Cerebroplacental Ratio in Intrauterine growth restriction and perinatal outcome

Dr. A.K. Bhattacharjee[1], Dr. M.K. Majumdar[2], Dr. Divya. M[3*]
[1]Professor, Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital, (Guwahati-781032), Under Srimanta Sankardev University of Health Sciences, Guwahati, Assam, India
[2]Assistant Professor, Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital, (Guwahati-781032), Under Srimanta Sankardev University of Health Sciences, Guwahati, Assam, India
[3]Post graduate student, Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital, (Guwahati-781032), Under Srimanta Sankardev University of Health Sciences, Guwahati, Assam, India

Abstract: The aim of this study is to study the utility of Cerebroplacental ratio (CPR) in assessing perinatal outcome. This is a prospective observational study done in pregnant females presenting with high risk factors for intrauterine growth restriction (IUGR). The study was conducted in antenatal outpatient department of Gauhati Medical College Hospital which is a tertiary care hospital located at Guwahati in the state of Assam, Northeast state of India. The study was conducted during the period of 1year w.e.f 1st September 2016 to 31st August 2017.The pregnant women were followed till discharge to know the perinatal outcome. Doppler ultrasound was done for all the selected patients and Cerebroplacental ratio was calculated. The primary outcome assessed was perinatal mortality and secondary outcomes were birth weight, neonatal intensive care unit admission and were compared with CPR.CPR<1.08 was taken to be the abnormal cut off based on previous studies by Baschat *et al.* [1] .Our study showed that there was significantly poor perinatal outcome when CPR is <1.08 in a pregnant women. Fetuses having CPR<1.08 had a statistically significant increased chance of perinatal mortality, NICU admission and low birth weight.
Keywords: Cerebroplacental ratio, perinatal outcome, perinatal mortality, NICU admission, Doppler.

INTRODUCTION

Intrauterine growth retardation (IUGR) is a fetal growth disorder where the fetal birth weight is below 10th percentile for the corresponding gestational age.

According to American College of Obstetricians and gynaecologists, IUGR is one of the most common problems of modern day obstetrics in view of poor detection rates, limited treatment options and increased perinatal morbidity. Before the era of ultrasound, assessment of fetal growth during pregnancy was restricted to measuring the fundal height and looking at the infant after delivery. In India, the recent UNICEF surveys reports 25-30% incidence of IUGR [2]. As Doppler ultrasound provides a unique, non-invasive and safe method of studying blood flow characteristics in both the fetoplacental and uteroplacental circulations, it is being used for clinical evaluation of high risk pregnancies. Circulatory adaptation of the human fetus in the presence of uteroplacental insufficiency in IUGR fetuses leads to preferential perfusion of vital organs such as the brain, heart, adrenal glands, and spleen. Changes in flow velocity waveforms are observed in various fetal vascular beds, and Doppler surveillance is based on the relationship between circulatory changes and fetal condition [3]. Recent studies suggest that the cerebroplacental Doppler ratio (CPR), which is a ratio of the pulsatility indices of the middle cerebral artery (MCA) to the umbilical artery, is a better index for predicting adverse outcomes in IUGR when compared with using either the umbilical artery Doppler values or the MCA values alone. The CPR has been shown to be a good predictor of the fetal oxygenation status at birth and can be used to identify pregnancies that are at risk for adverse outcomes. CPR <1.08 shows highest sensitivity and productivity in diagnosing IUGR in comparison with other Doppler indices [4]. Therefore, accurate measurement of the CPR is important.

This study was conducted to assess the utility of Cerebroplacental ratio in predicting perinatal outcome including perinatal mortality, NICU

admissions and birthweight. An analysis of perinatal outcomes in relation to Cerebroplacental ratio in the Indian population will provide important knowledge that may be used to further improve antenatal, obstetric and neonatal care and reveal risk groups that in particular may need more attention in antenatal care.

MATERIALS AND METHODS

In our study, all patients seen in the antenatal outpatient department were screened for the inclusion criteria and 50 cases were included in the study. Pregnant women with clinical presentation of IUGR in 3rd trimester and, or pregant women at high risk of developing IUGR viz. pregnancy induced hypertension, preeclampsia, eclampsia, chronic hypertension, cardiac disease, anaemia, advanced diabetes (class F or higher), infections such as rubella, cytomegalovirus, toxoplasmosis, syphilis, kidney disease, lung disease, malnutrition, hemoglobinopathies, autoimmune disease, thrombophilias, placental abnormalities, chronic abruption, placenta praevia, abnormal cord insertion, uterine anomaly were included in the study as per inclusion criteria. Patients were clinically examined after taking consent and thorough history and necessary investigations along with ultrasonogaphy with Doppler was done. With ultrasonography, fetal biometry and morphology scan was done. Doppler mode was switched on. The following vessels were studied:

- Umbilical artery
- Middle cerebral artery

The Doppler waves are taken from the above arteries during the time of fetal inactivity and apnoea with an angle of insonation being 30-60 degrees and when atleast four waves of equal height appear on the screen. The Doppler indices RI, PI and S/D were measured for each vessel.

Umbilical artery Doppler flow velocity waveforms were obtained from a free loop of cord and measurements were obtained when a clear waveform was acquired in absence of fetal body movement and fetal apnoea. The presence, absence or reverse end diastolic frequencies were noted.

For MCA Doppler, a transverse image of fetal head was obtained at the level of sphenoid bones. Color flow imaging was used to display the Circle of Willis. MCA in the near field was insonated about 1 cm distal to its origin from internal carotid artery. Measurements were taken when a clear waveform was obtained.

Cerebroplacental ratio was calculated based on the formula

$$Cerebroplacental\ ratio$$
$$= Middle\ cerebral\ artery\ P.I$$
$$\div Umbilical\ artery\ P.I$$

The cases were followed up till discharge and the correlation between Cerebroplacental ratio and perinatal outcome was analysed. The primary outcome analysed was perinatal mortality and birthweight and NICU admission were the secondary outcomes. CPR<1.08, Middle cerebral artery (MCA) PI<1.5 and Umbilical artery PI>1.42 was taken as abnormal based on previously done studies [1,5]. Institutional ethical committee clearance was taken. Data analysis was done using Statistical Package for the Social Sciences (SPSS) software package (version 19).p value<0.05 was considered significant.

RESULTS

Of 16,560 cases seen in Antenatal OPD, 50 cases fulfilling the inclusion criteria were selected. All the cases in our study were between 18 -35 years of age. Most of the cases were between the age group of 22 to 25 years of age comprising of 62% of the study group. In the study population, the distribution of abnormal CPR<1.08 was almost equal among all age groups. The mean gestational age at the time of recruitment in the study was 37.81±2.28 weeks of gestation (264±15.9 days). The number of primipara and multipara cases in our study was almost equal. 38% of the study population had an abnormal MCA PI value <1.5 which was about 19 cases while 62 % had a normal value. 24% of the study population had an abnormal UA PI>1.42(12 cases). The Mean CPR of the present study population was 1.42±0.55 .The range of CPR values of the patients with 0.34 to 2.75. The median CPR was 1.60 .Of the study group, 16 cases had an abnormal CPR<1.08 which comprised of about 32% of the study population. In our study group, 72% of the cases delivered by LSCS as compared to 28% delivered by spontaneous vaginal delivery.90% of the babies survived at the time of delivery in which 48% required admission to NICU.

Mean birthweight of the babies in the study was 2.06 kg with a standard deviation of 0.49 kg .The median birthweight was 2.1 kg while the birth weights ranged between as low as 1 kg to 3.4 kg maximum.78% of the babies born to the women included in the study were <2.5 kg (n=39).In our study cohort, 42% of the IUGR babies (n=21) got admitted at the time of delivery. Among these, birth asphyxia was the major cause for NICU admission in 8 babies (16%) whereas prematurity for 10 babies (20%) and neonatal sepsis in 13 babies (26%).

The Mean CPR of the present study population was 1.42±0.55 .The range of CPR values of the patients with 0.34 to 2.75. The median CPR was 1.60 .Of the study group, 16 cases had an abnormal CPR<1.08 which comprised of about 32% of the study population.43.8% of the foetuses having CPR <1.08 (n=7) died eventually in the perinatal period while only

5.9% of the foetuses having CPR>1.08 (n=2) died among the study population. This was found to be statistically significant (p value<0.001) as shown in the table 1 and figure 1.The odds of having poor perinatal outcome when CPR is <1.08 in a pregnant women with IUGR IS 12.44 TIMES (95% confidence interval 2.19 - 70.67) as compared to CPR>1.08.
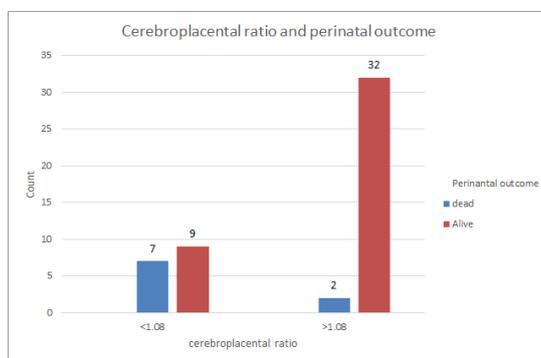

Fig-1: Distribution of perinatal outcome according to CPR

Table-1: showing CPR and association with perinatal outcome

CPR	Perinatal outcome		Total	P value
	Dead	Alive		
<1.08	7(43.8)	9(56.3)	16(100)	0.001
>1.08	2(5.9)	32(94.1)	34(100)	

Most of the cases with CPR<1.08 had a birth weight <2.5 kg (n=12) which comprised of 75% of the study population having abnormal CPR while 63.6% of the group with CPR>1.08 were found to have a birthweight >2.5 kg. 37.5% (n=6) of the IUGR babies having CPR<1.08 got admitted to NICU among the study population which was statistically significant (p-value<0.01) as shown in the below table 2 and 3.

Table-2: showing CPR in comparison with birth weight

CPR	Birth weight		Total	P value
	<2.5	**>2.5**		
<1.08	12(75)	4(25)	16(100)	0.001
>1.08	27(79.4)	7(20.6)	34(100)	
Total	39(78)	11(22)	50(100)	

Table-3: showing CPR in comparison with NICU admission

CPR	NICU admission		Total	P value
	Yes	**No**		
<1.08	6(37.5)	10(62.5)	16(100)	0.001
>1.08	15(44.1)	19(55.9)	34(100)	
Total	21(42)	29(58)	50(100)	

Only 55.6% of the study group had an abnormal UA PI>1.42(n=5) who had adverse perinatal outcome while 44.4% of women having normal UA PI also had poor outcome (n=4) which was not statistically significant. 66.7% of the study population having abnormal MCA PI<1.5 had very poor perinatal outcome whereas 33.3% of the population having a normal MCA PI >1.5 had adverse perinatal outcome (p-value<0.05).This has been summarized in the table 4.

Table-4: showing p-values of Doppler indices

	p-value	
CPR<1.08	0.001	Significant
UA PI>1.42	0.12	Not significant
MCA PI>1.5	0.05	Not significant

DISCUSSION

In the present study, we can find synergy with the findings of previous studies that the occurrence of IUGR is more common in the age group of 22-25 years. In our study, 62% of the cases were between 22-25 years of age. This was in concurrence with study done by Rajesh Malik *et al.,* [6] which also had 47% of the cases between the same age group. However there was no significant age difference noticed in the study done by Ropacka-Lesiak *et al.,* [7] Odibo *et al.,* [8], Shivani singh *et al.* This is probably because all high risk patients of IUGR are in reproductive age group.

We observed that 79% (n=39) had birth weight less than 2.5 kg which was comparable to others done previously. This was also already proved by study done by Rajesh Malik *et al.*[6], who found that 88% of the study population had babies with birth weight <2.5 kg as per Lubchenco classification. The mean birthweight of babies was 2.06 kg as per our study which corresponded with the study done by Urmila Sharma *et al.* In our study, we found that 42% of the babies had NICU admission .This was comparable to previous studies done by Garcio Simon *et al.* 2015, Khalil *et al.* [9], Bellido Gonzalez *et al.* [10], Bano *et al.*[11], Odibo *et al.*[8], and Shahinaj *et al.*[12]. Our study had found that 72% had delivered by LSCS which was in comparable to study by Shahinaj *et al.* [12], and Bano *et al.* [11] but this was in contradiction to the finding noted by GV. Prasad *et al.* [13] and Odibo *et al.*[8]. 43.8% of the foetuses having CPR <1.08 (n=7) died eventually in the perinatal period as inferred from our study which was found to be statistically significant (p<0.001).In study done by GV Prasad *et al.* [13] 20% mortality was found (n=7), of which 4 cases had reversal of diastolic flow and 3 had absent diastolic flow. There were limited data reported for perinatal mortality in many studies. Morales-Rosello *et al.* [14] reported six (0.05%) early neonatal deaths and six (0.05%) late neonatal deaths. The CPR data corresponding to these deaths however were not obtainable. Low CPR resulted in a more than two-fold increase in the likelihood of adverse perinatal outcomes as found by Figures *et al.* [15].

As per our study, 37.5% of patients having CPR<1.08 had babies admitted to NICU which was similar in studies done previously [4,10,13,16,17]. Between 21.9% (40) and 37.1% (33) of fetuses with an EFW<10th centile and an abnormal CPR required admission to NICU, the rates significantly higher compared to normal CPR cohorts 11.1% (40) to 21.3% (33). Irrespective of fetal size, a low CPR was independently associated with NICU admission (aOR 0.55, 95%CI 0.33-0.92, p < 0.021), outperforming that of birthweight centile.

According to our study, 66.7% of the study population having abnormal MCA PI<1.5 had very poor perinatal outcome whereas 33.3% of the population having a normal MCA PI >1.5 had adverse perinatal outcome. The p value of the same was 0.05 which was much less comparable to CPR in predicting perinatal outcome. This was also proven by Rajesh Malik *et al*. [6],which showed the association of abnormal fetal MCA PI with an abnormal outcome was not statistically significant(p value = 0.5834). This shows that MCA PI is not a good predictor of adverse perinatal outcome as compared to CPR. Similar results were obtained by Bano *et al*. [11].

In our present study, only 55.6% of the study group had an abnormal UA PI>1.42(n=5) who had adverse perinatal outcome while 44.4% of women having normal UA PI also had poor outcome.The association of abnormal umbilical artery PI with an abnormal outcome (SFD) was statistically significant(p value = 0.0132) in the study done by Rajesh Malik *et al.* [6].There is disparity between results of both the studies which is insufficient to reach a valid conclusion for the same.

All these results obtained in comparison to previously done studies point that CPR is a better predictor in comparison to UA PI or MCA PI in predicting perinatal outcome in IUGR patients.

CONCLUSION

From our study we conclude that pathological Doppler velocimetry of fetomaternal vessels were found to be a powerful predictor of adverse perinatal outcome. Perinatal mortality was found to be significantly higher with abnormal cerebroplacental ratio at presentation. Fetuses having abnormal cerebroplacental ratio had higher mortality in the perinatal period as compared to Middle cerebral artery pulsatility index and umbilical artery pulsatility index independently being abnormal. When Cerebroplacental Ratio (CPR) was <1.08, there was a higher number of low birth weight babies and more NICU admissions. Assessment of CPR in pregnant women with clinically suspected IUGR might help in predicting adverse perinatal outcome earlier and also help in risk stratification and prompt management for the prevention of the same. Therefore measuring CPR can be considered as an assessment tool during third trimester ultrasound irrespective of the individual umbilical and middle cerebral artery measurements.

Conflict of Interest

The authors declare no conflict of interest.

REFERENCES

1. Baschat AA, Gembruch U. The cerebroplacental Doppler ratio revisited. Ultrasound Obstet Gynecol

Off J Int Soc Ultrasound Obstet Gynecol. 2003 Feb;21(2):124–7.

2. Antonisamy B, Sivaram M, Richard J, Rao PS. Trends in intra-uterine growth of single live births in southern India. J Trop Pediatr. 1996 Dec;42(6):339–41.

3. Romo A, Carceller R, Tobajas J. Intrauterine growth retardation (IUGR): epidemiology and etiology. Pediatr Endocrinol Rev PER. 2009 Feb;6 Suppl 3:332–6.

4. Gramellini D, Folli MC, Raboni S, Vadora E, Merialdi A. Cerebral-umbilical Doppler ratio as a predictor of adverse perinatal outcome. Obstet Gynecol. 1992 Mar;79(3):416–20.

5. Arduini D, Rizzo G. Prediction of fetal outcome in small for gestational age fetuses: comparison of Doppler measurements obtained from different fetal vessels. J Perinat Med. 1992;20(1):29–38.

6. Role of Colour Doppler Indices in the Diagnosis of Intrauterine Growth Retardation in High-Risk Pregnancies [Internet]. [cited 2017 Sep 12].

7. Ropacka-Lesiak M, Korbelak T, Świder-Musielak J, Breborowicz G. Cerebroplacental ratio in prediction of adverse perinatal outcome and fetal heart rate disturbances in uncomplicated pregnancy at 40 weeks and beyond. Arch Med Sci AMS. 2015 Mar 16;11(1):142–8.

8. Odibo AO, Riddick C, Pare E, Stamilio DM, Macones GA. Cerebroplacental Doppler ratio and adverse perinatal outcomes in intrauterine growth restriction: evaluating the impact of using gestational age-specific reference values. J Ultrasound Med Off J Am Inst Ultrasound Med. 2005 Sep;24(9):1223–8.

9. Khalil AA, Morales-Rosello J, Morlando M, Hannan H, Bhide A, Papageorghiou A, Thilaganathan B. Is fetal cerebroplacental ratio an independent predictor of intrapartum fetal compromise and neonatal unit admission?. American journal of obstetrics and gynecology. 2015 Jul 31;213(1):54-e1.

10. Bellido-González M, Díaz-López MÁ, López-Criado S, Maldonado-Lozano J. Cognitive Functioning and Academic Achievement in Children Aged 6-8 Years, Born at Term After Intrauterine Growth Restriction and Fetal Cerebral Redistribution. J Pediatr Psychol. 2017 01;42(3):345–54.

11. 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.

12. 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 Prenat Med. 2010;4(2):17–21.

13. G V P, Jyothi J, Sarvottam S. Role of doppler study in the evaluation of intrauterine growth retardation. Vol. 2. 2015. 7266 p.

14. Morales-Roselló J, Khalil A, Morlando M, Bhide A, Papageorghiou A, Thilaganathan B. Poor neonatal acid-base status in term fetuses with low cerebroplacental ratio. Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol. 2015 Feb;45(2):156–61.

15. Figueras F, Gratacos E. Stage-based approach to the management of fetal growth restriction. Prenat Diagn. 2014 Jul;34(7):655–9.

16. Makhseed M, Jirous J, Ahmed MA, Viswanathan DL. Middle cerebral artery to umbilical artery resistance index ratio in the prediction of neonatal outcome. Int J Gynaecol Obstet off Organ int Fed Gynaecol Obstet. 2000 Nov;71(2):119–25.

17. Flood K, Unterscheider J, Daly S, Geary MP, Kennelly MM, McAuliffe FM, O'donoghue K, Hunter A, Morrison JJ, Burke G, Dicker P. The role of brain sparing in the prediction of adverse outcomes in intrauterine growth restriction: results of the multicenter PORTO Study. American journal of obstetrics and gynecology. 2014 Sep 30;211(3):288-e1.