

DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20205249>

Original Research Article

Doppler study (cerebroplacental ratio) as a predictor of adverse perinatal outcome

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Received: 01 October 2020

Revised: 11 November 2020

Accepted: 12 November 2020

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ABSTRACT

Background: Objective of the current study was to determine the importance of Doppler screening (cerebroplacental ratio i.e. CPR) in antenatal mothers and its effect on perinatal outcome of the baby so that appropriate management can be planned effectively for a better reduction in perinatal mortality and morbidity.

Methods: A prospective study conducted on hundred antenatal women in GMKMCH, Salem with gestational age >32 weeks, with singleton pregnancies. Doppler ultrasonogram of fetal middle cerebral artery and umbilical artery and thus CPR obtained.

Results: 25 out of the 100 patients in the study had $CPR < 1$. CPR was compared against factors such as maternal age, parity, associated risk factors, gestational age (GA) at diagnosis (LMP GA and scan GA), time duration to delivery from diagnosis, requiring neonatal intensive care unit (NICU) admission, duration of stay in NICU and perinatal mortality. The $CPR \leq 1$ has a good sensitivity of 68% but a very high specificity of around 98% in predicting neonatal complications which was found to be statistically significant with a p value < 0.0001 .

Conclusions: Since CPR has a high negative predictive value, $CPR > 1$ helps to rule out adverse perinatal outcomes. When $CPR < 1$, it acts as an effective tool in helping the obstetrician to decide on the mode of delivery to ensure that the baby is delivered within 12 hours of diagnosis, to improve the perinatal outcome of the baby.

Keywords: Doppler study, Cerebroplacental ratio, Perinatal morbidity, Perinatal mortality

INTRODUCTION

Antepartum fetal surveillance is the corner stone of preventive obstetric management aimed at reducing perinatal morbidity and mortality.¹ Specific and accurate methods for detection of fetus at risk of death or compromise in utero can result in early and appropriate intervention and thus reduce the adverse perinatal outcomes in the fetus.² Perinatal mortality rates are 4-8 times higher in infants with intrauterine growth restriction (IUGR) and morbidity is present in half of the surviving infants.³ Along with other tools for antepartum fetal surveillance, Doppler ultrasound plays an important role in

the antenatal fetal surveillance of high risk pregnancies. It is a non-invasive tool which allows evaluation of the fetal placental circulation and thus allows early diagnosis of placental failure.^{4,5} Doppler ultrasound has emerged as a vital tool for antenatal surveillance.⁶

IUGR is described as fetal weight less than 10th percentile for gestational age (GA).⁷ In pregnancies with IUGR, umbilical blood flow reduces due to increased placental vascular resistance.⁸⁻¹⁰

Pregnancies in which adverse intrauterine conditions result in failure of the fetus to reach its growth potential constitute the high risk group (hypertension,

oligohyramnios, diabetes mellitus, anemia).¹¹ Next to prematurity, IUGR is the second most common cause of perinatal mortality.¹² Because a growth restricted fetus subjected to compromised blood flow is particularly at high risk for hypoxia, Doppler flow velocimetry studies have been advanced as an important technique for distinguishing the compromised small fetus from a small fetus that is unlikely to experience serious perinatal outcomes.¹³

At any point of gestation, infants with low birth weight have relatively high morbidity and mortality. There is a strong association between IUGR and the development of metabolic syndromes later in life.¹⁴ Tools that are used in antepartum fetal surveillance are fetal kick count, non-stress test, biophysical profile, amniotic fluid volume, arterial and venous Doppler.

Doppler velocimetry has been shown to reliably predict these adverse outcomes.¹⁵ Doppler investigation of the fetal circulation can give important clues to fetal wellbeing in a number of fetal conditions. The future fetal growth velocity is in turn reflected with various Dopplers and their proportions. There is redistribution of the fetal circulation to major organs like heart, kidneys and brain in the presence of chronic hypoxia of the fetus.¹⁶ Hence compensatory vasodilation of middle cerebral artery with increase in diastolic flow results in a decrease in its pulsatility index (PI) and resistive index (RI) termed as 'brain sparing effect'.¹⁷ It is associated with low cerebral/umbilical PI ratio. A fetus is said to have brain sparing effect when cerebroplacental ratio (CPR) ratio is <5th percentile for GA. Even a slight suspicion of fetal growth restriction should lead to an adequate surveillance of fetal health and Doppler velocimetry plays an important role in the monitoring.¹⁸ Doppler study of the fetal umbilical and middle cerebral arteries helps us to predict the perinatal outcome and modify the obstetric management accordingly. The aims and objectives of the study included: diagnosis and timely management of delivery of IUGR babies using Doppler study of middle cerebral artery (MCA) and umbilical artery (UA) flow ratio (CPR); and earlier prediction of adverse perinatal outcome of IUGR using Doppler MCA: umbilical artery flow index may improve neonatal survival and quality of life.

METHODS

A prospective study conducted on 100 antenatal women in department of obstetrics and gynaecology, Government Mohan Kumaramangalam Medical College Hospital, Salem for a duration of 12 months from January 2018 to December 2018.

Inclusion criteria

In this study, the patients included were, antenatal mothers with GA>28 weeks with singleton pregnancy, patients with reliable dates and first trimester scans, high risk

pregnancies such as gestational hypertension, gestational diabetes mellitus, anemia, hypothyroidism, oligohydramnios.

Exclusion criteria

In this study, patients with multiple gestation, with gestational age <28 weeks, and those with unreliable dates were excluded.

Procedure

Written consent was obtained from the patients, following which detailed history taking and clinical examination of the patient was done. Elaborate history was taken to ensure that the details of the menstrual history were accurate, in order to calculate the GA correctly and to find out the associated risk factors.

After obtaining consent from the patients, they were subject to Doppler study following biometric scan. Biometric scan was done to correlate the GA calculated by scan and that by the last menstrual period of the patient.

Doppler study was done using the 2D convex probe of Mindray DC-N3 pro colour Doppler machine. Morphology and biometry scan were done and then colour Doppler mode was switched on.

Doppler study was done in patients with associated risk factors such as hypertension, diabetes mellitus, oligohydramnios, anaemia, heart disease complicating pregnancy and hypothyroidism.

Method of study

Umbilical artery

The transducer is placed over the anterior abdominal wall over the uterus and then carefully manipulated till a free loop of umbilical cord is seen by grayscale imaging and then colour Doppler is used to identify the umbilical artery. Thus umbilical artery waveform was obtained. Recordings of umbilical artery are obtained from free loops of the umbilical cord. Angle of insonation was adjusted to less than 60 degrees. An optimal Doppler signal was obtained and the PI was measured.

Foetal middle cerebral artery

Section of the fetal head used for BPD measurement was obtained and then the transducer was angled caudally till the middle cerebral artery was seen coursing along the sphenoid wings. Sample volume size and angle of insonation were adjusted after placing the cursor in the artery and the appropriate waveform signals obtained and the PI was measured. In IUGR, increased diastolic flow is expected due to cephalisation of blood flow and brain sparing effect, which is reflected by a decrease in the PI value.

CPR is then calculated by simply dividing the umbilical artery PI and the middle cerebral artery PI.

Data analysis

The data gathered was entered in excel spreadsheet and analysed using IBM. Statistical package for the social sciences (SPSS) statistics software 23.0 version. To describe about the data, descriptive statistics, frequency analysis, percentage analysis were used for the categorical variables and the mean and standard deviation (SD) were used for continuous variables. To find the significant difference between invariant samples, independent groups, the unpaired sample t-test was used. To find the significance in categorical data Chi square test was used.

RESULTS

In this study of 100 antenatal mothers who were admitted in GMKMCH, Salem, CPR was calculated. MCA PI is the calculated by subtracting the end diastolic velocity from the peak systolic velocity and then dividing the mean velocity. It normally has a high value. A low PI reflects the redistribution of cardiac output to the brain due to foetal brain sparing theory. UA PI is calculated similarly. UA Doppler is the most commonly used Doppler study for the detection of IUGR and its positive predictive value is increased with simultaneous measurement of other Dopplers and CPR. CPR is calculated by dividing the MCA PI and UA PI.

Table 1: Frequency of CPR.

CPR	Frequency	Percent
<1	25	25.0
>1	75	75.0
Total	100	100.0

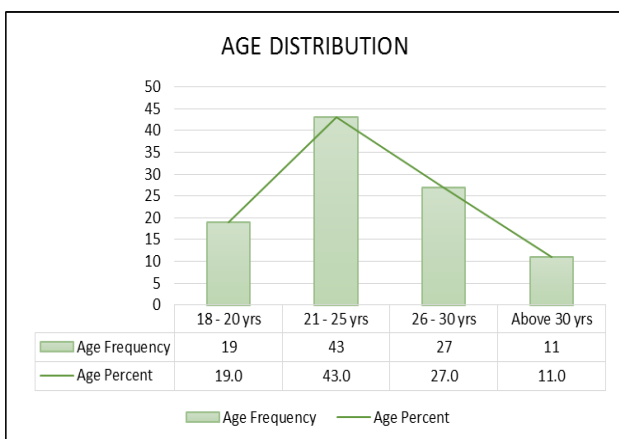


Figure 1: Age distribution.

In this study, 75 of them had CPR>1 and 25 of them had CPR<1. The mean age of the patients was 24.9 years. 52% of them were primi gravida and 48% of them were multigravida. The associated risk factors studied were

gestational hypertension, gestation diabetes mellitus, oligohydramnios, anemia, hypothyroid and others.

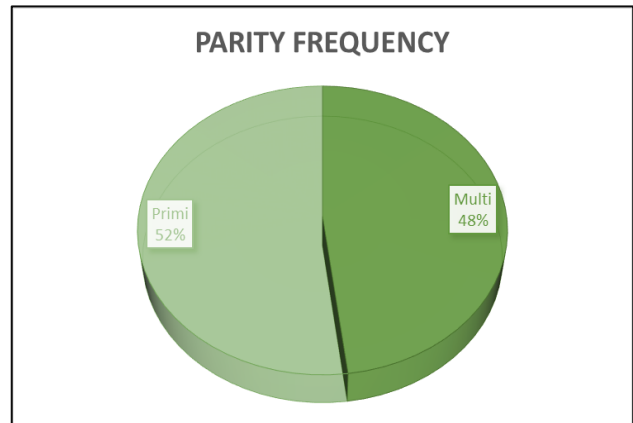


Figure 2: Distribution of parity.

Table 2: Incidence of high risk factors.

Comorbidities	Frequency	Percent
Gestational hypertension	70	70.0
Diabetes mellitus	13	13.0
Oligohydramnios	30	30.0
Anaemia	6	6.0
ASD closure	1	1.0
Hypothyroid	5	5.0

In this study, 57% of the patients were found to be of term gestation, i.e. 37 weeks according to their gestational age based on last menstrual period (LMP GA). In order to calculate the LMP GA, detailed history was elicited from the patients to ensure that they were sure of their dates. The LMP GA was then compared against the scan GA to further ensure accuracy in calculation of gestational age. However, only 25% of the cases were found to be term as per scan GA. From this it can be seen that a disparity in gestational age calculated by LMP and scan is prevalent in pregnancies at high risk for IUGR. Also, LMP GA was found to be statistically significant with a p value <0.01.

Table 3: Comparison of gestational age with CPR unpaired t-test.

CPR	N	Mean	S.D	t-value	P-value
<1	25	243.80	16.14	3.482	0.001**
>1	75	255.97	14.80		

**Highly significant at p<0.01 level

Taking into account the mode of delivery, 64% of the patients delivered by caesarean section and 36% by labour naturale. Of the patients taken up for LSCS, previous LSCS was the most common indication, followed by severe preeclampsia.

Out of the 36 patients who underwent labour naturale, 11 patients had induction of labour for severe preeclampsia, which was the most common.

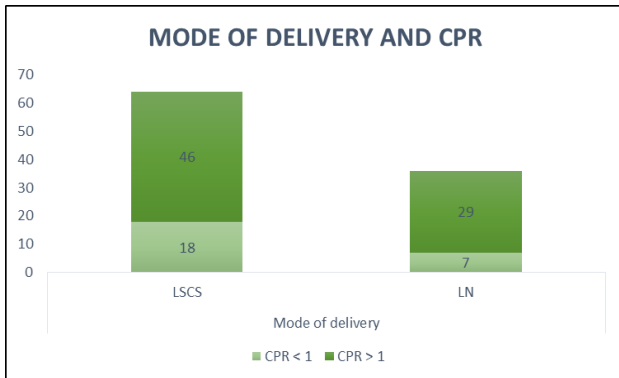


Figure 3: Incidence on mode of delivery and distribution of CPR.

Table 4: Comparison of time to delivery with CPR.

CPR	N	Mean	SD	t-value	P value
Time to delivery	<1	25	9.52	6.206	0.0005**
	>1	75	39.08		

**Highly significant at p<0.01 level

Another important factor included in the study was the time interval to delivery after Doppler study. In cases with CPR<1, the average time to delivery was 9.52 hours, whereas in cases with CPR>1, the average time to delivery was 39.08 hours. It showed high statistical significance with a p value=0.0005.

Table 5: Incidence of NICU admission with significance.

	Frequency	Percent	P value
No	37	37.0	0.001**
Yes	63	63.0	
Total	100	100.0	

**Highly significant at p<0.01 level

Perinatal outcomes were studied in babies based on the birth weight, Apgar score at 1 minute and 5 minutes, requiring NICU admission, their duration of stay in NICU and perinatal death. Of these factors, significant outcome in relation to CPR was seen in the babies who required NICU admission and the duration of their stay in NICU. 63% of the babies required NICU admission.

In relation to duration of stay in NICU, out of the 25 babies with CPR<1, 20 of them had a mean duration of stay in NICU for 10.10 days. It is a much longer duration when compared to the 5.49 days in babies with CPR>1.

Out of the 100 cases studied, 96% of the babies survived, 2 were IUD and 2 had perinatal death.

Table 6: Comparison of duration of NICU stay with CPR and its significance.

CPR	N	Mean	SD	t-value	P value
Dura-tion of stay	<1	20	10.10	2.479	0.019*
	>1	39	5.49		

**Highly significant at p<0.05 level

DISCUSSION

In this study, there was significant correlation between CPR and the gestational age at diagnosis. A study similar to this was conducted by Zohav et al in a university hospital in Israel in which they established a strong correlation between the gestational age, CPR and the pregnancy outcome.¹⁹ It is backed by another study conducted by Bano et al in Dr. Ram Manohar Lohia Hospital and PGIMER, New Delhi, in which it was inferred that decreased gestational age is a strong independent risk factor for IUGR and that CPR is a better predictor of small for gestational age fetuses and adverse perinatal outcome rather than the MCA PI or the UA PI being used alone.²⁰

From this study, it was inferred that, in relation to risk factors complicating pregnancy, gestational hypertension and gestational diabetes mellitus were found to have high negative predictive value. Such relation was not seen with other risk factors such as oligohydramnios, hypothyroid and others. Even though there is no significant correlation has been found between the CPR and gestational hypertension in our study, because of our limited sample size. It is found that CPR has a high specificity of around 77% with sensitivity around 26% in predicting the adverse perinatal outcome. Thus, it has a high negative predictive value, thereby emphasizing the need for CPR screening in all mothers having gestational hypertension and at high risk to predict the adverse outcome earlier, so that further management can be planned accordingly.

These findings were similar to a study conducted by Barati et al. This study established a relationship between CPR and diabetes mellitus, gestational hypertension, and maternal drug use. Diabetes and gestational hypertension had influence over the cerebroplacental ratio.²¹

A study by Gibbons et al concluded that, regardless of the type of treatment for GDM, a low CPR is associated with poorer neonatal outcome in women with GDM.²²

In other high factors like anaemia, hypothyroidism, heart diseases complicating pregnancies the adverse perinatal outcomes can be determined by measuring CPR and management can be planned accordingly.²³

On comparison of the data in this study containing 100 patients, no statistical significance was found between the

mode of delivery (whether being a caesarean section or labour natural) and CPR.

CPR has clinical significance in predicting the adverse outcome, there is nil statistic correlation between the mode of delivery and CPR. But many studies suggest that, if the duration taken for conduction of delivery is less than 12 hours the relative outcome is better. Hence clinically majority of the obstetricians prefer caesarian section over labour natural, if the $CPR \leq 1$ as time taken for delivery is much lesser and we can prevent the adverse outcomes. CPR has a sensitivity of around 28% but has a high specificity of around 81%. Thus, it is mandatory in predicting the adverse outcomes earlier, as it has higher negative predictive value. Thereby aiding the obstetricians in appropriate antenatal management and deciding the mode of delivery for earlier delivery of the baby to prevent the adverse outcome due to extended time taken for labour.

In this study, of the 25 babies who had $CPR < 1$, 18 of them were delivered by LSCS and only 7 of them were delivered by labour naturalis. Mode of delivery as LSCS had a positive predictive value of 72% which indicates that it is the preferable mode of delivery in IUGR babies even though statistics show no significance attached to it.

In another study conducted by Grutner et al, the comparison of patients with spontaneous delivery versus operative delivery showed no significant difference in the cerebroplacental index ($p=0.616$).²⁴

In a similar study by Dall'Asta et al, which was a prospective multicenter observational study conducted at three tertiary centers, the study concluded that, while reduced CPR is associated with a higher risk of obstetric intervention due to fetal distress and composite adverse perinatal outcome, it is a poor predictor of adverse perinatal outcome, indicating that there is no significant correlation between the mode of delivery and CPR.²⁵

However, it must be stressed that in all these studies, even though the mode of delivery has no statistical significance in relation to CPR, LSCS was the most common mode of delivery when taking into account that babies with $CPR < 1$ are more likely to undergo fetal distress when subject to the stress of normal delivery, especially when the time to delivery is prolonged.

The interval time to delivery from the antenatal diagnosis of IUGR in relation to the cerebro placental ratio is statistically highly significant with a p value < 0.01 .

A study by Odibo and Riddick in cerebro placental Doppler ratio and adverse perinatal outcomes in IUGR showed that there was a statistically significant relationship between the earlier interval between the last Doppler and delivery in cases with abnormal $CPR < 1$.

From this inference, it is seen that more than the mode of the delivery, it is the time taken between the diagnosis of

IUGR and the delivery of the baby which is more significant in predicting the adverse perinatal outcomes in the baby. Having said this, the duration to delivery can only be shortened when the mode of delivery is by LSCS rather than prolonging the duration of labour by waiting for labour natural unless and otherwise the obstetric conditions indicate that early delivery within 6 to 12 hours is anticipated in waiting for labour natural. Thus, this factor gives a guide to the obstetrician when to decide definitely to take up a patient for LSCS in a baby with IUGR, for non-obstetric indications.

The neonatal outcomes analysed in this study were the birth weight of the babies, Apgar score at 1 and 5 minutes, requiring admission to NICU, the duration of admission in NICU and perinatal death. In a prospective cohort study conducted by Chainarong et al it was concluded that negative predictive value (NPV) of CPR was significantly high and hence it can be used in stratifying pregnant women who may really benefit from a continuous fetal heart rate monitoring.²⁶

In our study we found a high level of statistical significance between NICU admission and significant CPR ratio. With highest specificity of about 97% and a sensitivity of about 38%. This means that when $CPR < 1$, the baby almost always needs admission to NICU, which is an indicator of adverse perinatal outcome.

A study by Yalte et al showed that the CPR was significantly associated with adverse perinatal outcomes such as respiratory distress syndrome, meconium aspiration syndrome and hypoxia. These findings show similarity to our study as indicated by the prolonged NICU stay of the babies with $CPR < 1$.

A study done at Jawaharlal Nehru Hospital, Aligarh in 2004 showed that the sensitivity of CPR is 60% and that the specificity is 82% in predicting adverse perinatal outcomes. This study shows that CPR has even higher specificity of 97% in predicting adverse perinatal outcomes.

In a study conducted at Thanjavur medical college from August 2015 to August 2016 by Rajarajeswari et al, the results clearly demonstrated the efficacy of umbilical artery Doppler in predicting the fetal outcome.²⁷

In our study we found a high level of statistical significance between NICU admission and significant CPR ratio. This again reiterates that CPR assessment in the antenatal period should be done to predict adverse perinatal outcomes and thus allowing the obstetrician in making timely decisions with regards to the mode of delivery and the duration taken for delivery.

In a meta-analysis study done by Moreta et al, data from 47 studies were taken. The analyzed retrospective data suggested a high statistical significance in the correlation of CPR in all outcomes but the low pH.

It concluded that CPR can be used in identifying foetuses which are at higher risk for operative delivery due to foetal distress, low Apgar score, NICU admission, neonatal morbidity as well as stillbirth and neonatal death rates.²⁸

Limitations

In this study, the sample size of 100 is relatively small and the duration of study for a period of one year is relatively short. There was no control group of antenatal mothers without high risk to compare in this study.

CONCLUSION

This study shows significant correlation of CPR with the gestational age of delivery of the baby, the time taken to deliver the baby after diagnosis of IUGR, admission to NICU, and the duration of stay in NICU.

It is learnt from this study that earlier diagnosis of IUGR in early third trimester (around 32 weeks of gestation by calculating CPR (MCA PI/UA PI) can better predict the adverse perinatal outcome in IUGR babies. This helps in deciding the mode of delivery of the baby, preferably LSCS, and the time within which the baby should be delivered (<12 hours) in order to reduce the perinatal morbidity and mortality in the baby.

The $CPR \leq 1$ has a good sensitivity of 68% but a very high specificity of around 98% in predicting neonatal complications which was found to be statistically significant with a p value <0.0001.

Since CPR has a high negative predictive value, $CPR > 1$ rules out adverse perinatal outcomes such as NICU admission, prolonged NICU stay or perinatal death to a great extent. When $CPR < 1$, it acts as an effective tool in helping the obstetrician to decide on the mode of delivery to ensure that the baby is delivered within 12 hours of diagnosis, to improve the perinatal outcome of the baby.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Sengodan SS, Mathiyalagan S. Doppler study (cerebroplacental ratio) as a predictor of adverse perinatal outcome. *Int J Reprod Contracept Obstet Gynecol* 2020;9:5068-74.