10.5005/jp-journals-10006-1439

ORIGINAL ARTICLE

Relationship of Fetal Complications in Monochorionic Diamniotic Twin Pregnancy with Placental Site Cord Insertion: A Retrospective Analysis of 30 Months Data in a Referral Fetal Medicine Center

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ABSTRACT

Aims: Among the increasing twin gestations, monochorionic twins occur in about 12 to 15% of all twin gestations and the occurrence is about 1 in 20 in assistive reproductive technology pregnancies. Early detection of twin to twin transfusion syndrome (TTTS) or selective intrauterine growth restriction (sIUGR) aids the obstetrician in counseling and therapy as required.

Materials and methods: This is a retrospective cohort study of monochorionic diamniotic (MCDA) pregnancies referred from January 2011 to June 2013. Those cases that had crown rump length and nuchal translucency measurements done in the first trimester and then at least one subsequent scan at >16 weeks, at the institution were chosen. The objective was to assess the utility of placental site of cord insertion in early second trimester scan to predict fetal outcome in monochorionic twin pregnancy.

The patient characteristics, placental cord insertion site, and neonatal outcomes were compared among TTTS, sIUGR, and normal groups.

Discussion: Of 89 MCDA pregnancies, only 60 had been referred for second trimester scan. Among these, in 48 (80%) of pregnancies, both babies were delivered and discharged alive and well. Cord insertions that were eccentric or central were classified as "type A". Marginal and velamentous cord insertions were classified as "type B". Pregnancies with both types A and B insertions were called "concordant cord insertions group" and the others were classified as "discordant cord insertions" group. The two groups were compared to look for the pregnancy complications – TTTS or sIUGR.

Results: The concordant cord insertions (n=33) had 84.8% of pregnancies having a normal pregnancy and 12.1 and 3.1% developing sIUGR and TTTS respectively. The discordant cord insertion group (n=27) had 59.2% with normal findings at the second scan and 14.8 and 26% developing sIUGR and TTTS respectively. The incidence of TTTS was 30% in twin pairs with discordant cord insertions and 3% in twin pairs with concordant cord insertions (p=0.0158). Cord insertions did not influence the occurrence of sIUGR in our study. (p=0.69). Significantly more pregnancies with concordant cord insertions had normal outcomes (p=0.02).

Conclusion: Determination of placental site of cord insertion should be incorporated into protocols of twin pregnancy care. This is a window of opportunity to gain valuable information regarding the pregnancy. Further large studies incorporating fetal biometric and Doppler parameters could show the relative utility of each parameter in the detection of MCDA vascular complications. If the MCDA pregnancy can be classified as "low risk" then reassessment intervals can be extended. This would help to reduce patient stress and costs involved in repeated scans.

Keywords: Cord insertion, Monochorionic diamniotic twins, Outcomes, Twin to twin transfusion.

How to cite this article: Andrew C, Suresh I, Seshadri S. Relationship of Fetal Complications in Monochorionic Diamniotic Twin Pregnancy with Placental Site Cord Insertion: A Retrospective Analysis of 30 Months Data in a Referral Fetal Medicine Center. J South Asian Feder Obst Gynae 2016;8(4):304-308.

Source of support: Nil

Conflict of interest: None

Date of received: 05 May 2016

Date of acceptance: 19 July 2016

Date of publication: October 2016

INTRODUCTION

Monochorionic twins occur in about 12 to 15% of all twin gestations, and the occurrence is about 1 in 20 in assistive reproductive technology (ART) pregnancies.[1] Monozygotic twin pregnancies are more complex because the interests of both twins are intertwined due to vascular anastomoses.[2] Ultrasound determination of chorionicity in the first trimester screening (FTS) is done by observation of number of placental masses and presence of the "lambda" or "T" sign. Chorionicity can be determined in 99.8% of the cases, with 100% sensitivity and 99.8% specificity by these methods.[3]

Monochorionic diamniotic (MCDA) twins are variably reported to be at 2- to 5-fold risk of perinatal mortality compared to dichorionic diamniotic (DCDA) twins.[4] Placental sharing and anastomoses between different vessels from both sides of the placenta can cause transfusion imbalances. These transfusion imbalances result in twin to twin transfusion syndrome (TTTS) or selective intrauterine growth restriction (sIUGR). Twin to twin transfusion syndrome may develop acutely, precipitating

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fetal demise within a few hours or days. Although acute conditions cannot be diagnosed, development of complications has subtle preceding findings that can be used to triage fetuses. Co-twin demise can result in catastrophic events in the fetus, resulting in demise or permanent brain damage. This influences timing of delivery and intrauterine therapeutic options.[5]

This data set is part of a study in which the first trimester and early second trimester scan in MCDA pregnancies were compared to determine the prediction of development of complications. In the second trimester along with fetal parameters, determination of cord insertion has been described to have a role in risk stratification. The combination of all factors may stratify obstetric risk within the MCDA cohort and aid in further counseling.[6]

Intrauterine growth restriction (IUGR) is defined as an estimated fetal weight (EFW) of one twin less than the 10th percentile for the period of gestation. Selective IUGR is discordancy in growth within the genetically identical twin pair. This condition has discordance between the weights of the two fetuses. The percentage weight discordance is calculated by difference in weights of the fetuses divided by that of the larger fetus multiplied by 100. Various definitions of significant discordance have been proposed.[7]

Although the growth discordance seen in both sIUGR and TTTS is highly unlikely due to different genetic potential of the fetuses, there could be an unequal split up of the blastomeres after twinning. This inequality may occur in the cells forming the trophoblasts and placenta.[8-10] The inequality in placental territory size may lead to discordance in the fetal weights when compared to normal controls. Here, the smaller twin is seen to have a smaller territory of the placenta.[10] This may form the pathologic basis of the etiology of sIUGR and growth discordance.

MATERIALS AND METHODS

This is a retrospective cohort study of cases, both routine and referred, over a period of 2½ years from January 2011 to June 2013. The study was carried out in the twin and fetoscopy unit at a Tertiary Referral Institute of Fetal Medicine. The patients to be studied were chosen by using the computerized database (SONOCARE, Medialogic) for retrieval of all the cases of monochorionic twin gestation within the study period. Those cases that had crown rump length (CRL) and nuchal translucency (NT) measurements done in the first trimester and then at least one subsequent scan at > 16 weeks, at the institution were chosen. These cases were then reviewed individually and those meeting the inclusion criteria were selected.

The objective of this study is to assess the placental site of cord insertion in early second trimester scan to predict fetal outcome in monochorionic twin pregnancy, and compare this with the available literature. The data set was extracted to study other multiple parameters in MCDA twins, including first trimester CRL and NT discrepancies, second trimester fetal biometry, liquor, and Doppler. In this study the relationship of location cord insertion in the placenta to the development of TTTS and sIUGR and the pregnancy outcomes alone will be discussed. The other factors have been described elsewhere.

First trimester screening scan was performed by Fetal Medicine Foundation accredited operators. The CRL and NT measurements were noted. Monochorionicity was diagnosed with the presence of a single placental mass, absence of lambda sign, and presence of "T" sign. The pregnancy date by last menstrual period was confirmed or reassigned using the CRL of the larger fetus if a 7 day discrepancy was noted. *In vitro* fertilization pregnancies were dated based on the embryo transfer date. Population-specific nomograms of CRL used for singleton pregnancies were used.

All patients were advised review at 16 weeks followed by fortnightly appointments in the absence of any complications. However, the second scan could be performed only when the patient was referred back by the attending obstetrician. In the second visit, placental site of cord insertion was noted. Estimated fetal weight was calculated using the Hadlock formula, and umbilical artery, middle cerebral artery, and ductus venosus were assessed by Doppler. The location of cord insertion was determined using power Doppler and tracing the cord to the placental insertion site. This was classified as velamentous, eccentric (more than 2 cm from the placental edge), marginal (less than 2 cm from the placental edge), and central.

Twin to twin transfusion syndrome was diagnosed with donor twin with deepest vertical pocket (DVP) of ≤2 cm and polyhydramnios in the recipient with DVP ≥8 cm. Selective IUGR was defined as 15% or greater difference in the birth weight for live born twins. The final confirmation of the diagnosis was done by one of the two unit heads. All the scans were performed using the Voluson® 730 Expert GE or Voluson® E6 GE.

Laser coagulation of vascular anastomoses was offered to patients with TTTS diagnosed at 26 weeks or less. For pregnancies with gestational age > 26 weeks, amniodrainage, elective preterm delivery, or exceptionally by cord coagulation in selected cases were offered. The management was based on technical feasibility and parental decisions.

The timing of delivery and mode of delivery were decided by referring obstetricians. The perinatal outcome was obtained over telephone from the parents or from the maternity units. The information was elicited from the families on voluntary basis and confidentiality assured. Approval was obtained from the ethics committee for communicating with the patients.

ANALYSIS

The patient characteristics, placental cord insertion site, and neonatal outcomes were compared among TTTS, sIUGR, and concordant groups. Location of the placenta was classified into groups and the outcomes were compared across the various groups. Preliminary analysis was made on Microsoft Excel. Fisher's exact test was used to compare the variables. A level of 0.05 was taken as statistically significant. Analysis was performed using Statistical Package for the Social Sciences (SPSS) version 11.5 (SPSS Inc., Chicago, USA).

RESULTS

A total of 529 MCDA pregnancies underwent FTS during the study period. Of the 97 women who fitted the inclusion criteria, outcome data was unavailable for eight. Among the remaining 89 patients, analysis of placental cord insertion was done in 60 patients who were scanned before 22 completed weeks of gestation. Due to technical limitations caused by fetal crowding, placental site of cord insertions could not be noted for older gestational ages and these were excluded from analysis. In total, almost 32% of cases did not have a 16 to 18 week scan for evaluation.

Cord insertions were classified as "type A", if the distance of insertion from the edge to the placenta was more than 2 cm (eccentric and central). The cord insertions that were less than 2 cm from the edge were classified as marginal. The marginal and velamentous cord insertion groups were grouped together as "type B." Then the pregnancies were separated into two subsets according to whether the cord insertions of both twins was similar (either both types A or B) which was called the concordant cord insertions group; or whether one twin was in type A and one cord insertion was in type B, which was called the discordant cord insertions group (Table 1). The two groups were compared to look for the development of TTTS or sIUGR.

Among the 60 pregnancies, in 48 (80%) pregnancies, babies were delivered and discharged alive and well. In 12 pregnancies (20%), pregnancy loss occurred. Live birth was recorded if the baby was alive at the time of discharge from the hospital.

Table 1: Cord insertions – study group split up (numbers in brackets are percentages of the cases within cord insertion subgroups)

	Cord insertion		
Study group	*Concordant n = 33 (%)*	*Discordant n = 27 (%)*	*Total*
Low risk	28 (84.8)	16 (59.2)	44
sIUGR	4 (12.1)	4 (14.8)	27
TTTS	1 (3.1)	7 (26)	6

The two subsets, i.e., concordant and discordant cord insertions which were classified as described above, were analyzed with regard to the development of sIUGR and TTTS and the pregnancy complications encountered (Table 2). The pregnancies with concordant cord insertions (n = 33) had 84.8% of pregnancies having a normal pregnancy and 12.1 and 3.1% developing sIUGR and TTTS respectively (Table 1). The pregnancies with a discordant cord insertion (n = 27) had 59.2% with normal findings at the second scan and 14.8 and 26% developing sIUGR and TTTS respectively (Table 1).

The cord insertion subsets were analyzed with regard to the outcomes of the pregnancies (Table 3). More pregnancies with both cord insertions concordant had normal outcomes. There was a significantly larger number of patients with discordant cord insertions having poor outcomes. This was statistically significant (p = 0.02) (Table 3). Comparing the outcomes of the pregnancies with respect to cord insertion between the two subgroups, there was a significant difference in the outcomes of the pregnancies with those having a discordant cord insertion having a poorer outcome than those with concordant central cord insertions. This reflects the poor outcomes seen in the twins who developed TTTS all of whom had loss of the entire pregnancy.

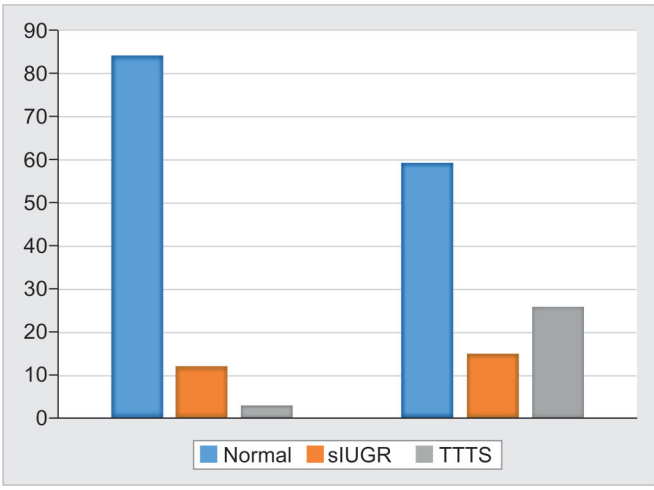
Ninety percent of pregnancies with both cord insertions concordant in location had a normal outcome (p = 0.02). The incidence of complications, such as TTTS

Table 2: Cord insertions and development of complications (numbers in brackets are percentages of pregnancies with complications among cord insertion subsets)

Cord insertion	*Low risk (n = 44)*	*TTTS (n = 8)*	*p-value*
Concordant (n = 29)	28 (96.6%)	1 (3.4%)	0.0158
Discordant (n = 23)	16 (66.3%)	7 (43.7%)	
Cord insertion	*Low risk (n = 44)*	*sIUGR (n = 8)*	*p-value*
Concordant (n = 32)	28 (87.5%)	4 (12.5%)	0.69
Discordant (n = 20)	16 (80%)	4 (20%)	

Table 3: Cord insertions and pregnancy outcome

	Outcome		
Cord insertion	*Fetal loss*	*Good outcome*	*p-value*
Concordant	3	30	0.02
Discordant	9	18	



Graph 1: Placental site of cord insertion and pregnancy complications

and sIUGR was more in the discordant cord insertions than in those with concordant velamentous insertions in this study (Graph 1).

DISCUSSION

The finding that when both cord insertions are concordant, the development of TTTS is reduced is similar to the study by Machin et al.[11] They described 60 placentae of MCDA pairs with birth weight discrepancy based on cord insertions seen after delivery. Velamentous cord insertions were seen in 45%, and discordant cord insertions were seen in 53% of those fetuses with >20% birth weight discrepancy and perinatal demise. Lewi et al[5,12] found that the site of cord insertion remained a significant variable in the prediction of poor outcome with an odds ratio = 3 ($p = 0.03$). When MCDA twins with concordant and discordant growth were compared, unequal placental sharing ($p < 0.001$) and velamentous placental cord insertion ($p = 0.0001$) are seen more commonly in cases with discordant growth.[10,13]

Weight discordance has also been shown to correlate with velamentous or eccentric cord insertion, which result in an unequal sharing of the placental territories.[9,10] The cord insertion may be velamentous due to a shift in the vascular equator or may be the cause of sIUGR.[11] Machin et al[11] classified cord insertions based on location and found that a central/velamentous combination had high rates of growth discordance >20% and poor outcomes. De Paepe et al[14] studied 319 MCDA placentae and showed that birth weight was more discordant in velamentous cord insertion and unequal placental sharing when compared with the placentae of babies which were concordant for birth weight. Both these studies concluded that determining the presence of a velamentous cord insertion could be useful in triaging pregnancies for closer monitoring.

Another study of 178 twin pairs showed that the MCDA twins complicated by early-onset growth discordance had a greater incidence of unequal sharing of placenta and larger arterio-arterial anastomoses, in contrast to those of twin with late onset discordant growth.[6]

In our study, the twin pairs with concordant cord insertions showed low incidence of TTTS and resultant good outcome. Among the twin pairs with discordant cord locations, there was an increased incidence of sIUGR among those with discordant cord insertions (Table 2). Among the concordant cord insertion fetuses, there was a 14% incidence of sIUGR compared to a 25% incidence among the pairs with discordant cord insertions. However, as the number of affected fetuses in both arms of this group was small, the numbers did not achieve statistical significance. The fetal outcomes in the sIUGR group were more favorable than those in the TTTS group and hence the overall outcomes of the group with concordant insertion were favorable and this was statistically significant (Table 3) with a p-value of 0.02.

CONCLUSION

Determination of placental site of cord insertion is important in the early second trimester examination of the MCDA pregnancy and should be incorporated into the protocols of twin pregnancy care. There is a need for dissemination of this information. This study revealed that in about 30% of known MCDA pregnancies there was no referral for early second trimester scan. This results in loss of a window of opportunity to gain valuable information regarding the pregnancy. The finding of both concordant placental cord insertions provides reassurance if other parameters are also normal that the pregnancy is likely to have an optimal outcome. The limitations of the study include that although the cord insertions were verified in pregnancies which required fetoscopy, the cord insertions could not be confirmed in all pregnancies because deliveries occurred in various centers across the country.

There is scope for further prospective studies incorporating all these parameters and post-natal placental examination to determine if the findings are optimal, the MCDA pregnancy can be classified as "low risk" and reassessment intervals can be extended. This would help to reduce patient stress and costs involved in repeated ultrasound examinations.

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