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Monochorionic Twin Pregnancy: Retrospective Analysis of Predicted Pregnancy Outcome

Ratko Matijević, Meliha Solak, Nika Kalogjera, Asim Kurjak

Department of Obstetrics and Gynecology, Zagreb University School of Medicine and Holy Ghost Hospital, Zagreb, Croatia

Aim. To assess the accurate establishment of chorionicity, perinatal complications, and outcome of monochorionic twin pregnancies managed in a tertiary referral center in Croatia and compare the findings with data published for other countries.

Methods. The retrospective analysis included data on a total of 24 monochorionic twin pregnancies delivered at the Department between January 1998 and May 2002. The data retrieved from the maternity ward birth register included the ultrasound establishment of chorionicity, demographic data, complications of the pregnancy (presence of twin-to-twin-transfusion syndrome, intrauterine growth restriction, and threatened or actual preterm labor rate), and pregnancy outcome. Perinatal morbidity and mortality were also analyzed.

Results. The establishment of chorionicity by ultrasound was accurate in all 24 monochorionic twin pregnancies. Five twins died in the perinatal period, and two in early neonatal period. The median gestational age at delivery was 35 weeks, ranging 29 to 38 weeks, and median birth weight was 1,990 g, ranging from 740 to 3,000 g. Intrauterine growth restriction was present in 18 cases, whereas twin-to-twin-transfusion syndrome complicated 2 monochorionic twin pregnancies. Symptoms of threatened preterm labor were present in 19 women, whereas actual preterm delivery rate was 16 out of 24.

Conclusion. The diagnosis of monochorionic twin pregnancy can be reliably made by ultrasound. Monochorionic twin pregnancies are characterized by a high complication rate, with threatened and actual preterm labor and delivery as the most common complications. These pregnancies are also accompanied with high perinatal mortality and morbidity.

Key words: *fetal growth retardation; fetofetal transfusion; infant mortality; labor, premature; pregnancy, high risk; twins, monozygotic*

In general, 1-2% of all pregnancies are twin pregnancies (1). They may be either dichorionic and diamniotic if 2 oocytes have been fertilized, or monochorionic and monoamniotic or diamniotic if they have originated from the fertilization of one egg that underwent subsequent mitotic division (1). The incidence of monochorionic pregnancies is constant throughout the world and accompanied by increased risk of complications, including miscarriage (2), preterm birth (3), and congenital anomalies and intrauterine growth restriction (4,5). Perinatal mortality is also significantly higher in monochorionic than in dichorionic twin pregnancies (6). Due to these reasons, it is important to establish the chorionicity in a twin pregnancy as early as possible and provide adequate counseling to future parents about potential complications. Moreover, determination of chorionicity can facilitate pregnancy management and potentially reduce perinatal mortality and morbidity.

The aim of this retrospective analysis was to assess the establishment of chorionicity by ultrasound, pregnancy complications, and outcome of monochorionic twin pregnancies managed in a tertiary referral center in Croatia.

Patients and Methods

We retrospectively analyzed data on 24 monochorionic twin pregnancies delivered at the Department of Obstetrics and Gynecology, Holy Ghost University Hospital in Zagreb, Croatia, between January 1998 and May 2002.

Identification and Data Collection

All women with twin pregnancies were identified in the maternity ward birth register. We reviewed their medical records and collected demographic data, data on antenatal assessment and potential complications, as well as perinatal morbidity and mortality. Demographic data included age, parity, and details about previous pregnancies. Perinatal morbidity was assessed by Apgar score and the length of the hospital and neonatal intensive care unit (NICU) stay. Antenatal assessment data in-

cluded chorionicity, hospitalization rate, the length of hospital stay, presence of twin-to-twin-transfusion syndrome, intrauterine growth restriction, threatened preterm labor, and preterm delivery rate.

Determination of Chorionicity

To establish the chorionicity, the placenta and dividing membrane between twins were examined by the ultrasound. Ultrasound criteria used for the determination of chorionicity in the first and early second trimester were the number of placental sites, the lambda or "T" sign, and the thickness of the inter-twin membrane (<2 or >2 mm) (7). Chorionicity was confirmed by histology examination of the placenta after delivery and by the same sex and blood group of the newborn infants.

Intrauterine Growth Restriction and Birth Weight Discordance

Intrauterine growth restriction was defined as estimated and actual fetal weight below the 10th centile for the gestational age, adjusted for a twin pregnancy (8,9). Discordant growth was determined by the difference in birth weight between the twins (10). According to the percentage of growth discordance, twins were divided into three groups: twins with less then 5% of growth discordance were considered concordant, those between 5% and 25% were defined as mildly discordant, and those with difference more than 25% as severely discordant (10).

Twin-to-Twin-Transfusion Syndrome

The criteria for twin-to-twin-transfusion syndrome were as follows: inter-twin weight discordance of 20% or more, polyhydramnios-oligohydramnios sequence, absent or persistently small bladder of the donor twin and large bladder of the recipient twin, single placental mass and same sex of the fetuses, with or without fetal hydrops. The syndrome was staged by internationally accepted criteria (11,12).

Outcome and Definitions

Perinatal mortality was defined as fetal death between 24 gestational weeks to 7 post-partum day. Perinatal morbidity was assessed by preterm delivery rate, birth weight, mode of delivery, Apgar score after 1 and 5 minutes, and neonatal hospital stay with admission to neonatal intensive care unit (NICU) and neonatal intervention and complications. Preterm delivery was defined as a delivery before 37 week of gestation, whereas early preterm delivery was defined as delivery before 32 weeks. Symptoms of threatened preterm labor included uterine contractions, vaginal bleeding, funneling, shortening, and dilatation of the cervix, diagnosed clinically or by ultrasound.

Statistics

Statistical analysis was performed by using Arcus Pro Stat software (Medical Computing, Aughton, UK). $P<0.05$ was considered statistically significant. The data were analyzed with chi square and Mann Whitney nonparametric tests.

Results

The search of maternity ward birth register identified 24 monochorionic twin pregnancies (Table 1). Among them, 21 were diamniotic and three monoamniotic. Twenty-one were first diagnosed and followed up at our Department, whereas three pregnancies underwent an antenatal assessment and follow up in some other institution but were delivered in our Hospital. Twenty-two women conceived spontaneously, one became pregnant after Clomiphene-induction of ovulation, and one after *in vitro* fertilization. The median maternal age was 29 years (range, 18-39). There was no significant difference in maternal age between monoamniotic and diamniotic group ($p=0.333$, Mann-Whitney nonparametric test). For eight women, it was the first pregnancy. The median gestational age at delivery was 35 weeks (range, 29-38). The median birth-weight of twins was 1,990 g; the median weight of the first twin was 2,055 g (range, 1,600-3,000) and 1,925 g (range, 740-2,570) of the second twin. The difference in birth weight was statistically significant ($p=0.002$, Wilcoxon's signed rank test). Perinatal death was the rarest in the discordance group between 5-25%, whereas preterm delivery before 32 weeks was the most frequent in the severe discordance group (>25%; Table 2).

Chorionicity

The diagnosis of chorionicity was made during the first trimester on the basis of an ultrasound scan

Table 1. Data on demographics, pregnancy assessment, and pregnancy outcome in women with monochorionic twin pregnancy, 1998-2002*

No./ amnionicity	Age (years)	Hospital stay (days)	G	P	GA at US diagnosis (wk)	GA at delivery (wk)	BW discordance (%)	Weight (g) first twin	Weight (g) second twin	Complications	Mode of delivery
1/MA	28	21	1	0	27	37	26	2,550	1,900	IUGR-1	NVD
2/DA	39	26	3	2	19	37	14	2,300	1,970	IUGR-1, TPL	NVD
3/DA	39	15	2	1	15	36	14	3,000	2,570	TPL	NVD
4/DA	27	31	3	2	38	38	4	2,400	2,500	None	NVD
5/DA	26	22	1	0	33	37	1	2,550	2,570	TPL	CS
6/DA	28	30	2	1	17	32	18	1,600	1,320	IUGR-2, TPL, TTTS	CS
7/DA	30	93	1	0	26	37	9	2,050	1,870	IUGR-2, TPL	CS
8/DA	35	66	1	0	17	37	0	2,190	2,200	IUGR-1, TPL	CS
9/DA	26	14	2	1	12	34	13	2,250	1,950	IUGR-1, TPL	CS
10/DA	27	95	4	0	25	33	13	1,720	1,500	TPL	CS
11/DA	34	40	3	0	25	29	50	1,480	740	IUGR-1, TPL	CS
12/DA	25	28	1	0	7	33	10	2,050	1,850	TPL	CS
13/DA	29	45	3	2	11	36	6	1,980	2,100	IUGR-1, TPL	CS
14/DA	36	15	4	2	35	35	12	1,900	2,150	IUGR-1,TPL	CS
15/DA	29	15	3	2	17	35	12	2,060	2,350	IUGR-1, TPL	NVD
16/DA	25	6	2	1	15	37	4	2,200	2,300	TPL	NVD
17/DA	35	2	3	2	37	38	17	2,600	2,150	IUGR-1	NVD
18/MA	37	21	2	0	10	36	5	2,000	1,900	IUGR-1, TPL	CS
19/MA	31	16	2	0	20	34	12	1,940	1,700	IUGR-2	NVD
20/DA	21	12	1	0	34	35	13	2,480	2,150	IUGR-1, TPL	CS
21/DA	27	36	1	0	25	35	34	2,200	1,450	IUGR-2, TPL	CS
22/DA	30	7	2	0	15	31	37	1,940	1,230	IUGR-1	CS
23/DA	32	32	1	0	11	36	8	2,000	1,850	IUGR-2, TPL	CS
24/DA	24	53	2	0	18	32	49	1,970	1,000	IUGR-2, TPL, TTTS	CS

*Abbreviations: DA – diamniotic twin, MA – monoamniotic twin, G – gravidity, P – parity, GA – gestational age, US – ultrasound, BW – birth weight, IUGR – intrauterine growth restriction (1 of one twin, 2 of both twins), TPL – threatened pre-term labor, TTTS – twin-to-twin transfusion syndrome, NVD – normal vaginal delivery, CS – cesarean section.

Table 2. Complications arising from discordant growth in 24 pairs of monochorionic twins

Complications	Discordance (No. of twins)		
	<5% (n=4)	5-25% (n=15)	>25% (n=5)
Perinatal death	2	1	2
Threatened preterm labor	3	13	2
Delivery before 32 weeks	0	0	2
Delivery between 32-37 weeks	0	12	2
Cesarean section	2	9	4

(ie, before 14 weeks) in five women, between 14 and 24 weeks in nine women, and after 24 weeks in 10 out of 24 women with twin pregnancies. In seven of them chorionicity was determined after 24 weeks of pregnancy due to a late hospital referral, and in thee women, who did not have antenatal assessment at our Department, the diagnosis was made on placental examination after delivery.

Pregnancy Complications and Outcome

As shown in Table 3, the threatened preterm labor was found in 19 out of 24 women with twin pregnancies, and actual preterm delivery rate before 37 weeks of pregnancy occurred in 16 of them (3). Out of these 16 preterm deliveries, 14 were between 32 and 37 weeks and two before 32 weeks of gestation. There were 15 intrauterine growth restriction cases in diamniotic group (n=21), and three intrauterine growth restriction cases in all three monoamniotic pregnancies (p=0.724, chi-square test). Growth restriction of one of the twins was found in six cases, and of both twins in 12 cases (p=0.142, chi-square test). All 18 cases of growth restriction diagnosed antenatally were confirmed postnatally by comparing the actual birth weight to the expected one for the gestational age.

Table 3. Complications and outcome of 24 monochorionic twin pregnancies

	No. of twin pregnancies
Complications:	
intrauterine growth restriction	18/24
threatened pre-term labor	19/24
pre-term delivery:	16/24
<32 weeks	2/16
>32 weeks	14/16
twin-to-twin transfusion syndrome	2/24
cesarean section	16/24
normal vaginal delivery	8/24
Outcome in twins:	
neonatal intensive care unit admission	37/48
perinatal mortality	5/48
early neonatal mortality	2/48

All but three women with monochorionic twin pregnancies were hospitalized during the course of pregnancy. The median length of antenatal hospital stay was 52 days (range, 4-85). Fetal demise occurred during the antenatal period in three out of 48 fetuses. Twin-to-twin-transfusion syndrome was diagnosed in two pregnancies. One pair of twins delivered at 32 weeks after a pregnancy complicated by severe twin-to-twin-transfusion syndrome died within seven days. The first one, with the birth weigh of 1,000 g, died because of meconium peritonitis and necrotizing enterocolitis. The second one, with the birth weight of 1,970 g, died because of multi-organ failure, with prominent acute renal insufficiency. The other pair of twins was delivered at 32 weeks of gestation, with birth weight of 1,600 g and 1,320 g respectively. The recipient twin had pronounced polyhydramnios, whereas the donor twin had persistent foramen ovale suspected after delivery and confirmed by post mortem examination. The indication for delivery was terminal fetal bradycardia on cardio-tocography (CTG) recording of the donor twin. After emergency cesarean section, resuscitation was unsuccessful and donor twin died, whereas the recipient is still alive and well.

Labor

The onset of labor was spontaneous in seven cases, and induced in a single case because of achieved gestational age of 38 weeks and favorable finding on the vaginal examination. The rest of the women delivered their twins via cesarean section. One of the indications for cesarean section was suboptimal fetal monitoring in six cases, diagnosed either by CTG in four cases (the presence of unprovoked decelerations with reduced variability or complicated fetal tachycardia with decelerations) or ultrasound/Doppler assessment of fetal circulation in two cases (reversed blood flow in umbilical artery). Other indications for caesarian section included abnormal fetal position in labor in six, pre-eclampsia in one, and maternal reproductive history in three cases.

Neonatal Problems

Regarding neonatal complications, the average length of hospital stay for newborn twins included in the study was 21 days (range, 4-145). One baby was excluded from the analysis because it was transferred to another institution due to the surgical management of omphalocele. The commonest indication for NICU admission was low birth weight and prematurity requesting close neonatal surveillance and monitoring. Endotracheal intubation and mechanical ventilation was indicated in 5 newborns. The indications were extreme prematurity, hypoxia, and respiratory distress syndrome. The average length of NICU stay was 19 days (range, 4-145), with 29 newborns spending more than 10 days in NICU.

The mean Apgar score at 1 minute for the first twin was 8.3 (range, 5-10), and 8.0 (range, 5-10) for the second twin (p=0.76). At 5 minutes, the median Apgar score for the first twin was 9.2 (range, 6-10), and 9.1 (range, 8-10) for the second twin (p=0.87). Among the twins included in the study, only two had 5 minute Apgar score less than 7. Both were delivered from the pregnancy complicated by twin-to-twin-transfusion syndrome, needed mechanical ventilation, and had signs of intra-cranial hemorrhage. There was a single case of the fetal chronic lung disease. Six infants developed sepsis, and five more had neonatal respiratory infection, whereas three had intra-cranial hemorrhage. The most common complication was

hyperbilirubinemia, occurring in 11 of the newborns, and anemia, which was present in seven infants.

Discussion

During the study period, there were 173 twin pregnancies delivered in our Department, giving an overall twins incidence of approximately 2%. This is on the upper margin of the expected incidence of twins in general population, but as our hospital is a tertiary referral center with assisted reproduction unit, this difference was expectable. Overall incidence of monochorionic twins during the study period was 0.3%, ie, within the expected limits of 0.3-0.5% of all pregnancies (6). The incidence of monochorionic twins compared to all twins delivered was 13%, slightly below the expected incidence of 20-30% (13). This finding was also expectable because in the recent years the number of twin pregnancies from assisted conception procedures has increased, and most such pregnancies are dichorionic.

Although the number of women with monochorionic twin pregnancies included in our study was relatively small, we found birth weights of delivered twins similar to those reported by Minakami et al (14), but slightly different from those found by Dube et al (1). Monochorionic twin pregnancy is characterized by high perinatal mortality mostly related to prematurity and placental morphologic characteristics, including complex vascular communication between the twins associated with twin-to-twin-transfusion syndrome and the tendency for the common placenta to be shared either symmetrically or asymmetrically (15). Perinatal mortality in our study was approximately 10%, which is excellent in comparison with the reported perinatal death rate as high as 50% (6). The reason for such a low perinatal mortality rate could be a relatively low number of twin pairs included in our study and low incidence of twin-to-twin-transfusion syndrome, but it could also be due to close fetal surveillance of every pregnant woman with monochorionic twin pregnancy, mostly in the hospital settings. The protocol for monochorionic twin pregnancy at our Department includes inpatient assessment on regular intervals. The first admission is planned for early second trimester and includes a detailed ultrasound scan, confirmation of chorionicity, ultrasound assessment of the cervix to detect possible signs of cervical insufficiency, and infection screening (cervical swabs, full blood count, C reactive protein, and interleukins). The second hospital admission is planned after completed 24 weeks of gestation and includes assessment of fetal growth, full blood count, C reactive protein, and administration of steroids. Ultrasound assessment of fetal growth and fetal well being by Doppler ultrasound of the blood flow in fetal circulation is performed twice a month as an outpatient procedure and steroids are re-administered at 30 weeks of gestation. After 34 weeks, all women with monochorionic pregnancy are admitted to the Department and followed up until delivery. In normal circumstances, they undergo non-stress test on daily basis and ultrasound assessment including biophysical profile and Doppler studies every week. As there is no day assessment unit in our hospital, this protocol results in high hospitalization rate and high number of inpatient bed days. All women with monochorionic twins are electively delivered not later than 38 weeks of pregnancy (16) and, since recently, all monoamniotic twins are delivered by elective caesarian section not later than 36 weeks.

It is very important to determine successfully the chorionicity in twin pregnancy because the management and antenatal care for monochorionic and dichorionic twin pregnancies differs (7). Therefore, we use ultrasound examination in the first or early second trimester, following the defined criteria (7). In our experience, ultrasound is an excellent diagnostic tool to make precise diagnosis of chorionicity (15).

The adverse outcome of monochorionic pregnancies is strongly associated with high incidence of preterm delivery (17). In our study, threatened preterm labor and preterm delivery were the most frequent antenatal complications (79% and 67%, respectively). Since we do not use routine prophylactic tocolytics, this difference is acceptable and reasonable. The incidence of preterm delivery was even more prominent in the subgroup of twins with discordant growth because all of them were delivered before term; however, more frequent obstetric intervention could be a possible source of bias. Discordant growth can be caused by hemodynamic misbalance caused by placental vascular anastomoses, fetal anemia, function of the uterine capacity to carry twins, decreased placental weight, and increased umbilical cord abnormalities (10,18,19). For the prediction of pregnancy outcome, 25-30% birth weight difference was found to be crucial for the most clinically relevant outcomes (ie, antenatal, perinatal, and early neonatal death; congenital anomalies; and periventricular leukomalacia) (10,20). There were five pairs of severely discordant twins in our study. All of them had a high incidence of neonatal morbidity and high rate of pregnancy complications, including early preterm delivery (before 32 weeks) and twin-to-twin-transfusion syndrome. Only one pair of twins in this subgroup was not delivered by caesarian section. We observed that symptoms of threatened preterm labor were more frequent in mildly discordant than in severely discordant twins. We believe that this difference is also caused by obstetric intervention, as four out of five severely discordant twins were delivered by elective caesarian section because of fetal hypoxia suspected either by cardiotocography recording or Doppler assessment of the blood flow in fetal circulation.

Growth restriction is a well-recognized phenomenon of monochorionic pregnancy. Intrauterine growth restriction and lower birth weights are usually affecting both twins (1,14). Severe intrauterine growth restriction occurs in approximately 25% of multiple gestations, with increased rate in monochorionic pregnancies. In our study, intrauterine growth restriction was present in 75% of monochorionic twins and was confirmed postnatally. Growth restriction was more frequent in monoamniotic pregnancies (100%) and less frequent in diamniotic pregnancies (71%).

There were six pairs of twins where only one twin was growth-restricted despite the absence of the obvious clinical signs of twin-to-twin-transfusion syndrome. All of them were diamniotic. Such selective intrauterine growth restriction occurs in 12.5-25% of all monochorionic pregnancies (21). However, this is a very important observation because it indicates close surveillance of the pregnancy. Such a growth-retarded twin is at higher risk of fetal death, which always carries a high risk of the concomitant death of the other twin and up to 30% risk for neurological complications (22).

Twin-to-twin-transfusion syndrome is the result of transfusion of blood from one fetal twin to another. It occurs when there is an anastomosis between placental vasculature. These anastomoses are present in monochorionic placenta, but twin-to-twin-transfusion syndrome exists in only 5-15% of monochorionic twin pregnancies and is associated with a perinatal mortality >80% during mid trimester if left untreated (23).

In our study, the incidence of twin-to-twin-transfusion syndrome was 8%. Both cases were managed conservatively, and there was no need for an amniodrainage since polyhydramnios was not excessive. The median gestational age at the onset of symptoms was 25 weeks in one pregnancy, and 29 weeks in the other, and both twin pairs were delivered at 32 weeks of gestation. Only one of these four twins survived; it is now three years old and has no major complications. Berghella et al (24) reported perinatal survival of untreated cases of 30% in cases where twin-to-twin-transfusion syndrome had been diagnosed before 28 weeks of pregnancy. We also analyzed post-delivery hospital stay, NICU stay, Apgar score, and neonatal complications to evaluate perinatal morbidity. It was reported that newborns with 5 minute Apgar score below 7 have increased perinatal mortality and neurologic morbidity (ie, cerebral palsy, epilepsy, and mental retardation) (25). In our study, only two newborns had Apgar score less than 7 after five minutes and both of them had serious neonatal complications including interventricular hemorrhage.

With all the limitations related to the retrospective design of the study and small number of cases, we can say that monochorionic twin pregnancy in Croatia is characterized by high perinatal mortality and morbidity, as well as pregnancy and neonatal complications. Early diagnosis of chorionicity, early referral to a tertiary health care centre, and close monitoring of such pregnancies are crucial for the improvement of pregnancy outcome.

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Correspondence to:
Ratko Matijević
Department of Obstetrics and Gynecology
Holy Ghost General Hospital
Sveti Duh 64
10 000 Zagreb, Croatia
ratko.matijevic@zg.tel.hr