Original Article

Placental pathology in birth weight discordant monochorionic and dichorionic twins

A. A. H. Priyani¹, N. M. Gamage¹, T. Dias², M. V. C. de Silva¹

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¹Department of Pathology, Faculty of Medicine, University of Colombo, Sri Lanka; ²Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Kelaniya, Sri Lanka

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Summary

Identification of placental parenchymal lesions (PPL) associated with birth weight (BW) discordance will be helpful in understanding the pathogenesis of BW discordance in twins. The aim of this study was to evaluate such association in monochorionic (MC) and dichorionic (DC) twins. This was a single centre, prospective study of placentas of consecutive twin deliveries. Gross and microscopic examination of placentas were done according to a protocol. Association of PPL count with the degree of BW discordance and the significance of the presence of each PPL in the lighter twin (LT) in comparison to the heavier twin (HT) were analysed. Of the 92 placentas studied 57.6% were DC and 42.4% were MC. Significant BW discordance was present in 28% (n=39) of MC and 26% (n=53) of DC twins. There was a positive correlation with the PPL count of the LT and the mean BW discordance in both MC (p=0.032) and DC twins (p=0.043). Increased incidence of distal villous hypoplasia in the placental territory of the LT in comparison to the HT was statistically significant in BW-discordant DC twins (P=0.04) and in both BW-concordant and BW-discordant MC twins (p=0.02 and p=0.03 respectively). In conclusion, this single centre prospective study showed a strong association between the PPL count and the degree of BW discordance in both MC and DC twins. Increased incidence of distal villous hypoplasia in the placental territory of the LT in comparison to the HT was statistically significant.

Keywords: twin, birth weight discordance, placental pathology, parenchymal lesions

Introduction

Twin pregnancy provides some of the greatest challenges in obstetric care and foetal medicine today. The rate of twin births has dramatically increased in the last decade,

mainly as a result of the development of assisted reproductive technology. One of the major complications unique to twin pregnancy resulting in significant morbidity and mortality is discordant foetal growth. Birth weight (BW) discordance is defined as the difference in birth weight of twins, which is expressed as a percentage of the weight of the larger twin (1). The BW difference of more

Author for correspondence: A.A.H.Priyani (MBBS, Dpath, MD), Department of Pathology, Faculty of Medicine, University of Colombo, Sri Lanka. E mail: priyaniaah@gmail.com

than 15-25% is used as definition for discordance (2). The significant BW discordance has been taken differently in different studies and most investigators have settled on either 15%, 20% or 25% as the cut off for significant BW discordance with clinical correlates to support all three.

Multiple factors may contribute to BW discordance including maternal, foetal and placental factors. Placental factors associated with BW discordance have been extensively investigated in monochorionic (MC) twins and twin-to-twin transfusion syndrome has been identified as an important placental factor (3). Other placental characteristics shown to be associated with BW discordance in MC twins are unequal sharing of placental territories and velamentous cord insertions (3-8). In a few studies done including both MC and dichorionic (DC) twins, decreased placental weight, velamentous cord insertion and single umbilical artery have been found significantly more in placentas of smaller BW discordant fetuses (9,10). Though gross placental characteristics of twin pregnancies have been investigated in many studies, systematic histological examination of placental parenchyma for pathological changes in MC and DC twins have been investigated in only a few studies (9-13).

The maternal and foetal placental vascular trees are dynamic structures which can be significantly altered by abnormal development, luminal obstruction and physical loss of integrity. Therefore, any event that occurs in one of this vasculature leads to the development of pathological changes in the corresponding placental territory. Identification of these pathological changes associated with BW discordance will be useful in understanding the pathogenesis of BW discordance.

This study was performed to describe the pathological characteristics associated with BW-discordant MC and DC twins and to correlate the number of pathological lesions with the mean BW discordance. The study further looked at the significance of the presence of each pathology in the placental tissue in the placental territory of the lighter twin (LT) compared to the heavier co-twin (HT).

Materials and Methods

This was a prospective study which included the placentas of consecutive twin deliveries at De Soysa Maternity Hospital, Colombo from 2010 to 2012. The placentas were examined at the Department of Pathology, University of Colombo, Sri Lanka. The placentas with unclear labelling of umbilical cords as to twin born first (T1) and twin born second (T2) and those with incomplete clinical information in the request forms were excluded. There were no triplet or quadruplet placentas.

The BWs of both twins were obtained from clinical records. The BW discordance was calculated for each twin pair by expressing the difference in BW as a percentage of the weight of the larger twin. The percentage of BW difference of >15% was categorized as BW-discordant and those of <15% as BW-concordant.

The placentas underwent fixation in 10% formalin at least for 24 hours. Systematic gross examination of the placentas was done by a resident in pathology under the supervision of two perinatal pathologists. The membranes, cords, foetal and maternal surfaces were examined first. Placental weight was obtained after trimming membranes along the site of their insertion and cutting the umbilical cord at 1 cm

distance from the site of its insertion. Those having two anatomically separate placental discs with two amniotic sacs were taken as DC. Those with a single placental disc with a single amniotic sac were taken as MC. The chorionicity was determined by both gross and histological examination of the inter-twine membrane in di-amniotic fused placentas. The foetal vascular distribution on the foetal surface was examined after stripping the amnion to identify the corresponding placental territories of T1 and T2 in the fused placentas. Maternal surface was examined to identify retro-placental haematoma. Placental discs were serially sliced at 10mm intervals and all gross focal lesions were measured and sampled for histological examination. Two representative samples from macroscopically normal placental tissue from each placental territory were taken for histological examination.

Microscopic examination of Haematoxylin and Eosin stained tissue sections was done by a single perinatal pathologist. The presence of distal villous hypoplasia, excessive fibrin deposition in the inter-villous space, chorangiosis, fibrotic avascular villi, foetal thrombotic vasculopathy, inter-villous thrombi, placental infarctions and retro-placental haematoma were identified according to the pre-defined criteria by both gross and microscopic examination of the placentas (Table 1), (Figures 1-4). From here onwards, these pathological changes will be referred to as placental parenchymal lesions in this article. The pathologist was blind to the BW discordance of twins when the placental examination was done.

The frequency of occurrence of placental parenchymal lesions was compared in MC and DC twin pregnancies. The significance of occurrence of each placental parenchymal

lesion in the LT in comparison to the HT was looked at. In both MC and DC twins, the number of different types of placental parenchymal lesions present in the territory of the LT was counted and stratified in to four groups, as having 0, 1, 2, 3 or more lesions. The placental parenchymal lesion count was correlated with the mean BW discordance of each stratum.

Statistical analysis was done by Chi-square, Fisher's Exact and t-test where applicable using SPSS software device version 16. A P-value of <0.05 was considered significant. Ethical approval was obtained from the Ethics Review Committee of the Faculty of Medicine, University of Colombo, Sri Lanka (EC/11/202).

Results

A consecutive cohort of 185 placentas was examined during the study period and 93 were excluded due to lack of information in identifying the placental territories as to T1 or T2. In the remaining 92 placentas, the age of the mother ranged from 18 to 42 years with 89.9% of cases being below 35 years. The period of gestation ranged from 32 to 41 weeks with 50.7% of cases being over 37weeks. Of the cases 36.2%, 42%, 15.9% were in their first, second and third pregnancy respectively.

Of the 92 cases included for the study, 53(57.6%) had DC placentas and the remaining 39(42.4%) cases had MC placentas. The trimmed placental weight of MC placentas ranged from 390 to 1150g with a mean placental weight of 636.85g. The trimmed placental weight of DC placentas ranged from 380 to 1100g with a mean weight of 676.51g. In fetuses with DC placentas, the BW discordance of co-twins ranged from 0 to 52.8% with a mean BW discordance of 12% (SD±11.47%). Only 26% (n=14) of DC twins

Table 1. Definition of placental parenchymal lesions

Variable	Definition
Distal villous hypoplasia	Diminished villous growth leading to small terminal villi (usually containing only one capillary), with absence of intermediate sized villi and the presence of large syncytial knots (containing more than 10 nuclei, often larger than the villi), giving the placental histology a look of only large and small villi with abundant open maternal spaces at a section of macroscopically normal placental tissue (14,15)
Excessive fibrin deposition	Excessive accumulation of amorphous fibrinoid material encasing at least 50% of the chorionic villi as seen on at least one slide (16)
Chorangiosis	Presence of more than 10 vessels per chorionic villous in more than 10 villi (15)
Fibrotic avascular villi	Degeneration and eventual loss of capillaries in the downstream villi, separated from normal villi (16)
Foetal thrombotic vasculopathy	Thrombosis of chorionic plate and stem villous vessels (16)
Inter-villous thrombi	Small foetal haemorrhages in to the inter-villous space resulting in thrombi formation in the inter-villous space (16)
Placental infarction	Local collapse of villi with loss of the inter-villous space and evidence of villous trophoblastic necrosis (15,16)
Retro-placental haematoma	Gross / microscopic evidence of an ante-partum haemorrhage over the maternal surface (15,16)

were BW-discordant when 15% or more of difference in birth weights of co-twins was taken as the cut off.

In fetuses with MC placentas, the BW discordance of co-twins ranged from 0 to 55.34% with a mean BW discordance of 14% (SD±11.42%). Only 28% (n=11) of MC twins were BW-discordant when 15% or more of the difference in birth weights of co-twins was taken as the cut off. Further analysis of the DC twin pairs, in terms of type of the placenta i.e. fused or separate, showed that 29% (n=8) of twins with fused placentas and 24% (n=6) of twins with separate placentas were BW-discordant.

Overall, 63.0% (n=58) of twins in this study group had a placenta that showed 1 or more of the placental parenchymal lesion assessed, in the placental territory of the LT. Lesions

were more frequently seen in the placentas of MC twins (74.4%, n=29) than in DC twins (54.7%, n=29). In both MC and DC twin pairs, the placental parenchymal lesion count of the LT was stratified as 0, 1, 2 and 3 or more, and the mean BW discordance of each group was calculated. The relationship of the placental parenchymal lesion count in the placental territory of the LT to the mean BW discordance of each group showed that the mean BW discordance increases linearly with the number of placental parenchymal lesions (Table 2 and Figures 5 and 6). There was a positive correlation with the placental parenchymal lesion count and the mean BW discordance (for MC twins $p=0.032$, for DC twins $p = 0.043$).

The distribution of placental parenchymal lesions in the placental territories of the BW-discordant DC twins showed distal villous

Figure 1. Placental territories of the co-twins showing distal villous hypoplasia in the territory of lighter twin (B) compared to that of the heavier twin (A). Large well vascularized villi with thin vasculo-syncytial membranes are seen in A (arrows). B shows small sparse villi with a few vessels and having large syncytial knots (arrow heads) (H & E X 10)

Figure 2. A. Placental infarct with villous trophoblastic cell necrosis B. Inter-villous fibrin deposition showing amorphous fibrinoid material encasing chorionic villi (H & E X 20)

Figure 3. Fibrotic avascular villi in the left upper corner of the field with loss of capillaries, separated from normal vascularized villi in the right lower half of the field. (H & E X 4)

Figure 4. Small foetal haemorrhages in to the inter-villous space resulting in thrombi formation in the inter-villous space. (H & E X 4)

hypoplasia, excessive fibrin deposition in the inter-villous space, chorangiosis, inter-villous thrombi, infarction and foetal thrombotic vasculopathy occurring more frequently in the placental territories of the LTs than those of the HTs (Table 3). The increased incidence of distal villous hypoplasia in the placental territory of the LT in comparison to that of the HT was statistically significant ($p=0.04$). Some placental parenchymal lesions were more frequently seen in the placental territory of the LT in BW-concordant twin placentas, but none of such lesions showed statistically significant difference in occurrence (Table 3).

The distribution of placental parenchymal lesions in the placental territories of both BW-concordant and BW-discordant MC twins showed distal villous hypoplasia, excessive fibrin deposition in the inter-villous space and fibrotic avascular villi occurring more frequently in the placental territories of the LT than those of the HT (Table 4). The increased incidence of distal villous hypoplasia in the placental territory of the LT in comparison to that of the HT was

significant in both BW-concordant and BW-discordant Twins ($p=0.02$ and $p=0.03$ respectively) (Table 4).

Discussion

The present study shows that the placental territories of the LTs have more placental parenchymal lesions than those of HTs in both MC and DC twins. The study also shows that there is a positive correlation between the placental parenchymal lesion count of the placental territory of the LT and the mean BW discordance in both MC and DC twins. Similar studies done by Eberle et al and Victoria et al also have shown that the significant BW discordance is attributed to the presence of greater number of placental parenchymal lesions in the LT than in the HT (9,10). However, they have shown this association only in DC twins but not in MC twin. This discrepancy may be because both these studies have looked at placental vascular thrombotic lesions, not looked at distal villous hypoplasia which was the most common

Table 2. Correlation between the PPL^a count and the mean BW^b discordance in both DC^c and MC^d twins

PPL ^a count	DC ^c Placentas		MC ^d placentas	
	No. of placentas	Mean BW ^b discordance	No. of placentas	Mean BW ^b discordance
0	24	9.8%	10	11.49%
1	16	13%	22	11.81%
2	11	14.8%	06	23.2%
3 or more	02	29%	01	33.65%

^aPlacental parenchymal lesion, ^bBirth weight, ^cDichorionic, ^dMonochorionic

Figure 5. Relationship between the placental parenchymal lesion count of the placental territory of lighter monochorionic twins to the mean birth weight discordance.

Figure 6. Relationship between the placental parenchymal lesion count of the placental territory of lighter dichorionic twins to the mean birth weight discordance.

placental pathology in our cohort. The recent study done by Kent et al has shown that the placental pathological lesions were more common in the MC twins than in DC twins which were the same in the present study. Kent et al has also shown a significant

association between the abnormalities in the placenta and the BW discordance in DC twins with a higher frequency of placental parenchymal lesions occurring in the LT, but a similar association has not been demonstrated in MC twins (11).

Table 3: Frequency of each PPL^a in the placental territories of BW^b-Concordant and BW^b-Discordant dichorionic twins and the significance of each lesion occurring in the territory of LT^c in comparison to that of HT^d

PPL ^a	BW ^b -Concordant				BW ^b -Discordant			
	LT ^c (n=39)	HT ^d (n=39)	X ² value	P value	LT ^c (n=14)	HT ^d (n=14)	X ² value	P value
Distal villous hypoplasia	17(43.6%)	12 (30.8%)	0.88	0.34	8 (57.1%)	2(14.3%)	3.89	0.04
Excessive fibrin deposition	1(2.5%)	1(2.5%)	0.51	0.47	2 (14.3%)	-	0.54	0.48
Chorangiosis	3(7.6%)	7(17.9%)	1.03	0.31	3 (21.4%)	1(7.1%)	0.29	0.58
Fibrotic avascular villi	4(10.2%)	2(5%)	0.18	0.67	1(7.1%)	1(7.1%)	0.54	0.46
Intervillous thrombi	3(7.6%)	2(5%)	0.00	1.00	2 (14.3%)	1(7.1%)	0.00	1.00
Foetal thrombotic vasculopathy	-	-	-	-	1(7.1%)	-	0.00	1.00
Infarction	1(2.5%)	1(2.5%)	0.51	0.47	1(7.1%)	-	0.00	1.00
Abruption	1(2.5%)	-	0.00	1.00	-	-	-	-

^a Placental parenchymal lesion, ^bBirth weight, ^c Lighter twin, ^dHeavier twin

In the present study, a significant number of BW-discordant DC twins had distal villous hypoplasia in the placental territory of the LT compared to the HT. The presence of distal villous hypoplasia in the placental territory of the LT showed a positive correlation with degree of BW discordance in DC twins. Distal villous hypoplasia which is also denoted as abnormal maturation of villi occurs as a result of impaired development of utero-placental circulation due to defective migration of trophoblastic cell in the process of development of the placenta (14,17). Therefore, this study supports the fact that a disproportionate utero-placental circulation to the placental territories of each twin may contribute significantly to the BW discordance in DC twins. The significant occurrence of distal villous hypoplasia in the placental

territory of the LT than in the HT in DC twins has also been shown in two previous studies (10,11).

Three studies done on placental pathology in BW discordant twins have shown that vascular thrombotic lesions and fibrotic avascular villi occurred more frequently in the placental territory of the LT than in the HT (9,12,13). The present study did not support those observations as the number of samples with fibrotic avascular villi and vascular thrombotic lesions were only a few in this study group. The reason for not detecting more cases with fibrotic avascular villi may be due to inadequate sampling of grossly normal placental tissue. The small sample size is another limitation in this study. However, the importance of this study is that the placental

Table 4: Frequency of each PPL^a in the placental territories of BW^b-Concordant and BW^b-Discordant mono chorionic twins and the significance of each lesion occurring in the territory of LT^c in comparison to that of HT^d

PPL ^a	BW ^b -Concordant				BW ^b -Discordant			
	LT ^c (n=28)	HT ^d (n=28)	χ ² value	P value	LT ^c (n=11)	HT ^d (n=11)	χ ² value	P value
Distal villous hypoplasia	13 (46.4%)	4(14.3%)	5.41	0.02	8 (72.7%)	2(18.2%)	4.58	0.03
Excessive fibrin deposition	1(3.6%)	-	0.00	1.00	2 (18.2%)	1(9.1%)	0.00	1.00
Chorangiosis	2(7.1%)	2(7.1%)	0.27	0.60	2 (18.2%)	1(9.1%)	0.00	1.00
Fibrotic avascular villi	1(3.6%)	-	0.00	1.00	1(9.1%)	-	0.00	1.00
Intervillous thrombi	-	-	-	-	-	-	-	-
Foetal thrombotic vasculopathy	-	-	-	-	-	-	-	-
Infarction	-	-	-	-	-	-	-	-
Abruption	-	-	-	-	(9.1%)	-	0.00	1.00

^a Placental parenchymal lesion, ^b Birth weight, ^c Lighter twin, ^d Heavier twin

parenchymal lesions were pre-defined and the histological examination of the placenta was done by a single pathologist minimising the inter-observer variability which may have affected the results of other studies done so far.

In MC twins, the presence of distal villous hypoplasia in the placental territory of the LT in comparison to the HT was statistically significant in both BW-concordant and BW-discordant twins. This category needs further investigations with a larger sample size before arriving at a conclusion as multiple other factors like twin-to-twin transfusion syndrome, inequalities in distribution of placental mass between the two fetuses and abnormalities in the cord insertion site have been shown to be associated with BW

discordance in MC twins in several studies (3,4,5). These other factors may have compensated the role of disproportionate utero-placental circulation resulting in distal villous hypoplasia in MC twins.

It is known that in the absence of twin-to-twin transfusion syndrome, the underlying pathophysiology for foetal growth restriction due to placental insufficiency in twins is the same as in singleton pregnancies. Similarly, in twin pregnancies with foetal growth restriction due to placental insufficiency, the growth-restricted foetus demonstrates the same abnormal umbilical Doppler changes as observed in singleton pregnancies with the same complication. Giles et al. has reported that histopathological evidence of reduction in the count of small arterial vessels in

placental tertiary stem villi restricted to the placenta of the affected foetus from twin pregnancies complicated by the presence of abnormal umbilical Doppler results are similar to those found in singleton pregnancies (18). Hence, this study adds further depth to the knowledge of understanding the pathogenesis of BW discordance in DC twins and highlights the importance of foetal growth monitoring and monitoring of umbilical cord Doppler changes to detect early placental insufficiency.

Placental histological examination is vital in the evaluation of intrauterine growth restriction. Studies in singletons have shown morphological changes in villous structure in placentas of fetuses affected by intrauterine growth restriction (11). Similarly, histopathological examination of placentas to study the villous morphology in BW discordant twins will be useful in practice for the obstetricians to justify vital decisions taken regarding early delivery of some fetuses due to the presence of abnormal umbilical Doppler results detected during ante-natal monitoring.

In conclusion, the study has shown that the placental territories of the LTs have more placental parenchymal lesions than those of the HTs and the lesion count in the LT shows a positive correlation with the degree of BW discordance in both MC and DC twins. In DC BW-discordant twins, distal villous hypoplasia in the placental territory of the LT due to disproportionate utero-placental circulation would have contributed significantly to the BW discordance. Hence, histopathological examination of twin placentas would be helpful in explaining the underlying pathogenesis of BW discordance in twins in the absence of twin-to-twin transfusion syndrome.

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