Original Research Article

Comparative performance of Cerebral Perfusion Ratio as compared to MCA PI and UA PI in prediction of adverse perinatal outcomes in intra uterine growth restricted fetuses

Jyotsna S. Shinde*, Madan P. Manmohan, Sanjay S. Pasoria, Thahir V. Ummer

Department of Radiology, Dr. D.Y. Patil Medical College, Nerul, Navi Mumbai, Maharashtra, India

*Correspondence:
Dr. Jyotsna S Shinde,
E-mail: jyotsna.radiology@gmail.com

ABSTRACT

Background: Intra uterine growth restriction (IUGR) is a common clinical sign seen due to chronic foetal hypoxemia and is considered a major contributor of perinatal morbidity and mortality. The aim of the present study was to determine and compare the sensitivity and specificity of umbilical artery pulsatility index (UA PI), middle cerebral artery (MCA) PI and cerebral perfusion ratio (CPR) in predicting adverse and poor perinatal outcomes in fetuses with IUGR.
Methods: The study included 100 pregnant women with post 24 weeks of gestation with clinical history of IUGR. Doppler examination parameters, including waveforms and measurements, of the umbilical artery, middle cerebral artery were recorded. The Cerebral Perfusion Ratio (CPR) was calculated from MCA PI and UA PI and a final comparison of accuracy of Doppler indices was done with perinatal outcome.
Results: The sensitivity of the UA PI was higher (49.3%) than that of the MCA PI (43.6%) and the CPR (37.7%). The specificity of the CPR was higher (87.1%) than that of the MCA PI (83.9%) and the UA PI (74.2%).
Conclusions: From the findings of the study, it can be concluded that UA PI is the most sensitive and CPR is the most specific parameter in predicting adverse perinatal outcomes in IUGR fetuses. Thus, in addition to pulsatility indices, CPR should be used as a tool for surveillance and included in the routine reporting formats of obstetric Doppler studies.

Keywords: Doppler velocimetry, Intra uterine growth restriction, Perinatal outcomes

INTRODUCTION

Intra uterine growth restriction (IUGR) is defined as the clinical circumstance of a foetus that is under achieving its growth potential. It is highly related to the perinatal morbidity and mortality. Hence it is necessary to make definitive diagnosis based on the superlative criteria to decrease perinatal mortality and morbidity in IUGR cases. The most important modality to diagnose IUGR antenatally is the analysis of Doppler blood flow velocity waveforms of fetal and maternal vessels.[1]

Changes in flow velocity waveforms are observed in various fetal vascular beds, and Doppler surveillance is based on the relationship between circulatory changes and the fetal condition.[2] Elevated impedance to blood flow in the placenta is reflected by abnormal umbilical artery velocimetry findings (early-stage Doppler abnormalities and an elevated pulsatility index).[3] In such situations, growth restriction due to placental insufficiency occurs, and there may also be a change in the fetal cerebral waveforms that suggests increased blood flow to the brain (brain-sparing reflex).[4]

However, abnormal early umbilical artery abnormalities and middle cerebral artery signals are of limited value in predicting the perinatal outcome in growth-restricted fetuses. In addition, examination of middle cerebral artery velocimetry in complicated pregnancies has indicated that the brain-sparing reflex is an early sign of fetal hypoxemia in fetuses that still have adequate reserves to cope with the stress of labor and vaginal delivery and therefore is of limited value for the prediction of the perinatal outcome and the optimal time for delivery.[5-7]

In this study we attempt to identify if cerebral perfusion ratio (CPR) is a better predictor of adverse perinatal outcomes than the individual pulsatility indices of the umbilical and middle cerebral arteries. This study is focused to give critical information on the use and value of CPR in pregnancies complicated with IUGR and the necessity to include this parameter in routine Doppler study of pregnancy and in the reporting format.

METHODS

A prospective observational study was conducted at the Department of Radio-Diagnosis at the Dr. D. Y. Patil Hospital and Research Centre, Nerul, Navi Mumbai from November 2015 (after Ethics Committee approval date) up to July 2017 after getting approval from Institutional ethics committee. The study included 100 patients with post 24 weeks of gestation (as calculated by their last menstrual period or by the first ultrasound) with EFW below 10th percentile and/or abnormal Doppler, with or without concomitant medical conditions. Patients not willing to give consent, fetuses with congenital anomalies, multiple gestation and those lost to follow up were excluded.

Obstetric ultrasonography was performed in all the patients using Mindray ultrasound machine using a 3.5 MHz convex probe. PNDT form i.e. form 'F' was obtained from all the patients. All relevant clinical history was obtained and the correct LMP was confirmed. An ultrasonography was performed with patient in supine position. Good acoustic coupling was obtained using synthetic ultrasound gel. Doppler velocimetry was performed on the umbilical and the MCA close to the transducer. The estimated fetal weight (EFW) was auto calculated by the ultrasound machine using Hadlock formula.[8]

The clinical examination result, obstetric color Doppler study, and perinatal outcome were recorded. In order to avoid, inter observer bias, the Investigator performed all the ultrasound scans on the same machine. The Doppler values of MCA PI and UA PI just before delivery were used for statistical analysis. The cerebral perfusion ratio (CPR) was calculated as the ratio of middle cerebral artery pulsatility index (PI) to umbilical artery pulsatility index (PI). Each of the study subjects was followed up during the intra partum and post- partum period. Adverse perinatal complications such as birth asphyxia, hypoglycemia, perinatal death, or admission to NICU were recorded.

Statistical analysis

The statistical analysis was done using statistical package for social sciences (SPSS) version 21 statistical analysis software. The values are represented in number (%) and Mean±SD. The statistical formulas used were sensitivity, specificity, positive predictive value and negative predictive value. P values <0.05 were considered as statistically significant.

RESULTS

In this study 100 pregnant women post 24 weeks of gestation were included. The mean maternal age was 26.45±4.58 years, falling in the age range between 18 to 38 years. Of them 49 were primigravidas. None of the study subjects had diabetes mellitus, maximum (29%) had concomitant pregnancy induced hypertension (PIH). All study subjects in this study were between 29 to 40 weeks of gestation at delivery. 23 had early onset IUGR and 77had late onset IUGR.

On ultrasound Doppler abnormal cases were noticed in 54 cases. On the basis of umbilical artery pulsatility index (UA PI) abnormality was seen in 42 patients when the 95th percentile of reference ranges for respective gestational ages were used as cut off for normal. Middle cerebral artery pulsatility index (MCA PI) abnormality was seen in 35 patients when the 5th percentile of reference ranges for respective gestational ages were used as cut off for normal. Abnormal cerebral perfusion ratio was seen in 30 patients (Table 1).

Table 1: Distribution of study subjects according to ultrasound Doppler results.

Doppler results	Number of patients (n=100)
Abnormal	54
Normal	46
Pulsatility index	
Abnormal UA PI at 95th percentile	42
Normal UA PI at 95th percentile	58
Abnormal MCA PI at 5th percentile	35
Normal MCA PI at 5th percentile	65
Abnormal CPR	30
Normal CPR	70

Figure 1 presents the distribution of study subjects according to expected foetal weights (EFW) values as compared to reference range for that gestational age.
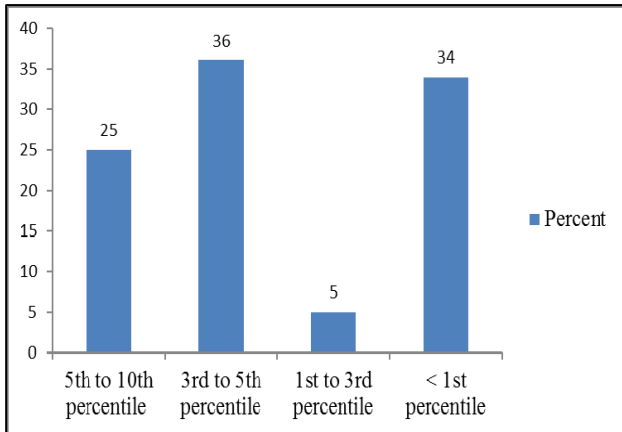
Figure 1: Distribution of study subjects according to EFW.

Out of 100 cases, 63 were full term babies and 37 were preterm babies. Still birth was noticed in 7 cases and 93 cases were survived. All the cases of still birth were observed in fetal stage with abnormal UA PI, MCA PI with significant correlation between them with p values of 0.002, 0.00043 and 0.00013 respectively.

A total of 62 neonates needed admission to NICU. Of them, 28 neonates had abnormality in MCA PI and 23 of them needed NICU admission. Out of 35 neonates with abnormality in UA PI, 27 was admitted in NICU and out of 23 patients with abnormality in CPR 19 neonates needed admission in NICU. The duration of NICU stay varied from a minimum of 2 days up to a maximum of 55 days with a mean of 11 days at a standard deviation of

12.7. A maximum number of neonates (n=10, 16.1%) were in the NICU for a period of 4 days, followed by 8 neonates each admitted for 2 days and 7 days respectively. 3 neonates were admitted for 55 days, 2 for 35 days and 3 for 32 days (Table 3).
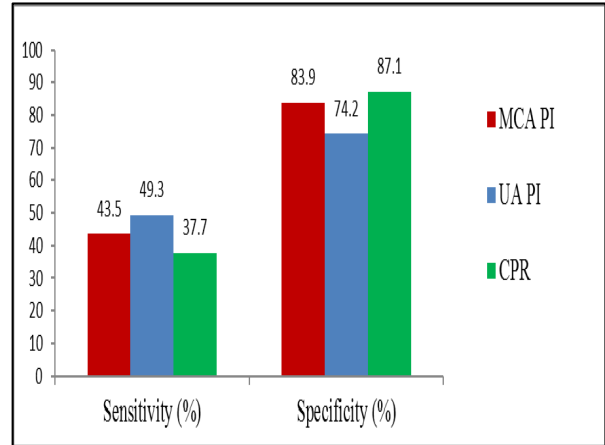
Figure 2: Comparison of sensitivity and specificity in MCA PI, UA PI and CPR.

Table 2: Status of neonates during and after birth.

Gestational status	No. of patients (n=100)
Full term	63
Preterm	37
Birth status	
Live birth	93
Still birth	7

Table 3: Comparative performances of all three pulsatility indices with respect to NICU admission.

		NICU admission required		Total	P Value by Chi square test
		Yes	No		
MCA PI	Abnormal	23	5	28	0.05
		37.1%	16.1%	30.1%	
	Normal	39	26	65	
		62.9%	83.9%	69.9%	
UA PI	Abnormal	27	8	35	0.09
		43.5%	25.8%	37.6%	
	Normal	35	23	58	
		56.5%	74.2%	62.4%	
CPR	Abnormal	19	4	23	0.06
		30.6%	12.9%	24.7%	
	Normal	43	27	70	
		69.4%	87.1%	75.3%	
Total		62	31	93	
		100.0%	100.0%	100.0%	

As given in Table 4, adverse perinatal outcome was noticed in 69 neonates. Of 35 fetuses with abnormal

MCA PI, 30 cases showed adverse perinatal outcomes. Out of 42 fetuses with abnormal UA PI 34 had adverse

perinatal outcome. Out of 30 foetuses with abnormal CPR, 26 had adverse perinatal outcome.

Table 4: Comparative performances of all three pulsatility indices with respect to perinatal outcome.

		Perinatal outcome		Total	P value by Chi square test
		Adverse	Normal		
MCA PI	Abnormal	30	5	35	0.01
		43.5%	16.1%	35.0%	
	Normal	39	26	65	
		56.5%	83.9%	65.0%	
UA PI	Abnormal	34	8	42	0.03
		49.3%	25.8%	42.0%	
	Normal	35	23	58	
		50.7%	74.2%	58.0%	
CPR	Abnormal	26	4	30	0.013
		37.7%	12.9%	30.0%	
	Normal	43	27	70	
		62.3%	87.1%	70.0%	
Total		69	31	100	
		100.0%	100.0%	100.0%	

Table 5: Comparative performances of all three pulsatility indices with respect to perinatal mortality.

		Perinatal mortality		Total	P value by Chi square test
		Yes	No		
MCA PI	Abnormal	9	26	35	0.03
		75.0%	29.5%	35.0%	
	Normal	3	62	65	
		25.0%	70.5%	65.0%	
UA PI	Abnormal	9	33	42	0.016
		75.0%	37.5%	42.0%	
	Normal	3	55	58	
		25.0%	62.5%	58.0%	
CPR	Abnormal	9	21	30	0.01
		75.0%	23.9%	30.0%	
	Normal	3	67	70	
		25.0%	76.1%	70.0%	
Total		12	88	100	
		100.0%	100.0%	100.0%	

Table 6: Final comparative performance of MCA PI, UA PI and CPR in predicting adverse perinatal outcomes in IUGR fetuses.

Index	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
MCA PI	43.5	83.9	85.7	40.0	56.0
UA PI	49.3	74.2	80.9	39.7	57.0
CPR	37.7	87.1	86.7	53.0	53.0

Out of 100 cases, perinatal mortality was seen in 12 cases. Of them 7 cases were still birth and 5 were early neonatal deaths. Of them total 9 cases were noticed with abnormal MCA PI, UA PI and CPR during their fetal stage (Table 5).

As shown in Table 6 and Figure 2, the sensitivity, specificity, positive predictive value and negative predictive value of the PI of the MCA in determining adverse perinatal outcomes in the pregnancies complicated with IUGR in this study calculated to be 43.5%, 83.9%, 85.7%, and 40% respectively. 49.3% sensitivity and 74.2% specificity was observed for umbilical artery Doppler in the study population which comprised of pregnancies complicated with IUGR. The positive predictive value was 80.9% and a negative predictive value was 39.7%. The sensitivity, specificity, positive predictive value and negative predictive value of the CPR in predicting adverse fetal outcome was found to be 37.7%, 87.1%, 86.7% and 53% respectively.

DISCUSSION

The prevalence of IUGR in India was found to be 54% in 2 independent studies according to Antoni Samy et al, and Pinheiro et al.[9,10] In India, according to recent UNICEF surveys, the per annum incidence of IUGR is 25-30%.[11] Out of the 100 pregnancies included in the study all fetuses were diagnosed with IUGR clinically.

All these fetuses were confirmed with IUGR postnatally on the basis of Ponderal index at birth. Hemlata et al, calculated an incidence of 15.6% per annum in their hospital.[12] According to a study conducted by Khanduri et al, 42 (70%) fetuses out of 60 were complicated with IUGR while 18 (30%) were falsely diagnosed with IUGR.[1]

The mean estimated fetal weight by the last ultrasound scan done before delivery was 1959.33±537.36 grams years, falling in the range between 574 to 2760 grams. NICU admission was mandatory for all fetuses detected with birth weight less than 2000 grams. This is due to standards protocols set in our hospital. For the sake of simplicity, we included all admissions in the NICU for a period of >48 hour due to any post-natal complication, as a component to define perinatal morbidity. In this study total of 62 neonates needed admission to NICU. According to Patange et al, in their study, 42% women with IUGR fetuses were required to admit their fetuses into NICU.[13]

Of the 100 patients enrolled in the study, 54 had an overall abnormal Doppler study. 37 patients had preterm delivery whereas 63 were full term at delivery. According to the Regional Health Forum, WHO (2005) approximately 3.3 million babies are still born each year.[14] In India the stillbirth rate is about 9 per 1000 births. The total stillbirth rate for the state of Maharashtra was 12 per 1000 births. In this study, 93 of the 100 fetuses delivered were live fetuses and 7 were stillbirths.

In this study a total of 12 growth restricted fetuses did not survive through the perinatal period (12% of pregnancies complicated with IUGR). According to Patange et al,

study 10% of neonates diagnosed with IUGR did not survive. Their findings showed similar results.[13]

In the evaluation of the fetal cerebral circulation, the MCA is the most accessible vessel. It can easily be located on an axial image of the fetal head. It is the main branch of the internal carotid artery and carries approximately 80% of cerebral blood flow to the ipsilateral cerebral hemisphere and a constant 3%-7% of the cardiac output throughout gestation. Hence, we used this vessel for the evaluation of the fetal cerebral circulation.

The sensitivity, specificity, positive predictive value and negative predictive value of the PI of the MCA in determining adverse perinatal outcomes in the pregnancies complicated with IUGR in this study calculated to be 43.5%, 83.9%, 40% and 56% respectively. The sensitivity is higher than that noted in a study conducted by Trudinger et al.[15] The sensitivity noted in this study was slightly lower than that noted in the studies conducted by Mari et al.[16]

Gudmundsson et al, performed a cross sectional study and demonstrated that in normal pregnancy umbilical artery Doppler indices decrease with advancing gestation.[17] In IUGR first there is decreased diastolic flow in the umbilical artery due to increase in the resistance that occurs in small arteries and arterioles of the tertiary villi.

This raises the S/D ratio, Pl and Rl of umbilical artery. As the placental insufficiency worsens, the diastolic flow decreases, then become absent, and later reverses. Ina study conducted by Bano et al, UA PI proved to be the most appropriate parameter in identifying IUGR.[18]

Further in this study we obtained 49.3% sensitivity and 74.2% specificity for umbilical artery Doppler in the study population which comprised of pregnancies complicated with IUGR. The positive predictive value was 80.9% and a negative predictive value was 39.7%. Mulders et al, found a sensitivity of 53.3% and a specificity of 87.9% for the UA PI in antenatal prediction of neonatal mortality.[19] However slightly lower sensitivity and specificity was obtained in this study. The sensitivity and specificity of the umbilical artery PI in predicting adverse foetal outcome were 50% and 59% according to a study published by Lakhar et al.[20]

In this study, 30 of 100 patients showed abnormal and 70 patients showed normal CPR values. Our specificity (87.1%), positive predictive value (86.7%) and negative predictive value (53%) were consistent with study conducted by Lakhkar et al, however our study showed less sensitivity of CPR (37.7%) in detecting adverse perinatal outcomes.[20] The sensitivity obtained in this study was comparable with that in a study conducted by Trudinger et al.[15]

The comparison of the Doppler indices in predicting neonatal morbidity with other published studies was not possible due to varied definitions of perinatal morbidities. Diverse end points were used by various authors. Some of the major outcomes included neurologic complication (major intracranial haemorrhage, periventricular leukomalacia), and necrotizing enterocolitis. The minor outcomes used by some authors were caesarean section for fetal distress, acidosis, low 5-minute Apgar scores, and admission to the neonatal intensive care unit were used.

CONCLUSION

Our study shows that umbilical artery PI is more sensitive, and CPR is more specific an indicator in detecting adverse perinatal outcomes in IUGR fetuses. On the basis of the current findings, we suggest that longitudinal monitoring of CPR values in IUGR fetuses in conjunction with PI of umbilical and middle cerebral arteries and ductus venosus Doppler is a logical approach to optimize the timing of delivery rather than watching and waiting for changes in fetal heart patterns and biophysical profile which, moreover, correlate poorly with the neonatal outcome.

Thus, a combination of longitudinal multivessel Doppler monitoring and biophysical profile scores together could provide a definitive indication for action in the management of severely IUGR fetuses. However, there is still the need for more well-designed longitudinal trials to devise protocols for grading and management of fetuses with IUGR.

REFERENCES

1. Khanduri S, Parashari UC, Bashir S, Bhadury S, Bansal A. Comparison of diagnostic efficacy of umbilical artery and middle cerebral artery waveform with color Doppler study for detection of intrauterine growth restriction. J Obstet Gynecol India. 2013;63(4):249-55.
2. Baschat AA, Gembruch U, Reiss I, Gortner L, Weiner CP, Harman CR. Relationship between arterial and venous Doppler and perinatal outcome in fetal growth restriction. Ultrasound Obstet Gynecol. 2000;16(5):407-13.
3. Divon MY. Umbilical artery Doppler velocimetry: clinical utility in high-risk pregnancies. Am J Obstet Gynecol. 1996;174(1):10-4.
4. Kaponis A, Harada T, Makrydimas G, Kiyama T, Arata K, Adonakis G, et al. The importance of venous Doppler velocimetry for evaluation of intrauterine growth restriction. J Ultrasound Med. 2011;30(4):529-45.
5. Hofstaetter C, Gudmundsson S, Dubiel M, Marsal K. Ductus venosus velocimetry in high-risk pregnancies. Eur J Obstet Gynecol Reprod Biol. 1996;70(2):135-40.
6. Gudmundsson S, Dubiel M, Gunnarson G, Stale H, Maesel A, Marsál K. Middle cerebral artery velocimetry as a predictor of hypoxemia in foetuses with increased pulsatility index in the umbilical artery. J Matern Foetal Invest. 1994;4:19.
7. Dubiel M, Gudmundsson S, Gunnarson G, Marsál K. Middle cerebral artery velocimetry as a predictor of hypoxemia in foetuses with increased resistance to blood flow in the umbilical artery. Early Hum Dev. 1997;47:177-84.
8. Hadlock FP, Harrist RB, Sharman RS, Deter RL, Park SK. Estimation of fetal weight with the use of head, body, and femur measurements-a prospective study. Am J Obstet Gynaecol. 1985;151(3):333-7.
9. Antonisamy B, Sivaram M, Richard J, Rao PS. Trends in intra-uterine growth of single live births in southern India. J Trop Pediatr. 1996;42(6):339-41.
10. Pinheiro A, David A, Joseph B. Pregnancy weight gain and its correlation to birth weight. Indian J Med Sci. 2001;55(5):266-70.
11. Gogate S. Intra-Uterine Growth Restriction-Obstetrician's Perspective. Int J Diab Dev Ctries [serial online]. 2001;21:51-6.
12. Dhand H, Kansal HK, Dave A. Middle cerebral artery Doppler indices better predictor for fetal outcome in IUGR. J Obstet Gynecol India. 2011;61(2):166-71.
13. Patange RP, Goel N. Role of Colour Doppler: Cerebral and Umbilical Arterial Blood Flow Velocity In Normal And Growth Restricted Pregnancy. JEMDS. 2014;3(13):3310-20.
14. The World Health Report 2005. Available at: http://www.who.int/whr/2005/whr2005_en.pdf. Accessed on 16 April 2018.
15. Trudinger BJ, Giles WB, Cook CM. Flow velocity waveforms in the maternal uteroplacental and fetal umbilical placental circulations. Am J Obstet Gynecol. 1985;152:155-63.
16. Mari G, Deter RL. Middle cerebral artery flow velocity waveforms in normal and small-for-gestational-age fetuses. Am J Obstet Gynecol. 1992;166:1262-70.
17. Gudmundsson S, Maršál K. Umbilical and uteroplacental blood flow velocity waveform in normal pregnancy - A cross-sectional study. Acta Obstet Gynecol Scand. 1988;67:347-54.
18. Bano S, Chaudhary V, Pande S, Mehta VL, Sharma AK. 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;20(1):20-5.
19. Mulders LG, Wijn PF, Jongsma HW, Hein, PR. A comparative study of three indices of umbilical blood flow in relation to prediction of growth retardation. J Perinat Med. 1987;15(1):3-12.

20. Lakhkar BN, Rajagopal KV, Gourisankar PT. Doppler prediction of adverse perinatal outcome in PIH and IUGR. Ind J Radiol Imaging. 2006;16(1):10-6.