Original Research Article

Doppler study of umbilical and fetal middle cerebral artery in severe preeclampsia and intra uterine growth restriction and correlation with perinatal outcome

Santosh Kumar Singh[1], Priti Mishra[2]*

[1]Department of Obstetrics and Gynecology, Command Hospital, Pune, Maharashtra, India
[2]Department of Obstetrics and Gynecology, Command Hospital Central Command, Lucknow, Uttar Pradesh, India

*Correspondence:
Dr. Priti Mishra,
E-mail: dr.mishrapriti@gmail.com

ABSTRACT

Background: Pre-eclampsia and IUGR are two conditions resulting from defective trophoblastic invasion of spiral arteries and an increase in vascular resistance in uteroplacental circulation. Doppler offers a non-invasive tool for evaluation of fetoplacental blood flow and correlate with fetal compromise giving early warning sign of fetal distress.
Methods: The study was conducted in Command Hospital, Lucknow in 100 singleton pregnancies with vertex presentation between 28-40 weeks of gestation with severe preeclampsia and/or IUGR. Doppler analysis of UA and MCA was done. Pregnancies were terminated depending on clinical condition and Doppler results.
Results: Abnormal Umbilical artery S/D ratio had strong statistical correlation with poor perinatal outcome. Elevated RI had 100% sensitivity in predicting APGAR<7 at 5 minutes. Elevated PI values was statistically significant in all parameters (except NICU stay>48hrs) in predicting poor perinatal outcome. PI values had highest sensitivity for predicting low APGAR values and highest specificity for predicting NICU admission. AEDF and REDF also correlated with adverse perinatal outcome. MCA S/D ratio had a high sensitivity (96.8%) in determining NICU stay>48h and specificity (70%) in determining NICU admissions. RI had highest sensitivity (71.8%) for NICU stay >48hrs and highest specificity for predicting NICU admissions (76.5%). MCA PI had a sensitivity of 66.6% in determining APGAR<7 at 5min and a specificity of 78.7% in determining NICU admissions. CPR had the highest sensitivity (100%) among all indices.
Conclusions: The study showed an adverse fetal outcome in cases of severe preeclampsia and or IUGR which showed abnormal Doppler results and thereby help to determine the optimal time for delivery.

Keywords: Doppler, Intra-uterine growth restriction, Middle cerebral artery, Perinatal outcome, Preeclampsia, Umbilical artery

INTRODUCTION

Pre-eclampsia is a major cause of maternal and perinatal mortality and morbidity worldwide causing 24% of all maternal deaths in India.[1,2] It accounts for a total of 7-10% of perinatal mortality in developed countries and 20% in developing countries. Early detection of preeclampsia may allow vigilant antenatal surveillance and appropriate timing of fetal delivery in order to avoid serious sequelae.

Human placentation relies on the trophoblastic invasion of the maternal decidua, myometrium and their blood vessels. Cytotrophoblastic cells invade and partially

replace the endothelium of the maternal spiral arteries, leading to progressive dilatation of these vessels. This process begins as early as 10th day post conception and continues all through pregnancy.[3,4]

Defective placentation is considered to be the major etiological factor in the development of pre-eclampsia and IUGR, both of which are major causes of perinatal mortality and morbidity worldwide.[5,6]

The decreased uteroplacental perfusion can result in fetal growth restriction, reduced amniotic fluid volume and an inability to tolerate the in utero environment leading to intrauterine death The timely diagnosis of fetal compromise is very important so that delivery can be affected before fetus suffers irreversible damage and dies in utero.

Doppler velocity study of placental and fetal circulation can provide important information about fetal wellbeing, thus providing an opportunity to improve fetal outcome various Doppler indices help to know about uteroplacental blood flow status.

The S/D ratio gives a simple evaluation of blood flow during diastole and provides estimation of downstream resistance. The pourcelot index or RI is useful when the diastolic flow is absent or reversed and the S/D cannot be calculated.[7] Hence it helps in comparing any waveform irrespective of its diastolic flow.

The pulsatality index considers the mean velocity as diameter i.e. the whole of the flow is given consideration not just the diastolic flow and hence can be used to analyze data from various vessels without encountering the excessive variation that can be caused by division by small numbers as with the other two indices.[8]

The aim of the study was to determine and compare the diagnostic performance of Doppler sonography of fetal middle cerebral artery (MCA) and umbilical artery (UA) in prediction of adverse perinatal outcome in suspected intrauterine growth retardation (IUGR) and severe PE.

METHODS

The study comprised of 100 women with singleton pregnancies with vertex presentation between 28 to 40 weeks of gestation complicated by severe preeclampsia and IUGR admitted to Command Hospital, Lucknow from March 2015 to February 2016.

Informed consent was taken from all the patients. Detailed history and through examination was done. All relevant investigations were carried out. The relevant data obtained was recorded in the standard prepared proforma.

Doppler waveform analysis of umbilical artery and middle cerebral artery was done.

Further management of the cases was decided depending on the clinical status of the patients and the Doppler report, and pregnancies were terminated as and when indicated.

Patients who continued pregnancy after the Doppler examination, Doppler was repeated at weekly interval. Doppler study done within 7 days prior to termination of pregnancy was taken into consideration for the study.

Mode of termination of pregnancy was decided depending on the clinical condition of patients and the indications. At the time of delivery details such as baby weight, APGAR score, meconium staining of liquor and neonatal intensive care unit admissions were noted.

Statistical analysis

Chi-square test was used for statistical comparison. Statistical significance was set at p <0.05. All the statistical calculations were done through SPSS for Windows (v 16.0).

RESULTS

One hundred singleton pregnancies between 28 and 40 weeks of gestation complicated by intrauterine growth restriction and severe pre-eclampsia or both were prospectively examined with Doppler ultrasonogrpahy of the UA and MCA and were correlated with fetal outcome out of which there were severe PE (47 cases), IUGR (7 cases) and severe PE+IUGR (46 cases). Age of the patients ranged from 18 to 36 years with a mean age of 22.8 years (S.D 3.6 years).

Of them 69% were primigravida and 31 were multigravida. Gestational age of the patients ranged between 28-40 weeks. Maximum number of patients (60%) belonged to 37-40 weeks group. All patients were subjected to Doppler waveform analysis of Umbilical and MCA and all the indices were noted.

Umbilical artery waveform analysis

Umbilical artery Doppler studies revealed that 52 patients had elevated S/D ratio, 58 had elevated RI and 63 had elevated PI. The perinatal mortality was highest in the elevated RI (31%) group when compared to elevated S/D (25%) and elevated PI (28.5%) group. Amongst the umbilical artery waveforms highest LSCS for fetal distress was done in those with an elevated RI (27.6%). Meconium stained liquor incidence (53.4%) was also highest amongst the elevated RI group.

Number of cases with birth weight<10th percentile was equal (58.6%) in elevated RI and PI group. Umbilical RI also had a 100% sensitivity in predicting APGAR<7 at 5min. The highest specificity (74.4%) was for S/D ratio in predicting NICU admissions (Table 1-3).

Table 1: Umbilical artery S/D ratio correlation with fetal outcome.

Fetal outcome	Increase in S/D ratio		Normal S/D ratio		p value	Sensitivity	Specificity
	No. (N=52)	%	No. (N=40)	%			
Birth weight <10th percentile	30	57.7	10	25.0	<0.05	75%	57.6%
LSCS for fetal distress	10	19	2	5	<0.05	19.23%	95%
Meconium stained liquor	27	51.9	6	15.0	<0.05	81.8%	61.8%
APGAR<7 (5 min)	28	53.8	1	2.5	<0.05	96.5%	66.1%
NICU admission	41	78.8	8	20	<0.05	83.6%	74.4%
NICU stay >48hrs	27	51.9	3	7.5	<0.05	90%	26.3%
Perinatal mortality	4	7	1	2.5	NS	7.69%	97.5%

Table 2: Umbilical RI values correlation with fetal outcome.

Fetal outcome	Elevated RI		Normal RI		p-value	Sensitivity	Specificity
	No. (N=58)	%	No. (N=42)	%			
Birth weight <10th percentile	34	58.6	11	26.2	<0.05	75%	56.3%
LSCS for fetal distress	16	27.6	1	2.38	<0.05	27.5%	97.62%
Meconium stained liquor	31	53.4	6	14.28	<0.05	83.7%	64.2%
APGAR<7 (5 min)	33	56.8	0	-	<0.05	100%	71.1%
NICU admission	45	77.5	8	19	<0.05	84.9%	72.3%
NICU stay >48hrs	29	50	3	7.1	NS	90.6%	23.8%
Perinatal mortality	10	17	0	-			

Table 3: Umbilical PI correlation with fetal outcome.

Fetal outcome	Elevated PI		Normal PI		p-value	Sensitivity	Specificity
	No. (N=63)	%	No. (N=37)	%			
Birth weight <10th percentile	37	58.7	8	21.6	<0.05	82.2%	52.7%
LSCS for fetal distress	16	25.4	1	2.7	<0.05	25.4%	97.3%
Meconium stained liquor	32	50.7	5	13.5	<0.05	86.4%	57.1%
APGAR<7 (5 min)	32	50.7	1	2.7	<0.05	96.9%	61%
NICU admission	46	73	7	18.9	<0.05	86.7%	63.8%
NICU stay >48hrs	29	46	3	8.1	NS	90.6%	19.0%
Perinatal mortality	10	15	1	2.7	NS	2.9%	88.4%

Umbilical artery waveform analysis

Umbilical artery Doppler studies revealed that 52 patients had elevated S/D ratio, 58 had elevated RI and 63 had elevated PI. The perinatal mortality was highest in the elevated RI (31%) group when compared to elevated S/D (25%) and elevated PI (28.5%) group. Amongst the umbilical artery waveforms highest LSCS for fetal distress was done in those with an elevated RI (27.6%). Meconium stained liquor incidence (53.4%) was also highest amongst the elevated RI group. Number of cases with birth weight<10th percentile was equal (58.6%) in elevated RI and PI group. Umbilical RI also had a 100% sensitivity in predicting APGAR<7 at 5min. The highest specificity (74.4%) was for S/D ratio in predicting NICU admissions (Table 1-3).

Five cases of 100 had AEDF and 3 had REDF. Perinatal mortality was worst amongst the REDF group wherein all delivered stillborn fetuses.Perinatal mortality and birth weight <10th percentile in those with AEDF was 60%.

80% had APGAR<7 at 5 min and meconium stained liquor.

MCA waveform analysis

MCA Doppler studies revealed that when there was an increase in the umbilical artery resistance there was a decrease in the values of MCA indices showing a brain sparing effect. Fifty-eight cases had an abnormal MCA S/D ratio,47 had abnormal RI and 43 had abnormal PI. Amongst the MCA indices perinatal mortality was highest for abnormal PI (41.8%) when compared to 34% (abnormal RI) and 31% (abnormal S/D).

Both abnormal S/D and PI correlated with 60.3% of birth weights <10th percentile. LSCS for fetal distress was highest, 30.2% amongst the abnormal PI group. Meconium stained liquor incidence was highest in the abnormal S/D group (50%) and was equal in the other two abnormal indices groups (44%). Incidence of APGAR<7 at 5 min also was highest amongst abnormal

S/D group (53.4%). NICU admission was comparable amongst the three groups (~76%). However abnormal S/D ratio had the highest specificity of 96.8% for predicting NICU stay >48 hrs (Table 4-6).

Table 4: MCA S/D ratio with fetal outcome.

Fetal outcome	Abnormal S/D		Normal S/D		p-value	Sensitivity	Specificity
	No. (N=58)	%	No. (N=42)	%			
Birth weight <10th percentile	35	60.3	10	23.8	<0.05	77.7%	58.1%
LSCS for fetal distress	15	25.8	2	4.76	<0.05	25.86%	95.24%
Meconium stained liquor	29	50.0	8	19.0	<0.05	78.3%	60.7%
APGAR<7 (5 min)	31	53.4	2	4.76	<0.05	93.9%	67.7%
NICU admission	44	75.8	9	21.4	<0.05	83%	70.2%
NICU stay >48hrs	31	53.4	1	2.3	<0.05	96.8%	38.0%
Perinatal mortality	5	8	0		-		

Table 5: MCA RI with fetal outcome.

Fetal outcome	Abnormal RI		Normal RI		p-value	Sensitivity	Specificity
	No. (N=47)	%	No. (N=53)	%			
Birth weigt <10th percentile	27	57.4	18	34	<0.05	60%	63.6%
LSCS for fetal distress	12	25.5	5	9.4	<0.05		
Meconium stained liquor	21	44.6	16	30.2	BS	56.7%	66.0%
APGAR<7 (5 min)	23	48.9	10	18.8	<0.05	69.6%	72.8%
NICU admission	36	76.5	17	32.1	<0.05	67.9%	76.5%
NICU stay >48hrs	23	48.9	9	16.9	NS	71.8%	38.0%
Perinatal mortality	16	34	2	3.7			

Table 6: MCA PI with fetal outcome.

Fetal outcome	Abnormal PI		Normal PI		p-value	Sensitivity	Specificity
	No. (N=43)	%	No. (N=57)	%			
Birth weight <10th percentile	26	60.4	19	33.3	<0.05	57.7%	65.4%
LSCS for fetal distress	13	30.2	4	7	<0.05	30.23%	87.72%
Meconium stained liquor	19	44.1	18	31.5	NS	51.3%	67.8%
APGAR<7 (5 min)	22	51.1	11	19.2	<0.05	66.6%	76.2%
NICU admission	33	76.7	20	35	<0.05	62.2%	78.7%
NICU stay >48hrs	13	30.2	18	31.5	NS	41.9%	57.1%
Perinatal mortality	9	20.9	-				

Cerebro placental ratio analysis

In all the fetuses with a brain sparing effect the CPR was <1.08 (57 cases). Perinatal mortality rate was 31.5% in those with a CPR <1.08, 80.7% needed NICU admission and 57.8% babies had APGAR<7 at 5mins.

Sixteen patients (28.1) with CPR <1.0 8 underwent LSCS for fetal distress and 36 (63.1%) had birth weight <10th percentile. CPR had 100% sensitivity in predicting NICU stay >48hrs and APGAR<7 at 5mins.

Specificity of CPR was 76.5% in determining NICU admissions. Overall highest CPR had the highest sensitivity (100%) and MCA PI had the highest specificity (78.7%).

DISCUSSION

The role of Doppler ultrasound in the study of uteroplacental and fetoplacental circulation is well known. It helps in detecting the extent of placental pathology and also predicts the fetal outcome. In normal pregnancy, the three indices; S/D; Pl and Rl decrease with advancing gestation.[8] But 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. Some fetuses have decreased diastolic velocity that remains constant with advancing gestation and never become absent or reversed which

may be due to a milder form of placental insufficiency. The prevalence of perinatal death in fetuses with absent or reversed end diastolic flow velocity is reported to be over 40%.[9] Numerous studies have been conducted to know the association between Doppler waveforms and perinatal outcome and have had variable results.

The present study showed that abnormal Doppler waveforms was associated with adverse perinatal outcome.

When umbilical artery velocity was correlated to fetal outcome in the present study, it was shown that there was an increase in the perinatal morbidity and mortality in cases with an abnormal umbilical artery S/D ratio. Yoon et al demonstrated in their study that absent umbilical artery waveform is a strong and independent predictor of adverse perinatal outcome.[10] When umbilical artery S/D ratios were compared to the study of Trudinger et al also showed that abnormal waveform are associated with adverse perinatal outcomes.[11]

Brar et al. noted that when umbilical artery S/D ratio is >3 than there is a greater chance of SGA, APGAR score<7 at 5 minutes, caesarean section for fetal distress and thick meconium in labour that correlated with the present study.[12] Similar findings were also noted by Yelikar.[13]

When the fetoplacental flow is severely affected there is an increased impedance to flow resulting in end diastolic flow becoming absent. With further hemodynamic compromise there will be reversal of flow in the umbilical arteries.

Such a development is ominous and results in a profoundly adverse perinatal outcome.In our study it was seen that AEDF or REDF correlated with poor perinatal outcome with an increase in the perinatal mortality and morbidity. Bhat CJ, Malhotra N also reported similar outcome.[14,15]

The perinatal mortality rate in those with a REDF in study was 100%. Hence from the above correlation and the results of the present study it is evident that in women with AEDF/REDF, if the baby is salvageable and NICU facilities are available, it is safer to deliver the baby for a better perinatal outcome.

Delivery can be delayed by 1-2 weeks if desired, with very intensive fetal surveillance in cases of AEDF, but immediate delivery is advocated when REDF sets in. REDF is a terminal event associated with an extremely high perinatal mortality.

The present study showed that UA PI >2SD is associated with poor perinatal outcome and birth weight <10th centile. Similar outcomes were shown in study by Bano, Chalubinski and Roy.[16-18]

Redistribution of blood flow occurs as an early stage in fetal adaptation to hypoxemia (brain-sparing reflex), wherein there will be an increased end diastolic flow resulting in decrease in Middle Cerebral Artery PI and RI. Present study showed similar findings of decrease in the MCA Doppler indices with an elevated umbilical artery resistance.

Low index of pulsatility in the MCA associated fetal compromise has been described by many authors.[19] In present study it was found that low MCA PI was associated with 60.4% of SGA babies and 41.8% of perinatal mortality.

MCA/UA pulsatality index ratio or the Cerebroplacental ratio is potentially more advantageous in predicting perinatal outcome as it not only incorporates data on the placental status but also on fetal response. Diagnostic performance of CPR in relation to perinatal outcome was similar to other studies.[20,21]

CONCLUSION

The present study noted an adverse fetal outcome in cases of severe preeclampsia and or IUGR which showed abnormal Doppler results. The finding of REDF is ominous and AEDF also correlated with poor fetal outcome with a perinatal mortality of 60%. In our study CPR had the highest sensitivity of 100% in predicting adverse fetal outcomes. Because CPR incorporates data not only on the placental side but also the fetal response it can be considered potentially more advantageous. Doppler patterns follow a longitudinal trend with early changes in the umbilical artery followed by middle cerebral artery. Doppler investigation of the fetal circulation plays an important role in monitoring the redistributing fetus and thereby may help to determine the optimal time for delivery.

REFERENCES

1. WHO. WHO International Collaborative study of Hypertensive disorders of pregnancy. Geographic variation in the incidence of Hypertension in pregnancy. Am J Obstet Gynecol. 1988;158:80-3.
2. Confidential Enquiry into maternal deaths: Why mothers die? 2000-2002. The sixth Report of the confidential Enquiries into maternal deaths in UK. London: RCOG Press;2004.
3. Pijnenborg R, Dixon G, Robertson WR, Brosens F. Trophoblastic invasion of human decidua from 8-18 wks of pregnancy. Placenta. 1980;1:3-19.
4. Kam EPY, Gardner L, Loke YW, King A. The role of trophoblast in physiological change in decidual spiral arteries. Human Reprod. 1999;14:2131-8.

5. Brosens IA. Morphological changes in the uteroplacental bed in pregnancy Hypertension. Clin Obstet Gynecol. 1977;4:573-93.
6. Kohnen G. Villous development and the pathogenesis of IUGR in intrauterine growth restriction. Br J Obstet Gynecol. 1990;99:342-8.
7. Porcelot L. Applications cliniques de I examen Doppler transcutane In: Perommeau P, ed. Velocimetric ultrasonoic Doppler. Paris: INSERM;1974:213-40.
8. Gudmundsson S, Maršál K. Umbilical artery and uteroplacental blood flow velocity waveforms in normal pregnancy: a cross- sectional study. Acta Obstetr et Gynecologic Scandinavica. 1988;67(4):347-54.
9. Madazli R. Prognostic factors for survival of growth - restricted fetuses with absent end - diastolic velocity in the umbilical artery. J Perinatol. 2002;22:286-290.
10. Yoon Bh, Lee CM, Kim SW. An abnormal umbilical artery waveform; a strong and independent predictor of adverse perinatal outcome in patient with pre eclampsia. Am J Obstet Gynecol. 1994;171:713-721.
11. Trud1nger BJ, Cook CM. Doppler umbilical and uterine flow waveforms in severe pregnancy hypertension. Br J Obstet Gynecol. 1990;97:142-8.
12. Brar HS, Medearis AL, De Yore GR. A comparative study of fetal umbilical velocimetry with continuous and pulsed wave Doppler ultrasonography in high pregnancies its outcome. Am J Obstet Gynecol. 1989;160:375.
13. Yelikar KA, Prabhu A, Thakre GG. Role of Fetal Doppler and Non-Stress Test in Preeclampsia and Intrauterine Growth Restriction. J Obstet Gynecol India. 2013;63(3):168-7
14. Bhatt CJ, Arora J, Shah MS. Role of color Doppler in pregnancy induced hypertension (a study of 100 cases). Indian J Radiol Imaging. 2003;13:417-20.
15. Malhotra N, Chanana C, Kumar S, Roy K, Sharma JB. Comparison of perinatal outcome of growth-restricted fetuses with normal and abnormal umbilical artery Doppler waveforms. Indian J Med Sci. 2006;60:311-7.
16. Bano S, Chaudhary V, Pande S. 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.
17. Chalubinski KM, Repa A, Stammler-Safar M, Ott J. Impact of Doppler sonography on intrauterine management and neonatal outcome in preterm fetuses with intrauterine growth restriction. Ultrasound Obstet Gynecol. 2012;39(3):293-8.
18. Roy A, Mukherjee S, Bhattacharyya SK, Banerjee P, Das B, Patra KK. Perinatal outcome in pregnancies with intra-uterine growth restriction by using umbilical and middle cerebral artery colour Doppler. J Indian Med Assoc. 2012 Mar;110(3):154-7.
19. Lakhkar BN, Rajagopal KV, Gourisankar PT. Doppler prediction of adverse perinatal outcome in PIH and IUGR. Indian J Radiol Imaging. 2006;16:109-16.
20. Rani S, Huria A, Kaur R. Prediction of perinatal outcome in preeclampsia using middle cerebral artery and umbilical artery pulsatility and resistance indices. Hypertens Pregnancy. 2016;35(2):210-6.
21. Shahinaj R, Manoku N, Kroi E, Tasha I. 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 Prenatal Med. 2010 Apr;4(2):17.