

# Role of First Trimester Ultrasound Scan as a Predictor of Monochorionic Diamniotic Complications

Amilia Afzan binti Mohd Jamil<sup>1\*</sup>, Shuhaila Ahmad<sup>2</sup> and Nor Azlin Mohamed Ismail<sup>2</sup>

<sup>1</sup>Department of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia

<sup>2</sup>Department of Obstetrics & Gynaecology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Cheras, Kuala Lumpur, Malaysia

\*Corresponding author: Amilia Afzan Binti Mohd Jamil,  
Email: amilia@upm.edu.my

Received: 29 March 2017; Accepted: 01 August 2017; Published: 08 August 2017

## Abstract

**Introduction:** Monochorionic twin pregnancies come with substantially higher complications compared to their dichorionic counterparts, which include intrauterine fetal death, fetal loss prior to 24 weeks, selective intrauterine growth restriction and twin-to-twin transfusion syndrome (TTTS).

**Objectives:** This work aims to examine the inter-twin discrepancy in nuchal translucency thickness (NT), crown-rump length (CRL), fetal heart rate (FHR) and ductus venosus Doppler (DV), as predictors of complications in monochorionic diamniotic twins (MCDA).

**Methods:** This is a retrospective study that involves 118 MCDA pregnancies followed-up in a tertiary centre, from January, 2011 to June, 2016. NT was measured at 11 to 13+6 weeks' gestation in 23 MCDA pregnancies. Regression analysis was employed to determine the significance of the association between inter-twin discrepancy in NT, CRL, FHR and DV Doppler with intrauterine death of both fetuses and monochorionic (MC) complications such as TTTS, selective intrauterine growth restriction (sIUGR) and twin anemia and polycythemia sequence (TAPs).

**Results:** Multiparous mothers (53.8%) aged between 19 and 35 years (89.9%) contributed to the majority of MCDA twin pregnancies. Among a total of 118 MCDA pregnancies, 16.8% (n=20) developed complications. About 3.4% (n=4) of them had TTTS, and 10.9% (n=13) had sIUGR, while only 0.9% (n=1) developed TAPs and intrauterine fetal death (IUFD) of both fetuses each. A significant prediction of MC complications and intrauterine death was provided by discordant NT of 35% or more (p= 0.021) with a relative risk of 4.0 (95% CI 1.23-12.99), a sensitivity of 57.1% and a specificity of 88.2%. Otherwise, there exist no significant associations between discrepancy in CRL, FHR and DV Doppler and MC complications.

**Conclusions:** Inter twin discordance in NT of 35% or more was reported in about 25% of MCDA twins in this group, with the risk of developing MC complications and intrauterine death of over 40%. Among other parameters, it is the early predictors of hemodynamic imbalance between both twins that significantly contribute to a more reliable screening tool for MCDA pregnancies with high specificity.

**Keywords:** Monochorionic pregnancies; Twin-to-twin transfusion syndrome; Adverse perinatal outcomes; First trimester scan

## Introduction

Multiple pregnancy is associated with a higher risk of fetal

complications and neonatal deaths. Monochorionic diamniotic (MCDA) twin pregnancies have substantially higher complications compared to dichorionic pregnancies, along with a substantially higher risk of intrauterine fetal death, fetal loss prior to 24 weeks, intrauterine growth restriction and twin to twin transfusion syndrome (TTTS) [1].

The reason underlying all these complications in monochorionic twin pregnancies is largely due to the presence of vascular anastomoses connecting the two fetal circulations. These inter-twin anastomoses are nearly always present, and account for a broad range of pregnancy complications, including TTTS, which damage the surviving twin in the event of intrauterine demise of its co-twin [1]. Additionally, the single monochorionic placenta has to care for two fetuses, and is often unequally shared, which may cause growth restrictions and severe discordant birth weight [1].

The current recommendation for complications screening is a two weekly scan for MCDA twins. However, it is not a standard practice at all centers and even with two weekly follow-ups, some cases might be missed, while others may be lost due to late diagnoses. Moreover, since most MCDA pregnancies do not develop TTTS (90%), such an approach drains a great deal of resources [2].

Therefore, efforts to predict which MCDA twin pregnancies are at an increased risk of developing TTTS and other complications are warranted. Published data to date has investigated the role of first trimester nuchal translucency (NT), crown-rump-length (CRL) and ductus venosus Doppler (DV), as predictive tools [1,3-5]. Although an increase in inter-twin discrepancy in NT or CRL and abnormal DV flow have been reported as early signs of haemodynamic imbalance predisposing to TTTS, published data are not univocal. Other markers such as amniotic fluid discrepancy, membrane folding, arterio-arterial placental anastomosis detection by Doppler ultrasound and maternal circulating mRNA levels, were also proposed as predictors of TTTS later in pregnancy [2,6-8].

To date, no research has been carried out to predict and screen monochorionic twins which have high likelihood to develop TTTS in the context of Malaysia. Hence, this study is a designed to investigate the parameters taken during the first trimester scans in monochorionic pregnancies, in an attempt to determine the association with the outcome later.

Therefore, this study aims to evaluate the possible value of inter-twin discrepancy in nuchal translucency thickness (NT), crown-rump length (CRL), fetal heart rate (FHR) and ductus venosus Doppler (DV) as a predictor of complications in monochorionic diamniotic twins (MCDA).

## Patients and Methods

### Study design

This is retrospective study approved by the Research and Ethics of Institutional Board

### Study population

A total of 118 MCDA pregnancies were followed-up in a tertiary center from January, 2011 to June, 2016 and then recruited. Diagnoses of MCDA twin pregnancies were carried out during the first trimester scan by the presence of T-sign and absence of Lambda- sign [9]. Demographic data which included maternal age, ethnic origin, parity and method of conception, were taken to compare their association with the MC complications. Congenital malformations detected during first trimester scan were excluded from the study.

Among the 118 identified MCDA twins, about 23 of them had NT, CRL and FHR; and DV Doppler was measured at 11 to 13+6 weeks' gestation using a Voluson 730 expert (GE Medical Systems, Zipf, Austria) with a multifrequency transabdominal probe maintaining the thermal and mechanical index value below 0.6 [10]. Both transabdominal and transvaginal approaches were employed according to the needs of the examination.

The gestational age was computed by CRL measurement. The largest fetus CRL was used for gestational age determination when early CRL discrepancy was detected. NT was measured as previously described to define the risk of aneuploidy [11]. The percentage discrepancy for NT was determined as the percentage difference relative to the lower value of NT. Also, the percentage discrepancy of CRL was determined as the percentage difference relative to the larger value for CRL.

The scan was done by experienced sonographers accredited to perform NT scans by the center. The DV Doppler examinations were carried out by accredited and experienced sonographers using strict criteria [12].

A magnified image of right ventral mid-sagittal view of the fetal trunk was obtained for the DV Doppler. With the use of colour flow mapping, the pulsed Doppler sample volume was placed on the yellowish aliasing area, directly above the umbilical sinus, during fetal quiescence. The insonation angle was maintained below 30 degrees, with a high-pass filter set as 50-60 Hz and with high sweep speed (2-3 cm/s) for better visualization of the A-wave. The DV was considered abnormal if the A-wave was absent or reversed.

Subsequently, the MC twins were assessed fortnightly for complications such as IFUD, TTTS, selective intrauterine growth restriction (sIUGR), twin reverse arterial perfusion syndrome (TRAPs) and twin anemia and polycythemia sequence (TAPs); and were then analysed.

### Outcome of study

The development of TTTS, as defined by Quintero et al. (1999) and sIUGR, is when there exists an EFW discordance of >25% on an ultrasound above 24 weeks' gestation [13]. Twin anemia and polycythemia sequence (TAPs) were defined by a discrepancy of hemoglobin between two monozygotic fetuses, leading to one fetus being anemic, while the other being polycythemic, without any sign of twin oligo-polyhydramnios sequence [15].

### Statistical analysis

In each pregnancy, the inter-twin discordance of NT, CRL and FHR were calculated as the difference in each measurement between the two fetuses (NT1-NT2, CRL1- CRL2 and FHR1-FHR2 respectively), and then expressed as a percentage of the larger measurement. The DV Doppler was compared between both normal and at least one of the fetuses having an absent A-wave. The distribution of measurements in the two groups of pregnancies was determined and compared. The first group included MCDA pregnancies with normal outcomes in which both babies were lifeborn without any antenatal complications. The second group comprised the MCDA pregnancies with adverse outcomes such as IUD, TTTS, selective intrauterine growth restriction (sIUGR), twin reverse arterial perfusion syndrome (TRAPs) and twin anemia and polycythemia sequence (TAPs).

Regression analysis was employed to determine the significance of the association between discordance in measurements and adverse outcomes. Data were analyzed using the R for Statistical Computing software application (version 3.3.2).

Receiver operating characteristic (ROC) curves (plot of "Sensitivity versus 1-Specificity") were plotted for inter-twin discrepancy in NT, CRL and FHR to determine the cut-off point that maximises the ability

to predict the adverse outcomes. The areas under the curves (AUCs) and their 95% confidence intervals (CIs) were used to determine their statistical significance at predicting adverse outcomes. Using the optimal cut-points identified from the ROC curves, sensitivity, specificity and positive and negative predictive values were determined for each variable. The prediction of adverse outcomes was derived by logistic regression analysis with backwards elimination of variables that were not significantly different to each other with p-values over a value of 0.05 ( $P < 0.05$ ).

### Results

Maternal characteristics of the MCDA twins included in this study are shown in Table 1. About 89.9% of women conceived MCDA twins were aged between 19 to 35 years old, most of them were multiparous (51.3%), and only 0.8% conceived with assisted reproductive techniques. Among the 118 MCDA pregnancies, 19 (16.85%) had at least one adverse outcome, in which about 3.4% (n=4) of them had TTTS, 10.9% (n=13) had sIUGR and 0.9% (n=1) developed either, TAPs or intrauterine death. However, there was no association between maternal age, parity and method of conception with development of complications, as shown in Table 2.

About 23 among 118 women underwent the first trimester scan, in which the NT, CRL, FHR and DV Doppler were recorded. A total of 26.1% (6 out of 23 MCDA pregnancies) developed adverse outcomes ranging from IFUD, TTTS, selective intrauterine growth restriction (sIUGR) and twin anemia and polycythemia sequence (TAPs).

When a significant p value was taken at less than 0.05, the study demonstrated that an NT discrepancy of >35% was significantly associated with adverse complications, relative risk of 4.0 (95% CI 1.23-12.99), a sensitivity of 57.1% (95% CI 18.4%-90.1%) and a specificity of 88.2% (95% CI 63.6 -98.5%).

The sensitivities, specificities, positive predictive values and negative predictive values of all the first trimester scan parameters as screening in predicting any adverse outcomes are shown in Table 2.

The ROC curves for NT, CRL and FHR discordances for the combined adverse perinatal outcome are shown in Figure 1.

NT discordance with an AUC of 0.80 (95% CI, 0.012, 0.81; p value 0.032) was a better predictor than CRL discordance with an AUC of 0.71 (95% CI 0.023, 0.1146; p value 0.571), and FHR discordance with an AUC of 0.57 (95% CI 0.047, 0.863; p value 0.775) for adverse perinatal outcomes. The optimal values for predicting any adverse outcomes derived from the ROC curves for NT were > 41.2%, for CRL were > 7% and for FHR were > 7%.

As a conclusion, NT discordance had a better diagnostic ability than CRL, FHR and DV Doppler for any adverse outcome in MCDA twins, with higher positive predictive values, which were substantially higher than the prevalence for outcomes.

**Table 1:** Maternal characteristics of the study cohort.

Characteristics	n= 23 (Mother)	Percentage (%)
Age (years)		
19-35	106	89.9
>35	12	10.1
Gravida- n		
1	55	46.2
2 to 5	60	51.3
>5	3	2.5
Conception		
Assisted Reproduction	1	0.8
Spontaneous	117	99.2
Complications		
Yes	19	16.8
No	99	83.2

**Table 2:** Association between Maternal characteristics and complications.

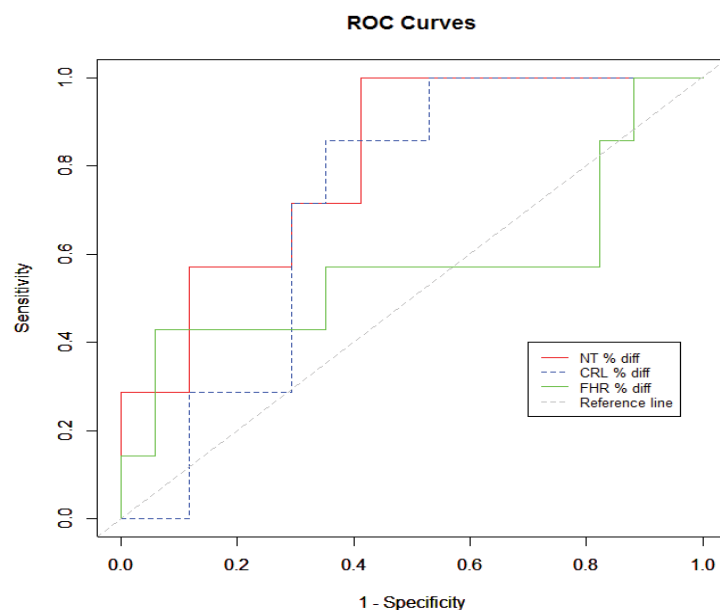
Characteristics	n= 118	Complications		Odds Ratio	95% confidence interval	p-value
		Yes	No			
Age (years)						
19-35	106	16	90	0.567	0.139- 2.311	0.428
>35	12	3	9	1.764	0.433 – 7.197	
Parity- n						
0	55	10	45	1.200	0.459 - 3.139	0.571
1 to 5	60	9	51	0.941	0.360 - 2.461	
>5	3	0	3	0.673	0.033 - 13.525	
Conception						
Assisted Reproduction	1	0	1	1.602	0.630 - 40.726	0.775
Spontaneous	11	19	98	0.624	0.025 - 15.876	

**Table 3:** Association between 1<sup>st</sup> trimester scan and complications.

	n= 23	Complications		Likelihood Ratio	95% confidence interval	p-value
		Yes	No			
NT Discrepancy (%)						
<35%	18	3	15	5.12	0.012 – 0.812	0.032
>35%	5	3	2			
CRL Discrepancy (%)						
<5	11	1	10	4.33	0.083- 0.88	0.571
>5	12	5	7			
FHR (%)						
0-7	20	4	16	2.10	0.047-0.863	0.775
>7	3	2	1			
DV						
Normal	19	5	14	0.33	0.023-0.1146	0.532
At least one twin with abnormal DV	4	1	3			

**Table 4:** Diagnostic accuracy of discordant in NT, CRL, FHR and DV Doppler for any adverse outcomes.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	p value
NT discrepancy >35%	57.1	88.2	66.7	83.3	< 0.05
CRL discrepancy >5 %	85.7	58.8	46.2	90.9	0.07
FHR discrepancy > 7%	28.6	94.1	66.7	76.2	0.07
At least 1 fetus with abnormal DV	28.6	82.3	40.0	73.7	0.53



**Figure 1:** The ROC curves for NT, CRL and FHR discordance for the combine adverse perinatal outcomes.

## Discussion

Adverse pregnancy outcome in MCDA twins is attributed to unequal placental sharing, making the twins at a higher risk of getting TTTS, sFGR, TAPs and intrauterine death of one or both twins, which endangers the entire pregnancy [2,16,17]. The risk of developing at least one adverse fetal outcome in MCDA pregnancies in this study was 16.8%, which corresponds to a study carried out in Australia by Zipori et al., in which 20% of the MCDA twins were at risk of adverse outcomes [18].

Both increased NT and CRL discordances offer the first window of opportunity to assess the potential for later MCDA complications. Despite the controversy in the related body of literature, there exists a general understanding that increased NT discordances among MCDA twins mandate a close surveillance for potential complications [1,19]. Several studies demonstrate that increased NT discordances were a better diagnostic tool at predicting adverse perinatal outcomes [18], and emerging evidence does not support a significant role for CRL discordance as a major predictive marker of complications in MCDA pregnancies [20,21].

We found that NT discordances > 35% were associated with significant combined adverse outcome complications. The overall positive predictive value of NT screening was rather high in predicting any adverse outcomes at 66.7%, and the lack of NT discordance can be seen as reassuring, with a negative predictive value of 83.3%. Both of these values must be considered relative to the prevalence of 16.8%, so neither NT or CRL discordance are likely to modify the intensive monitoring required for these very high-risk pregnancies.

A possible explanation for these findings is provided by the hypothesis of 'asymmetric reduction in placental anastomoses' [22], which states that there are progressive spontaneous closures or eruptions of bidirectional arteriovenous connections present in all early monochorionic twins with advancing gestation. It is thus possible that some pregnancies may possess an asymmetrical flow at 11 to 13 +6 weeks, causing a large discordance in NT. With advancing gestation, the random disruption of arteriovenous anastomoses restores symmetry in flow, and thus the spontaneous resolution of the early signs of TTTS [1].

CRL discordance appears to have less value in predicting adverse outcomes in MCDA twins compared to NT discordance [1,2,18]. This was also seen in the recent STORK study, in which the predictive accuracy of CRL discordance was poor for fetal loss < 24 weeks, perinatal mortality, EFW discordance, birth weight discordance, or preterm birth < 34 weeks [20]. CRL discordance > 5% in our study group was not a significant predictor of potential adverse outcomes. A limitation of this study was the small size of the cohort, with only 23 among 118 MCDA twin pregnancies having NT and CRL measurements, as well as known pregnancy outcomes.

Our study suggests an insignificant association and low diagnostic accuracy of abnormal DV with adverse outcome of MCDA twins. However, abnormal DV Doppler in combination with increased NT and CRL discordance increased the diagnostic accuracy and predictive value of MCDA twins' complications. This finding is also supported by Matias et al. and Lewi et al., who demonstrate that the combination of the difference in NT and DV blood flow represent useful first-trimester predictors of adverse outcomes in MCDA pregnancies [2,12].

In conclusion, NT discordance of > 35% identifies MCDA twin pregnancies of having higher risk of potential complications. CRL discordance is of limited value in predicting any adverse outcomes. Absence of substantial NT and CRL concordances, however, may be somewhat reassuring for prospective parents and their healthcare providers.

## References

- Kagan K, Gazzoni A, Sepulveda-Gonzalez G, Sotiriadis A, Nicolaides K. Discordance in nuchal translucency thickness in the prediction of severe twin-to-twin transfusion syndrome. *Ultrasound in Obstetrics and Gynecology*. 2007; 29:527-532.
- Lewi L, Lewi P, Diemert A, Jani J, Gucciardo L, Van Mieghem T, et al. The role of ultrasound examination in the first trimester and at 16 weeks' gestation to predict fetal complications in monochorionic diamniotic twin pregnancies. *American Journal of Obstetrics and Gynecology*. 2008; 199:493.e1-493.e7.
- El Kateb A, Nasr B, Nassar M, Bernard J, Ville Y. First-trimester ultrasound examination and the outcome of monochorionic twin pregnancies. *Prenatal Diagnosis*. 2007; 27:922-925.
- Fratelli N, Prefumo F, Fichera A, Valcamonico A, Marella D, Frusca T. Nuchal translucency thickness and crown rump length discordance for the prediction of outcome in monochorionic diamniotic pregnancies. *Early Human Development*. 2011; 87:27-30.
- Zoppi M. Nuchal translucency screening in monochorionic twin pregnancies. *Ultrasound in Obstetrics and Gynecology*. 2009; 34:491-493.
- Lin T, Lin C, Shih J, Su Y, Wu E, Lee C. Effect of arterioarterial anastomosis on early-onset umbilical artery flow abnormality in a monochorionic-diamniotic twin. *Ultrasound Obstet Gynecol*. 2012; 40:371-372.
- Stagnati V, Zanardini C, Fichera A, Pagani G, Quintero R, Bellocco R, et al. Early prediction of twin-to-twin transfusion syndrome: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2016; 49:573-582.
- Yamamoto R, Ishii K, Muto H, Kawaguchi H, Murata M, Hayashi S, et al. The Use of Amniotic Fluid Discordance in the Early Second Trimester to Predict Severe Twin-Twin Transfusion Syndrome. *Fetal Diagn Ther*. 2013; 34:8-12.
- Sepulveda W, Sebire NJ, Hughes K, Kalogeropoulos A, Nicolaides KH. Evolution Of The Lambda Or Twin-Chorionic Peak Sign In Dichorionic Twin Pregnancies. *Obstetrical & Gynecological Survey*. 1997; 89:439-441.
- European Committee for Ultrasound. What Happens When You Alter The Settings On Your Diagnostic Ultrasound Machine? — Safety Considerations. *European Journal of Ultrasound* 2.4. 1995; 329-330.
- Snijders RJ, Noble P, Sebire N, Souka A, Nicolaides KH. UK Multicentre Project On Assessment Of Risk Of Trisomy 21 By Maternal Age And Fetal Nuchal-Translucency Thickness At 10–14 Weeks Of Gestation. *The Lancet*. 1998; 352:343-346.
- Matias A, Montenegro N, Loureiro T, Cunha M, Duarte S, Freitas D, et al. Screening for twin-twin transfusion syndrome at 11-14 weeks of pregnancy: the key role of ductus venosus blood flow assessment. *Ultrasound in Obstetrics and Gynecology*. 2010; 35:142-148.
- Quintero R, Morales W, Allen M, Bornick P, Johnson P, Kruger M. Staging of Twin-Twin Transfusion Syndrome. *Journal of Perinatology*. 1999; 19:550-555.
- Khanduri S, Chhabra S, Raja A, Bhagat S. Twin Reversed Arterial Perfusion Sequence: A Rare Entity. *Journal of Clinical Imaging Science*. 2015; 5:9.
- Bae Jin Young, Jin Ju Oh, Seong Yeon Hong. Prenatal Diagnosis of Spontaneous Twin Anemia-Polycythemia Sequence and Postnatal Examination of Placental Vascular Anastomoses. *Obstetrics & Gynecology Science*. 2016; 59:539.
- Acosta-Rojas R, Becker J, Munoz-Abellana B, Ruiz C, Carreras E, Gratacos E. Twin chorionicity and the risk of adverse perinatal outcome. *International Journal of Gynecology & Obstetrics*. 2007; 96:98-102.
- Gratacós E, Ortiz J, Martínez J. A Systematic Approach to the Differential Diagnosis and Management of the Complications of Monochorionic Twin Pregnancies. *Fetal Diagnosis and Therapy*. 2012; 32:145-155.
- Zipori Y, Reidy K, Gilchrist T, Doyle L, Umstad MP. The Outcome of Monochorionic Diamniotic Twins Discordant at 11 to 13+6 Weeks' Gestation. *Twin Research and Human Genetics*. 2016; 19:692-696.
- Salomon L, Örtqvist L, Aegerter P, Bussières L, Staracci S, Stirnemann J, et al. Long-term developmental follow-up of infants who participated in a

- randomized clinical trial of amniocentesis vs laser photocoagulation for the treatment of twin-to-twin transfusion syndrome. *American Journal of Obstetrics and Gynecology*. 2010; 203:444.e1-444.e7.
20. D'Antonio F, Khalil A, Dias T, Thilaganathan B. Southwest Thames Obstetric Research Collaborative. Crown-rump length discordance and adverse perinatal outcome in twins: analysis of the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort. *Ultrasound in Obstetrics & Gynecology*. 2013; 41:621-626.
21. Johansen M, Oldenburg A, Rosthøj S, Maxild J, Rode L, Tabor A. Crown-rump length discordance in the first trimester: a predictor of adverse outcome in twin pregnancies? *Ultrasound in Obstetrics & Gynecology*. 2014; 43:277-283.
22. Sebire N, Talbert D, Fisk N. Twin-to-Twin Transfusion Syndrome Results from Dynamic Asymmetrical Reduction in Placental Anastomoses: A Hypothesis. *Placenta*. 2001; 22:383-391.