ORIGINAL RESEARCH

Cerebroplacental Ratio: Can It Be Taken as a Single Predictor of Adverse Perinatal Outcome in Singleton Uncomplicated Pregnancy at Term

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Abstract

Introduction: The brain-sparing (BS) phenomenon is considered an adaptive mechanism of the fetus, which is activated to protect the fetal brain in adverse conditions. The current challenge is, therefore, to identify vulnerable fetuses at risk of hypoxic complications, particularly within an apparently low-risk cohort before the onset of labor. The cerebroplacental ratio (CPR) is emerging as an important predictor of adverse pregnancy outcomes, and this has implications for assessment of the well-being of SGA and AGA fetuses close to term.

Materials and methods: It was a hospital-based prospective observational study. After obtaining informed consent from the patient, she was subjected to detailed history-taking and examination and underwent antenatal USG with color Doppler for CPR calculation.

Observations and results: The mean age of females enrolled in the study was 25.95 ± 3.50 years. About 63.5% patients had normal vaginal delivery, 35.0% had cesarean delivery, and 1.5% had instrumental delivery for intrapartum fetal compromise. Patients were divided into groups on the basis of Doppler findings, i.e., CPR ≤1.08 (n = 50) and CPR >1.08 (n = 150), adverse outcomes were significantly higher in groups with CPR ≤1.08 than in groups with CPR >1.08. CPR ≤1.08 was found to be 56.25% sensitive and 95.83% specific in predicting the poor outcome.

Conclusion: With the high specificity and positive predictive value of CPR, it is likely that those having normal CPR will have very less chance of adverse perinatal outcomes and, therefore, their delivery can be conducted at a peripheral center, and those with low CPR should be timely referred to a higher center where there are facilities for extensive fetal monitoring during the intrapartum period with availability of the neonatal unit (NNU).

Keywords: Cerebroplacental ratio, Color Doppler, Intrapartum fetal compromise.

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Introduction

Fetal hypoxia is one of the biggest contributors to severe perinatal outcomes (stillbirth, hypoxic–ischemic brain injury, and various neurodevelopmental disorders) globally as well as one of the main reasons of high perinatal morbidity and mortality.[1] As labor proceeds, fetal hypoxia is caused by uterine contractions, which are associated with a considerable reduction in uterine artery flow rate, placental perfusion, and placental perfusion.[2]

Lower middle cerebral artery resistance index (MCA RI) values are the result of cerebral vasodilation and reduced vascular resistance caused by decreased partial pressure of oxygen (pO_2).[3]

It is thought that the brain-sparing (BS) phenomenon is a fetal adaptation process that is engaged to safeguard the fetal brain under challenging circumstances.

It is challenging to anticipate intrapartum fetal problems because the majority of cases of intrapartum hypoxia occur in pregnancies without prenatal risk factors.

Consequently, the present challenge is to spot susceptible fetuses at risk of hypoxia consequences, particularly in the cohort that initially appears low-risk.

As the cerebrolplacental ratio (CPR) becomes a more significant indicator of unfavorable pregnancy outcomes, it has implications for determining the health of SGA and AGA fetuses who are nearing term.[4]

An obstetric ultrasonography tool called the CPR illustrates how hypoxia and increased placental resistance cause the heart's cardiac output to be redistributed into the cerebral circulation. The MCA Doppler indices are divided by the umbilical artery to determine CPR (MCA PI/UA PI). Although PI has recently been the calculation of choice,[5] S/D ratio, RI, and PI have all been reported in CPR calculations. The fetal brain vascular resistance has slightly decreased, whereas placental resistance has slightly increased, according to CPR.

Recent research has revealed that some healthy fetuses that are considered to be suitable for gestational age (AGA, or fetuses with estimated fetal weights between the 10th and 90th percentile) have impaired growth rates and do not reach their genetic growth potential, putting them at risk for a negative pregnancy outcome.[6]

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Even AGA fetuses with low CPR ratios at term are more likely to be compromised during labor, which raises the likelihood of obstetric interventions and increases the risk of morbidity and mortality for newborns.

The investigation of the relationship between fetal CPR and poor perinatal outcomes in simple-term AGA pregnancies was the primary goal of the study.

Materials and Methods

It was a hospital-based prospective observational study. Cases were selected from women attending antenatal OPD and being admitted to the labor room for delivery at the Department of Obstetrics and Gynaecology at Muzaffarnagar Medical College and Hospital, Muzaffarnagar, Uttar Pradesh. The period of study was 18 months. Enrolled patients were 200 in accordance with the following criteria.

Inclusion Criteria

- Patient gives consent.
- Term pregnancy.
- Singleton gestation.
- Primiparous or previous normal vaginal delivery or previous cesarean section.

Exclusion Criteria

- Patient refusing to give informed consent.
- Preterm.
- Multiple pregnancies.
- Congenital malformations.
- Intrauterine fetal death.
- Medical illness complicating pregnancy.
- Malpresentation.

After taking informed consent from the patient, she was subjected to detailed history-taking and examination and underwent antenatal USG with color Doppler for CPR calculation.

Procedure for CPR Calculation

Umbilical Artery Pulsatility Index (UA PI), Middle Cerebral Artery Pulsatility Index (MCA PI), and Cerebro Placental Ratio = [(MCA PI)/(UA PI)] were measured by a single trained practitioner with the patient lying in a semirecumbent position.

Doppler parameters were measured according to the recommendations by the International Society of Ultrasound in Obstetrics and Gynaecology, i.e., using an angle of insonation <30° in the absence of maternal and fetal movements and using an automated trace of at least three consecutive waveforms. Cerebral placental ratio was calculated as the simple ratio between the MCA PI and the UA PI. A single cutoff value of CPR 1.08 was taken. CPR ≤1.08 was considered as abnormal, while CPR >1.08 was considered as normal.

Outcomes

A. Mode of delivery:
   - Instrumental deliveries for fetal compromise.
   - Cesarean section for fetal compromise.

B. Neonatal outcomes were assessed by:
   - Primary outcome:
     - Perinatal outcome.
     - APGAR score at 1 and 5 minutes.
   - Secondary outcome:
     - Perinatal morbidity (NICU admission).
     - Perinatal mortality.

The perinatal outcomes were correlated with CPR.

Observation and Results

All the females enrolled in the study were between age 19 and 37 years. The mean age of females enrolled in the study was 25.95 ± 3.50 years. The majority of females were from rural areas (70.0%). About 55.0% of the females enrolled in the study were illiterate. About 51.50% of the females belonged to upper–lower SES. Majority of the females enrolled in the study were nullipara (63.0%) followed by primipara (26.0%). Only 22 (11.0%) females enrolled in the study were multipara (Table 1; Figs 1 to 3).

Table 1: Distribution of cases according to demography and obstetrical history

Age group	*No.*	*%*
≤25 years	92	46.0
26–30 years	96	48.0
31–35 years	10	5.0
>35 years	2	1.0
Habitat		
Rural	140	70.0
Urban	60	30.0
Literacy status		
Illiterate	110	55.00
Literate	90	45.00
Socioeconomic status		
Upper-middle (2)	01	0.50
Lower-middle (3)	70	35.00
Upper-lower (4)	103	51.50
Lower (5)	26	13.00
Parity		
Nullipara (P0)	126	63.00
Primipara (P1)	52	26.00
Multipara (≥P2)	22	11.00

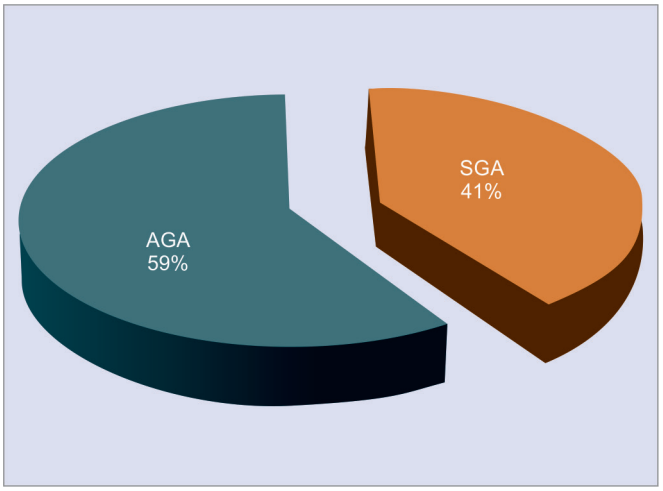

Fig. 1: Groupwise distribution of study population (*n* = 200)

Out of 200 term pregnancies, 118 (59.0%) pregnancies were AGA in which 25.00% had CPR ≤1.08 and 75.00% had CPR >1.08.

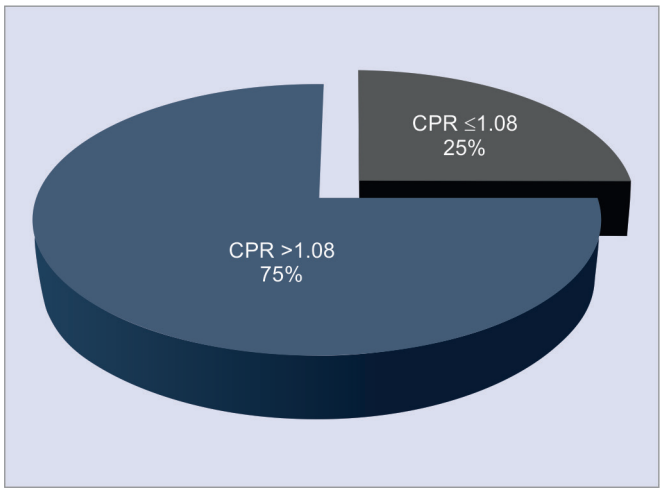

Fig. 2: Distribution of study population (*n* = 200) according to CPR*

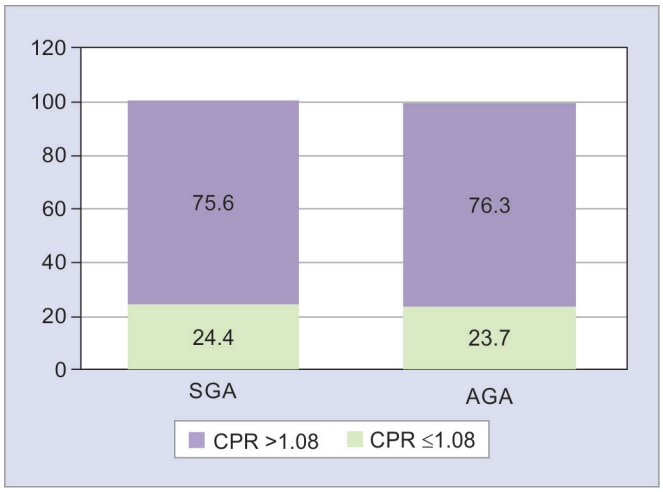

Fig. 3: Distribution of cases according to CPR levels in SGA and AGA groups

Among a total of 82 (41.0%) SGA pregnancies, 25.00% patients had CPR ≤1.08 and 75.00% patients had CPR >1.08 (Table 2).

Out of 200 patients, 63.5% patients had normal vaginal delivery, 35.0% had cesarean delivery, and 1.5% had instrumental delivery for intrapartum fetal compromise.

The rate of vaginal delivery was significantly high in normal CPR group (76.7% vs 22.7%, $p < 0.001$), while the rate of lower (uterine) segment caesarean section (LSCS) and instrumental delivery for IFC was higher in low CPR group (72% vs 22.7%, $p < 0.001$ and 4% vs 0.6%, $p < 0.001$, respectively) (Fig. 4).

In total, 200 patients when divided into two groups on the basis of Doppler findings, i.e., CPR ≤1.08 ($n = 50$) and CPR >1.08 ($n = 150$), adverse outcomes were found to be significantly high in the group with CPR ≤1.08 than in the group with CPR >1.08 (90% vs 23.3%; $p < 0.001$); odds ratio 23.54 (95% CI: 9.28–59.71). The major causes of perinatal morbidity were hypoxic ischemic encephalopathy, neonatal sepsis, respiratory distress syndrome, and birth asphyxia.

Out of 200 total term pregnancies, 50 had CPR ≤1.08, and 150 had CPR >1.08. The proportion of patients with CPR ≤1.08 was found to be significantly higher as compared to those with CPR >1.08 for all the adverse outcomes, i.e., LSCS (72% vs 22.7%; $p < 0.001$), instrumental delivery (4% vs 0.6%; $p < 0.001$), Apgar <7 at 5 minutes (18% vs 0.0%; $p < 0.001$), intrauterine death (2% vs 0.00%; $p = 0.015$), and NNU admissions (52% vs 0.1%; $p < 0.001$).

The proportion of patients with no adverse outcome was found to be significantly higher among patients with CPR >1.08 as compared to those with CPR ≤1.08 (76.6% vs 10%, $p < 0.001$) (Table 3).

Out of a total of 200 term-pregnant patients, 50 (25%) had CPR ≤1.08, in which 45 (90%) had poor outcomes and rest 5 (10%) had normal outcomes, while in the rest 150 (75%) pregnant patients with CPR >1.08, 115 (76.67%) had normal outcomes and the rest 35 (23.33%) had poor outcomes. CPR ≤1.08 was found to be 56.25% sensitive and 95.83% specific in predicting the poor outcome. Positive predictive value and negative predictive value of CPR was 90% and 95.83%, respectively. The overall diagnostic accuracy of CPR ≤1.08 was found to be 80%.

Discussion

The intrapartum period has always been a very crucial condition since the placental circulation is most challenged, and it is very

Table 2: Distribution of cases according to mode of delivery and adverse outcomes

		CPR ≤1.08 (n = 50)		*CPR >1.08 (n = 150)*		*Total (N = 200)*		*Significance of differences*	
SN	*Mode of delivery*	*No.*	*%*	*No.*	*%*	*No.*	*%*	χ^2	*p-value*
1	*LSCS for *IFC	36	72	34	22.7	70	35	28.763	<0.001
2	Instrumental delivery for IFC	2	4	1	0.6	3	1.5	13.844	<0.001
3	Normal vaginal delivery	12	24	115	76.7	127	63.5	44.4	<0.001
	Total	50	100	150	100	200	100		
			CPR ≤1.08 (n = 50)		*CPR >1.08 (n = 150)*			*Significance of differences*	
SN	*Adverse outcome*	*No.*	*No.*	*%*	*No.*	*%*		χ^2	*p-value*
1	*LSCS for IFC	70	36	72	34	22.7		28.763	<0.001
2	Instrumental for IFC	3	2	4	1	0.6		13.844	<0.001
3	Apgar <7 at 5 m	9	9	18	0	0.0		21.193	<0.001
4	Perinatal mortality	1	1	2	0	0.0		5.902	0.015
5	NNU admission	28	26	52	2	0.1		62.360	<0.001
6	No adverse outcome	120	5	10	115	76.6		64.732	<0.001
	Total	231	79		152				

IFC, interferential current therapy; LSCS, lower (uterine) segment caesarean section

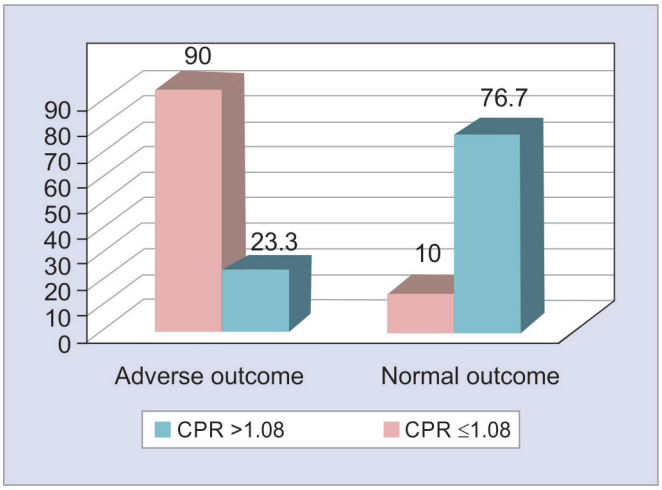

Fig. 4: Association of CPR with perinatal outcome

Table 3: Performance of CPR in the prediction of adverse outcome in study population ($n = 200$)

CPR levels	*Poor outcome (n = 80)*		*Normal outcome (n = 120)*	
CPR ≤1.08 ($n = 50$)	45 (True positive)		5 (False positive)	
CPR >1.08 ($n = 150$)	35 (False negative)		115 (True negative)	
Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
56.25	95.83	90	95.83	80

difficult to categorize patients who will be forced to land by cesarean section for fetal problems and who will have adverse perinatal outcomes. Consequently, there is a need for a tool that can anticipate a bad perinatal result. Herein lies the function of CPR, which is demonstrated to be a very promising method for enhancing the detection of fetuses at danger. It also seems to be a sign that growth potential will not be realized in a timely manner.

This study was designed to determine the association between fetal CPR and perinatal outcome at term in prenatal women.

The patients who were enrolled in the study had an average age of 25.95 ± 3.50 years in our study sample. Patients ranged in age from 19 to 37 years old. At the time of the USG Doppler scan, the average gestational age was 267.04 + 7.84 days. Delivery gestational age was 269.83 + 7.78 days on average. Based on estimated fetal weight, a study group of 200 term pregnancies was divided into AGA and SGA (EFW between the 10th and 90th percentile was defined as AGA), 200 individuals in total, with 59% having AGA and 41% having SGA. Since most high-risk pregnancies are referred to our institution, which provides tertiary care, there was a very high rate of SGA.

The study population was further divided into two groups based on Doppler velocimetry with a CPR cutoff of 1.08.[7,8] A CPR less than or equal to 1.08 was considered abnormal or low, and higher was considered normal.

When demographics were compared in the two groups divided by CPR cutoff, we found no significant difference between the two groups in terms of age, literacy, habitat, socioeconomic status, and parity. A similar study by Giles and Trudinger[9] also reported no difference in age, ethnicity, habitat, or literacy status between different percentile groups of CPR/CU ratio.

In this study, when the association between CPR and perinatal outcome was analyzed in the total study population ($n = 200$), we found that 90% of patients in the abnormal CPR group had an adverse outcome compared with 23.3% in the normal CPR group [$p = < 0.001$; odds ratio 23.54 (95% CI: 9.28–59.72)]. This was consistent with the findings of a study by Arias,[10] who reported that more than half of fetuses with low CPR had adverse perinatal outcomes (50.7% vs 6.3%, $p = < 0.05$).

In this study, out of a total of 200 patients, 70 (35%) patients had an urgent LSCS, 3 (1.5%) patients had an instrumental delivery for fetal distress, and 127 (63.5%) patients had a normal vaginal delivery. The rate of normal vaginal delivery in the low CPR group was significantly lower compared with the normal CPR group (24% vs 76.7%, $p < 0.001$). Giles and Trudinger[9] also observed in their study that normal vaginal delivery was up to three times more likely with normal CPR. Of the 51 patients in the low CPR group, only 12 (23.5%) had a vaginal delivery, of these, 6/12 (50%) children had an adverse outcome. Of these 6 children, 2 had intrauterine fetal deaths and 4 (33.3%) of these children required admission to a neonatal unit (NNU).

When examining the association between fetal CPR and low APGAR scores, we found that the group with abnormal CPR had more infants born with an APGAR <7 at 5 minutes after birth [18% vs 0.0%, $p < 0.001$; odds ratio 19.73 (95% CI: 2.31–168.25)]. This was true for both SGA and AGA pregnancies (15% vs 0.0, $p = 0.018$ and 21.4 vs 0.0, $p = 0.001$). Ebrashy et al.[11] reported a higher proportion of infants with low APGAR scores in the abnormal CPR group (27.5% vs 1.3%, $p < 0.001$).

This study also reported that admission to the NNU was higher in the group with abnormal CPR [52% vs 0.1%, $p < 0.001$, odds ratio – 39.98; 95% CI (11.23–142.24)]. A study by Low et al.[2] also found that decreased or abnormal CPR was independently associated with NICU admission, regardless of fetal size (OR 0.55, 95% CI: 0.33–0.92, $p < 0.021$).

There was one perinatal mortality reported in our study, in the SGA group with low CPR, this patient did not have any other known risk factor and she had an intrauterine fetal demise at 37 weeks 3 days just 2 days after the Doppler scan.

The number of AGA and SGA pregnancies was so low that there was no statistically significant difference in perinatal mortality in low and normal CPR ($p = 0.57$ and $p = 0.09$, respectively). When comparing perinatal mortality in the study population, a significant difference was observed between the low and normal CPR groups (2% vs 0.0%, $p = 0.015$). However, Parer and King[12] reported significantly higher perinatal mortality in the low CPR group (18% vs 0%, $p < 0.05$), similar to our findings.

Recent studies and this study have demonstrated that AGA fetuses with abnormal CPR have a high incidence of adverse outcome.[2,3,9] Because these AGA fetuses may not be identified using traditional clinical tools, it is prudent to consider routine late third-trimester evaluation of growth as well as measurement of CPR for identifying AGA fetuses that could suffer from placental insufficiency and fail to meet their genetic growth potential at term.

Our study suggests that a normal CPR assures the clinician of fetal well-being. Its high specificity 95.83% and low false-positive rate 5% will prevent unnecessary tests and interventions. On the other hand, a good positive predictive value of CPR (90%) suggests that pregnancies with abnormal CPR are at high risk of adverse perinatal outcome and should be delivered at a center with good monitoring facility.

Conclusion

In order to maximize the identification of at-risk fetuses, CPR assessment integrating both umbilical and MCA Doppler index appears to be a very promising method.

This assessment of the CPR ratio in term pregnancies can be used as part of antenatal testing in the third trimester, thanks to the declining cost of USG equipment and the availability of USG Doppler technology at the peripheral health center. Once they have received the necessary training, doctors may consistently perform these Doppler examinations (UA PI and MCA PI) in a matter of minutes.

This method of calculating CPR can be used to categorize at-risk pregnancies, which will then help determine how and where to deliver the baby. Given the high specificity and positive predictive value of CPR, it is likely that those whose CPR is normal will have a much lower risk of a poor perinatal outcome and that their delivery can be managed in a peripheral center, while those whose CPR is low should be referred as soon as possible to a higher center with the resources for intensive fetal monitoring during the intrapartum period and the availability of a neonatal ward.

Strengths of the Study

The use of cerebroplacental ratio as a single noninvasive tool in the prediction of adverse neonatal outcome is proving to be a boon in identifying at-risk fetuses and helping in timely intervention to prevent neonatal morbidity and mortality.

Limitations of the Study

Currently, due to paucity of color Doppler facilities to the rural population, a large group of antenatal women do not have access to such a tool.

Larger randomized controlled studies are required in a larger population group to find out the effectiveness of CPR as a single predictor for adverse outcomes.

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