741.24	**0.0001**		

Note: §: not include fetuses with fetocide
ψ: cases from 1-30 in Table 1
¥: not include fetuses with cord occlusion or alcohol ablation
Comparison of each parameter was always made with the control group (first line)

Table 4

Comparison of Abnormal Cases with Expectant and Interventional Management for Birthweight and Gestational Weeks at Delivery

	Dichorionic twins					Monochorionic twins		
	Expectant all cases (*n* = 26)	Expectant major anomalies (*n* = 19)	Intervention (*n* = 11) §	p1 (*n* = 11)	p2 (*n* = 7) ¥	Expectant	Intervention	*p*
Birthweight (g, mean ± *SD*)	2081 ± 704	1838 ± 645	2331 ± 882	0.32	0.08	2203 ± 670	2291 ± 879	0.659
Gestational week (weeks, mean ± *SD*)	33.6 ± 3.8	32.4 ± 3.8	34.9 ± 4.7	0.192	0.12	34.26 ± 4,17	34.66 ± 2.84	0.856

Note: § Interventions as fetocide and amniodrainage
¥ Interventions as bipolar cord occlusion, alcohol ablation and amniodrainage
p1: significance between all DC cases with expectant management and DC intervention group
p2: significance between major anomalies DC cases with expectant management and DC intervention group

Table 5

Perinatal outcome for expectant and interventional management with at least one surviving normal twin

	Dichorionic twins					Monochorionic twins		
	Expectant — all cases	Expectant — major anomalies	Intervention	p1	p2	Expectant	Intervention	*p*
Cases	26	19	11	0.72	0.57	11	7	0.39
At least one surviving normal twin	23	17	10			8	7	

Note: p1: significance between all DC cases with expectant management and DC intervention group
p2: significance between major anomalies DC cases with expectant management and DC intervention group

1994). Our results showed statistical significance for an earlier gestational age in DC twins associated with major fetal abnormalities (Table 3), but the results for birth weight were insignificant. Interventions showed no statistical improved outcomes (Tables 4 and 5), as in other studies, for detection and observation of anencephaly (Lust et al., 2008; Vandecruys et al., 2006). However, our total number of 37 DC twins with malformations was not sufficient to conclude a better/final conclusion for management options (Tables 4 and 5), or as a temporary result. The final decision on these two options will depend on the prevailing laws for the particular country and moral, religious, or psychologic issues for each family (Vandecruys et al., 2006). Nevertheless, other studies recommend SF in DC twins be postponed into the third trimester with better outcomes, which is associated with other ethical problems (Shaley et al., 1999).

In MC twin pregnancies, placentation with several vascular connections between both twins demands a special and more complicated treatment policy. SF should be performed by laser, bipolar cord coagulation, or in special circumstances, by alcohol ablation, which is a technically more complex intervention than intracardiac injection of KCL and only applicable in the early second trimester, with only six cases in our

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study (Eddleman et al., 2002; Evans et al., 1994; Lust et al., 2008; Vandecruys et al., 2006). The death of the malformed fetus increases the risk of mortality and morbidity with severe brain damage of the normal co-twin (Evans et al., 1994; Lust et al., 2008; Vandecruys et al., 2006), thus SF appears to be the preferred management option for MC twins. However, previous studies (Lust et al., 2008; Vandecruys et al., 2006) and our results (Table 3–5) showed no advantages in perinatal survival of normal co-twins with interventional treatment for MC twins.

All these studies and outcomes showed an evident bias, resulting from clinical risk estimation made by physicians in each case contributed to safety of a chosen intervention and the potential risk to decide not to intervene, related to their own experience. Randomization can hardly set up for such situations, so retrospective evaluation and review of data in different perinatology clinics is important, also for doctors behavior and counseling strategies. A recent study, evaluating MC and DC twins discordant for anencephaly (Lust et al., 2008) showed improved outcome for DC twins with longer gestations and higher birthweight, but does not reduced perinatal mortality. They could also not put a clear recommendation in MC twins for intervention.

In conclusion, the management of twin pregnancies with one malformed fetus is complex. The first step is to distinguish the chorionicity because of different management options in MC and DC twin pregnancies. Severe abnormalities should also be differentiated. The presence of a fetus with one major fetal malformation in a DC twin gestation increases the risk of preterm delivery. Active management in DC twins improved with gestational age and birth weight, but showed no statistically significance in our study. SF does not have a positive effect on yielding at least one normal fetus at discharge from the hospital. In MC twins it is uncertain whether the best management is expectant or intervention. The preliminary results do not improve fetal outcome with active management, although a possible negative influence should always be kept in mind. However, the number of cases in each group was too small to allow any definitive conclusion, as to the best approach to maximize the chances of survival of the normal co-twin and prevent preterm delivery. In a larger cohort study or meta analysis, a same tendency may very well become statistically significant.

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