Role of colour doppler evaluation of middle cerebral and umbilical arteries in intrauterine growth restriction and prediction of adverse perinatal outcome

Vishwanath G Kumbar[1*], Vijayalakshmi N[2], Vinod Xavier Joseph[3], Richard Thomas[4], Tessa N Kaneria[5], Sandeep M B[6], Gouri B Kaveriappa[7]

[1]PG Resident, [2,3]Senior Resident, [4,5,6,7]Assistant Professor, Department of Radio diagnosis, Father Muller Medical College, Mangalore, Karnataka, INDIA.
Email: drkumbar@gmail.com

Abstract

Background and Objectives: Objective of our study was to evaluate the usefulness of middle cerebral artery (MCA) and umbilical artery (UA) Doppler in the diagnosis of intrauterine growth restriction (IUGR) and its prediction of adverse perinatal outcome in clinically suspected IUGR pregnancies and to establish the role of Doppler ultrasound in the management of IUGR pregnancy. **Materials and Methods:** Data were analysed from 40 cases with clinical suspicion of IUGR between 31 to 40 weeks of gestation from June 2011 to June 2013. Pulsatility index (PI) was used as the Doppler index. The UA and MCA PI was considered abnormal if the value was >95th percentile and <5th percentile of previously published values for gestational age, respectively. Cut-off value of 1.08 was used for MCA/UA PI ratio; velocimetry above 1.08 was considered normal and if below abnormal. The fetus was considered IUGR if the estimated fetal weight (EFW) was <10th percentile of previously published values for gestational age. Pregnancies with documented major congenital abnormality and multiple gestations were excluded from the study. Findings of Doppler studies were correlated with the EFW and the following adverse perinatal outcomes: perinatal death, emergency caesarian section for fetal distress, low Apgar score (5min Apgar <7), and admission to neonatal intensive care unit for complications of IUGR, pregnancy outcome was considered favourable when these were absent. **Results:** Cerebroplacental ratio (MCA/UA PI) was the most sensitive parameter (95.8%) to predict adverse outcome. It was more sensitive than UA PI (91%) and MCA PI (87.5%). Diagnostic accuracy of cerebroplacental ratio (90%) was better than UA PI (88%) and MCA PI (66%) in predicting adverse outcomes. MCA/UA PI had less diagnostic accuracy (65%) in diagnosing IUGR than predicting its adverse outcome (90%). **Conclusion:** Cerebroplacental Ratio (MCA/UA PI) is a better predictor of adverse perinatal outcome than an abnormal MCA PI or UA PI, however has less diagnostic accuracy in the diagnosis of IUGR compared to prediction of adverse perinatal outcome.
Key words: Cerebroplacental Ratio; Intrauterine growth restriction; Middle cerebral artery pulsatility index; Umbilical artery pulsatility index.

*Address for Correspondence:
Dr. Vishwanath G Kumbar, Resident, Department of Radiodiagnosis, Father Muller Medical College, Kankanady, Mangalore 575002 Karnataka, INDIA.
Email: drkumbar@gmail.com

Access this article online	
Quick Response Code:	Website: www.statperson.com
	DOI: 10 October 2014

INTRODUCTION

Intrauterine growth restriction (IUGR) is classically defined as a fetus with an estimated weight below the 10th percentile for gestational age.[1,2] Pregnancies suspected of IUGR are a heterogeneous group. Some are constitutionally small and healthy, but others fail to reach their predestined growth potential due to lack of nourishment, chromosomal aberrations or external factors that influence growth like drugs or infections.[3,4] Doppler

ultrasound examination helps to identify heterogenous group of small for gestational age fetuses that includes fetuses with IUGR, fetuses with small constitution and fetuses which are misdiagnosed as IUGR.[3] IUGR is associated with increased perinatal morbidity, mortality and impaired neurological development.[1,4,5] The correct detection of compromised IUGR fetus to allow for timely intervention is the main objective of the antenatal care. Doppler velocimetric studies are most rigorously evaluated non invasive test of fetal well being. A meta-analysis of various randomized control trials of Doppler velocimetry demonstrated that its use was associated with a trend toward reduction of perinatal mortality and morbidity. [5,6] Perinatal complications have been found to be statistically correlated with abnormal indices of flow resistance suggesting a potential role of Doppler ultrasound in the management of high risk pregnancies.[5,7] Doppler USG studies of the human fetal circulation have shown that in fetuses with IUGR there is a significant reduction of MCA PI when compared with those in normal fetuses. At cordocentesis, a significant correlation has been observed between hypoxemia in fetuses with IUGR and an abnormal MCA PI. Results of various studies suggest that the MCA/UA PI ratio is more accurate in the prediction of adverse perinatal outcome than UA Doppler USG alone.[5-8] Differences in the study designs, inclusion criteria for patient selection, the definition of adverse outcomes, different cut-off levels between normal and abnormal test results and the small number of patients studied, make direct comparison of the studies difficult. Our study was an effort at establishing the role of MCA PI, UA PI and MCA/ UA PI in diagnosing IUGR and its prediction in perinatal out come in clinically suspected IUGR pregnancies, and to determine the role of Doppler velocimetry in clinical management of such pregnancies.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Radiodiagnosis, Father Muller Medical College for a period of two years from June 2012 to June 2013. Data for the study was collected by purposive sampling technique from pregnant women with clinically suspected IUGR referred to the Department of Radiodiagnosis, Father Muller Medical College.

Doppler USG technique

We used PHILIPS HD 7 with the transducer frequency of 3.5–5.0 MHZ with medium filter. The patients were allowed to rest for 10 to 15mins in a semi-recumbent position prior to commencing the ultrasound investigation. Fetal biometry was performed initially. The waveforms were obtained during fetal inactivity and apnoea. Umbilical artery Doppler flow velocity

waveforms were obtained from a free loop of cord, and measurements taken when a clear waveform was acquired in the absence of fetal breathing or body movement. The pulsatility index (PI) was measured, and the presence or absence of end-diastolic frequencies was noted. For MCA Doppler USG, a transverse image of the fetal head was obtained at the level of the sphenoid bones. Color flow imaging was used to display the circle of Willis. The MCA in the near field was insonated about 1 cm distal to its origin from the internal carotid artery.

OBSERVATIONS AND RESULTS

Of the 40 pregnancies studied acceptable wave forms were obtained from all the 40 cases. Out of 40 pregnancies 18 pregnancies had pregnancy induced hypertension (PIH), 2 pregnancies had anemia, 2 pregnancies had diagnosed gestational diabetes mellitus (GDM) on treatment with insulin, 2 pregnancies were Rh negative, 1 had hypothyroidism and 1 pregnancy with congenital heart disease. (**Table 1**)

Table 1: Distribution of associated Maternal Complications

Maternal complications	Number	Percentage (%)
PIH	18	45
GDM on insulin	2	5
Anemia	2	5
Rh negative	2	5
CHD	1	2.5
Hypothyroidism	1	2.5
Miscellaneous	14	35

Table 2: Pregnancy Outcome

Pregnancy outcome	No of cases	Percentage (%)
Adverse	19	47.5
Uneventful	21	52.5

Table 3: Distribution of adverse Outcomes

Adverse Outcomes	No of cases
Deaths (intrauterine and perinatal)	4
Emergency CS	7
Low Apgar score	12
Admission to NICU	11

Mean gestational age at the first Doppler US examination was 35.8 weeks +/- 3.46 weeks (2SD). 47.5% (n=19) fetuses had at least one abnormal outcome, of those some (n=11) had more than one abnormal outcome. Remaining 21 fetuses had normal outcome. (**Table 2**) Of the 40 pregnancies there were 2 intra uterine deaths and 38 live births. Of the 38 live births 2 neonates died in first week, 11 Neonates were admitted to NICU. 12 neonates had 5 min Apgar score of <7 and 7 babies were born by emergency caesarian section. Median birth weight at delivery was 2kg. 80% of neonates (n=30) had birth weight of less than 2.5 kg. (**Table 3/ Graph 1**)
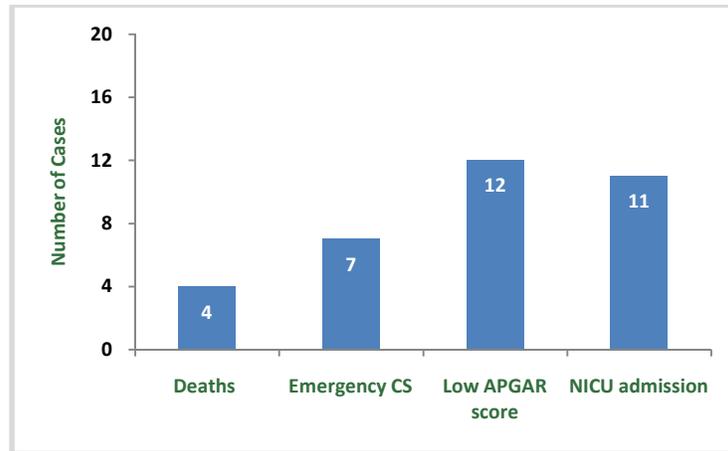
Graph 1: Distribution of adverse Outcomes

Both IUDs had reversal of diastolic flow (**Figure 2a**) and both neonatal deaths had absent diastolic flow in umbilical artery (**Figure 3a**). In all cases with reversal of diastolic flow, IUD of the fetus occurred within one week of diagnosis and both were preterm cases. **(Table 4)**

Table 4: Spectral characteristics of Umbilical Artery

Spectral Characteristics	No. of Cases	Perinatal Deaths	Mortality (%)
Absent EDF	04	2	50
Reversed EDF	02	2	100

Cerebroplacental ratio (MCA/UA PI Ratio) was most sensitive (94.7%) parameter. It was more sensitive than either UA PI (91%) or MCA PI (78.9%) alone in predicting any adverse out come. Cerebroplacental ratio was most specific (90.4%) than UA PI (85.7%) or MCA PI (68.4%) alone. Cerebroplacental ratio had highest Positive Predictive Value (90%) followed by UA PI (85%) and MCA PI (65.2%). Negative predictive value of cerebroplacental ratio was 95% when compared to 90% for UA PI and 76.4% for MCA. Diagnostic accuracy of cerebroplacental ratio (92.5%) was better than UA PI (87.5%) and MCA PI (70%) in predicting adverse outcomes. Of the 40 pregnancies studied 27 pregnancies had an estimated birth weight of less than 10th percentile and 13 pregnancies had birth weight more. **(Table 5)** Cerebroplacental ratio (MCA/UA PI Ratio) was most

sensitive (94.7%). It was more sensitive than either UA PI (91%) or MCA PI (78.9%) alone in diagnosing IUGR. Cerebroplacental Ratio was most specific (90.4%) than UA PI (85.7%) or MCA PI (68.4%) alone. There was no much difference in PPV of PI of UA, MCA and their ratio (95%). Negative Predictive Value of MCA PI (41.1%) was found to be higher when compared to UA PI and MCAPI/UAPI (35%). Diagnostic accuracy of MCA PI was higher (72.5%) compared to cerebroplacental ratio and UA PI which had similar accuracy of 65% in diagnosing IUGR. **(Table 6)**

Table 5: Performance Characteristics of Doppler indices in predicting perinatal outcome

	UA PI	MCA PI	MCA/UA PI Ratio
Sensitivity	89	78.9	94.7
Specificity	85.7	68.4	90.4
Accuracy	87.5	70	92.5
Positive Predictive value	85	65.2	90
Negative Predictive value	90	76.4	95

Table 6: Performance characteristics of doppler indices in diagnosing IUGR

	UA PI	MCA PI	MCA/UA PI Ratio
Sensitivity	58.3	68.7	58.3
Specificity	87	87.5	87
Accuracy	65	72.5	65
Positive Predictive value	95	95.65	95
Negative Predictive value	35	41.1	35

| Figure 1 (a) | Figure 1 (b) | Figure 2 (a) |

| Figure 2(b) | Figure 3(a) | Figure 3(b) |

Legend:
Figure 1 (a): Umbilical artery shows reduced diastolic flow and high pulsatility index
Figure 1 (b): MCA shows reduced pulsatility index
Figure 2 (a): Umbilical artery shows absent diastolic flow
Figure 2 (b): MCA shows reduced pulsatility index
Figure3 (a): Umbilical artery shows reversal of diastolic flow
Figure 3 (b): MCA shows reduced pulsatility index

DISCUSSION

When fetal growth restriction is suspected clinically, it is necessary to decide whether the fetus is "constitutionally" small or small as a consequence of impaired placental perfusion. Doppler flow velocity analysis can be valuable in resolving this question. The umbilical-placental and cerebral vascular beds are directly involved in the haemodynamic adjustments of fetal growth retardation. In IUGR, umbilical blood flow is significantly reduced, mainly due to changes in the placental vascular resistance. Giles et al [9] have found that a decrease in the number of resistance vessels in the tertiary stem villi in the placenta causes an increase in resistance, leading to decreased flow through the UA and an increase in the UA PI. This is described as umbilical placental insufficiency. In IUGR complicated by pregnancy-induced hypertension, there is inadequate trophoblastic invasion of the spiral arteries, leading to increased resistance in the spiral arteries and decreased blood flow in the placental vascular bed and in the UA, thereby resulting in an increase in the UA PI. This is described as uteroplacental insufficiency. In this situation of low oxygen tension there will be increased blood flow to the brain causing reduction in the MCA PI. Gramellini et al [7] calculated the cerebroplacental ratio and found that it remained constant in the last 10 weeks of pregnancy. We, therefore, used a single cut-off value of 1.08 for all cases of 31–40 weeks of gestation. Above this value, Doppler velocimetry was considered normal and, below it, abnormal. We chose perinatal death, emergency section for fetal distress, NICU admission for more than 7 days and low Apgar score as outcome variables in concurrence with previous studies done. For the diagnosis of IUGR estimated fetal weight was taken into consideration. We studied about 40 pregnancies with clinical suspicion of IUGR. 27 pregnancies had estimated fetal weight $< 10^{th}$ percentile. Median birth weight at delivery was 2 kg. 75% of neonates (n=30) had birth weight of less than 2.5 kg. 47.5% (n=19) fetuses had at least one adverse outcome; some (n=11) had more than one adverse outcome. Remaining 21 fetuses had favorable outcome. There were 2 intra uterine deaths and 38 live births. Of the 38 live births 2 neonates died first week, 11 neonates were admitted to NICU. 12 neonates had 5 min Apgar score of <7 and 7 babies were born by emergency caesarian section. By using the first Doppler US results for analysis, the MCA/UA PI ratio had a higher Sensitivity, Positive predictive value for adverse perinatal outcome than did the MCA PI and the UA PI alone. Differences in study design, including the criteria for patient selection, the definition of adverse outcomes, different cutoff levels between normal and abnormal test results, and the small number of patients studied, make direct comparison of the studies difficult. Our findings correlated with the results of the several studies that have shown MCA/UA PI Doppler ratio to be more useful than UA PI or MCA PI in predicting adverse outcome. (**Table 7 and 8**)

Table 7: Comparison of present study with Bano et [5] al in diagnosing adverse perinatal outcome

Doppler index		Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)	Diagnostic accuracy(%)
UAPI	**Bano *et al***	79.2	92.4	79.2	92.4	88.9
	Present study	89	85.7	85	90	87.5
MCAPI	**Bano *et al***	16.7	100	100	76.7	77.8
	Present study	78.9	68.4	65.2	76.4	70
MCAPI/ UAPI	**Bano *et al***	83.3	100	100	94.3	95.6
	Present study	94.7	90.4	90	95	92.5

Table 8: Comparison of present study with Bano et [5] al in diagnosing IUGR

Doppler index		Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)	Diagnostic accuracy(%)
UAPI	Bano *et al*	46.7	93.3	87.5	63.6	70
	Present study	58.3	87	95	35	65
MCAPI	Bano *et al*	8.9	100	100	52.3	54.4
	Present study	68.7	87.5	95.6	41.1	72
MCAPI/	Bano *et al*	44.4	100	100	64.3	72..2
UAPI	Present study	58.3	87	95	35	65

The differences in the outcome of present study with Bano et al[5] may be due to small study group, different study design where we considered estimated fetal weight instead of HC/AC ratio to diagnose IUGR, different MCA nomogram and no control group.

SUMMARY

We studied about 40 pregnancies with clinical suspicion of IUGR. Among them 27 pregnancies had estimated birth weight of less than 10th percentile. Median birth weight at delivery was 2 kg. 47.5% (n=19) fetuses had at least one adverse outcome; some of them (n=11) had more than one adverse outcome. Remaining 21 fetuses had favorable outcome. There were 2 intrauterine deaths and 38 live births. Of the 38 live births, there were 2 neonatal deaths in first week, 11 neonates were admitted to NICU, 12 neonates had 5 min Apgar score of less than 7 and 7 babies were born by emergency caesarian section. In our study MCA/UA pulsatility index ratio had a higher sensitivity, positive predictive value for adverse perinatal outcome than did the MCA pulsatility index and the UA PI separately. Our findings correlated with the results of the studies that have shown MCA/UA PI ratio to be more useful than UA PI or MCA PI in predicting adverse outcome. [5,10] Our studies confirm with those of Gramellini *et al* that best results are obtained when we used MCA/UA PI ratio, rather than PIs of middle cerebral artery and umbilical artery separately. [10] Diagnostic accuracy of MCA/UA PI ratio 92.5% when compared to 88% for UAPI and 70% for MCA PI. There were 2 IUDs which had reversal of diastolic flow in umbilical artery and 2 neonatal deaths which had absent diastolic flow in umbilical artery. In all cases with reversal of diastolic flow IUD occurred within one week of diagnosis and both were preterm. In our study, mortality in case of reversed end diastolic flow was 100% and 50% in absent diastolic flow indicating grave prognosis. In diagnosing IUGR, Doppler indices had similar specificity and positive predictive value. However, when compared to UAPI and MCA/UA PI, MCAPI had better sensitivity, negative predictive value and diagnostic accuracy.

CONCLUSION

In clinically suspected IUGR,
I. Cerebroplacental ratio (MCA/UA PI) is a better predictor of adverse perinatal outcome than MCAPI or UAPI.
II. Cerebroplacental ratio (MCA/UA PI) has less diagnostic accuracy in the diagnosis of IUGR compared to prediction of adverse perinatal outcome.

Therefore, fetal Doppler velocimetry helps in the recognition of compromised growth restricted fetus, thus plays an important role in the management of the growth restricted fetus allowing timely intervention.

REFERENCES

1. Ozyüncü O, Saygan-Karamürsel B, Armangil D, Onderoğlu LS, Yiğit S, Velipaşaoğlu M, Deren O. Fetal arterial and venous Doppler in growth restricted fetuses for the prediction of perinatal complications. Turk J Pediatr. 2010 Jul-Aug;52(4):384-92.
2. Turan OM, Turan S, Gungor S, Berg C, Moyano D, Gembruch U, Nicolaides KH,Harman CR, Baschat AA. Progression of Doppler abnormalities in intrauterinegrowth restriction. Ultrasound Obstet Gynecol. 2008 Aug;32(2):160-7.
3. Ghosh GS, Gudmundsson S. Uterine and umbilical artery Doppler are comparable in predicting perinatal outcome of growth-restricted fetuses. BJOG. 2009 Feb;116(3):424-30.
4. Figueroa-Diesel H, Hernandez-Andrade E, Acosta-Rojas R, Cabero L, Gratacos E. Doppler changes in the main fetal brain arteries at different stages of hemodynamic adaptation in severe intrauterine growth restriction. Ultrasound Obstet Gynecol.2007 Sep;30(3):297-302.
5. Bano S, Chaudhary V, Pande S, Mehta V, Sharma A. Color doppler evaluation of cerebral-umbilical pulsatility ratio and its usefulness in the diagnosis of intrauterine growth retardation and prediction of adverse perinatal outcome.Indian J Radiol Imaging. 2010 Feb;20(1):20-5.
6. Rozeta Shahinaj, Nikita Manoku, Enriketa Kroi, and Ilir Tasha .The value of the middle cerebral to umbilical artery Doppler ratio in the prediction of neonatal outcome in patient with preeclampsia and gestational hypertension. J Prenat Med. 2010 Apr-Jun; 4(2): 17–21.
7. Gramellini D, Folli MC, Raboni S, Vadora E, Merialdi A. Cerebral-umbilical Doppler ratio as a predictor of adverse perinatal outcome. Obstet Gynecol 1992; 79:416-20.
8. Arias F. Accuracy of the middle-cerebral-to-umbilical-artery resistance index ratio in the prediction of neonatal outcome in patients at high risk for fetal and neonatal complications. Am J Obstet Gynecol 1994; 171:1541-5.
9. Giles WB, Trudinger BJ, Cook CM: Fetal umbilical artery flow velocity-time waveforms in twin pregnancies. Br J Obstet Gynaecol 1985; 92:490.
10. Wang Y, Zhao S. Vascular Biology of the Placenta. San Rafael (CA): Morgan and Claypool Life Sciences; 2010