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# **Original Research Article**

# The role of cerebro placental ratio as a predictor of adverse perinatal outcome in uncomplicated term pregnancies

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#### ABSTRACT

**Background:** Aim of the study was to study role of cerebro placental ratio (CPR) as a predictor of adverse perinatal outcome in uncomplicated term pregnancies.

**Methods:** This prospective observational study took place at the Department of Obstetrics and Gynecology in SNMC Agra. We enrolled 140 uncomplicated antenatal cases with gestational age between 37 to 41 weeks, based on specific inclusion and exclusion criteria. Each participant underwent comprehensive assessments, including history-taking, examinations, and ultrasound color Doppler evaluations. We then analyzed perinatal outcomes in correlation with CPR. **Results:** Adverse perinatal outcomes i.e., asphyxia and NICU admissions were found to be significantly higher in patients with CPR<1. We also observed APGAR<7 at 1 and 5 minutes, cord blood ABG with pH<7.3, pO<sub>2</sub><50, PCO<sub>2</sub>>45 in patients with CPR<1.

**Conclusions:** CPR serves as a noninvasive means to identify fetal compromise in seemingly healthy pregnancies, aiding in the decision-making process regarding the mode of delivery. Clinical significance-CPR can assist in stratifying at risk pregnancies, subsequently influencing decisions regarding the mode and place of delivery.

Keywords: CPR, APGAR, Perinatal asphyxia, Cord blood pH, CTG

## **INTRODUCTION**

On a global scale, hypoxia continues to be the primary cause of stillbirth, hypoxic-ischemic encephalopathy, and cerebral palsy.<sup>1</sup> These complications have profound and enduring psychosocial and financial implications for parents and families. Embryogenesis, foetal growth, and survival of the perinatal period all depend on optimal maternal health and normal placental development.<sup>12</sup> Remarkably, a significant portion of these devastating events occur even in the absence of apparent risk factors.

CPR is an important obstetric ultrasound tool used for assessment of foetal oxygenation. It is a non-invasive technique that yields immediate results.<sup>2</sup> Prediction of perinatal compromise in pregnancies close to or at term is challenging. The CPR has emerged as a dependable indicator of compromised placental function, regardless of fetal weight, indicating its potential as a screening tool for perinatal issues in more recent times. The CPR is the ratio of the middle cerebral artery pulsatility index (MCAPI) divided by the umbilical artery pulsatility index (UAPI).<sup>3</sup>

Existing evidence indicates that CPR on its own may have utility in identifying appropriate for gestational age (AGA) foetuses in pregnancies affected by placental insufficiency, fetal hypoxemia and adverse perinatal events.<sup>4</sup>

This study was conducted to assess efficacy of CPR so that it can be used as non-invasive tool to predict any adverse perinatal event in seemingly uncomplicated term pregnancies.

#### METHODS

This was a prospective hospital-based study conducted at the Department of Obstetrics and Gynaecology in SN medical college, Agra. We selected one hundred and forty cases from the antenatal patients who presented to labor room and met specified inclusion and exclusion criteria between study period of August 2021 to July 2022.

Before conducting the study, we obtained informed consent from each patient and provided them with detailed information about the procedure. All cases underwent thorough history taking, examinations, ultrasound color Doppler assessments, and a correlation was made between perinatal outcomes, including APGAR scores and cord blood ABG, with CPR.

#### Inclusion criteria

Antenatal patients with term and singleton gestation were serially recruited.

#### Exclusion criteria

The patients with multiple gestation, antenatal congenital malformations, intrauterine foetal death, malpresentations and medical illness complicating pregnancy were excluded from the study.

#### Procedure for CPR calculation

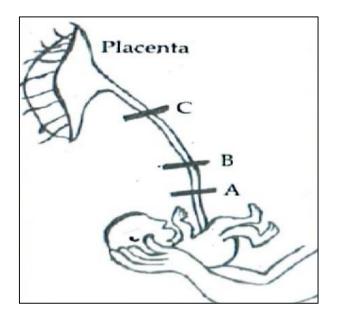
Color doppler was carried out by a trained practitioner, with the patient in a semi-recumbent position, to measure the UAPI, MCAPI, and CPR (MCAPI/UAPI). These Doppler parameters were assessed in line with the recommendations of the international society of ultrasound in obstetrics and gynecology. This involved maintaining an angle of insonation below 30°, ensuring the absence of maternal and fetal movements, and capturing an automated trace of at least three consecutive waveforms.<sup>4</sup>

Women with CPR value less than 1 were taken for emergency caesarean section whereas women with CPR value more than 1 were be either allowed for spontaneous onset of labour else induction of labour was done.<sup>4</sup>

#### Procedure for collection of cord blood

The standard technique of sampling cord blood for acidbase analysis as per AIIMS NICU Protocol 2019 (Figure 1):<sup>11</sup>After the delivery of the baby, the obstetric team (OB) applies two clamps (A and B) on the cord and cuts the cord between two clamps. The baby is then handed over to the newborn team for post-birth care. The OB team places third clamp (C) on the placental segment of the umbilical cord approximately 10 cm away from the clamp B. This clamping provides as segment of umbilical cord between two clamps B and C for umbilical cord arterial blood (UCAB) sampling. The blood in this segment of the cord is reflective of fetal acid-base status that is not affected by postnatal changes in the neonate or the mother. After delivery of the placenta, neonatal team can take UCAB sample for fetal acid-base status. The UCAB sample must be taken from umbilical artery and not umbilical vein. Use one ml syringe with 2-gauge needle. Draw one drop of heparin in it, move the plunger up and down and expel the residual heparin. Withdraw a minimum of 0.2 ml blood. Expel any air from the syringe before capping. Label the syringe and process the sample within 30 minutes. Document in records.

After the collection of cord blood, the following parameters were analyzed: pH, pO<sub>2</sub>, pCO<sub>2</sub>, base excess



**Figure 1: Site for umbilical arterial blood sampling.** (The cord is cut between 'A' and 'B'. An additional clamp 'C' isolates a segment of cord (BC) for sampling) AIIMS NICU protocol 2019.

#### Statistical analysis

Descriptive analysis was employed to outline the study participants' characteristics. The perinatal outcomes and CPR within the study population were assessed using the  $\chi^2$  test, with p calculated accordingly. Additionally, we computed the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) for the cerebro-placental ratio.

#### RESULTS

Study group of 140 patients was divided on basis of age of the patient which showed maximum patient belonging to age group 26-30 years (48%), followed by  $\leq$ 25 year (45%) and 7 cases in 31-35 years (5%) and 3 cases in >35 year (2%). Majority of the patient included in our study belonged to lower middle socioeconomic status 51% followed by upper lower socioeconomic status 35%. The percentage of patients with abnormal CPR was found to be significantly higher in patient with lower socioeconomic status (upper lower and lower) (p=0.000573). Majority of patients were nulliparous i.e., 58.57% followed by primiparous 32.14%. Study population was further divided on basis of period of gestation which reports maximum number of cases i.e., 99 in POG 37W-37W6D (71%),

followed by 21 cases in POG 38-38W6D and 16 cases in 39W-39W6D (11%). Total number of cases with CPR≥1 was 105 (75%) and CPR<1 was 35 (25%) (Table 1). Study population was distributed on the basis of their CTG tracing and we found out that maximum no. of patients have normal CTG. When we assessed intrapartum fetal compromise in both group rate of abnormal (pathological) CTG and indeterminate were significantly high in group with low CPR (p<0.0001). Outcome of patient with abnormal CTG (pathological and indeterminate) was studied and it was found that 86.2% of the patients with abnormal CTG have adverse outcomes in comparison to patients with normal CTG who have 23.42% patients having adverse outcomes (p<0.0001) (Table 2). In our study out of 140 total patients 35% patients had emergency LSCS, 5% patients had instrumental delivery for fetal compromise and 60% patients had normal vaginal deliveries. The rate of normal vaginal delivery in low CPR group was significantly less compared to normal CPR group (p<0.0001). On looking at various adverse outcome individually in total study population the rate of caesarean and instrumental delivery for intrapartum fetal compromise (IFC) was significantly higher in abnormal CPR group [p<0.001; odds ratio (95%) CI): 5.8237(2.5477 to 13.3125)] (Table 3).

While looking for association between fetal CPR and low APGAR scores we found significantly higher number of babies born with APGAR<7 at 1 min and 5 min of birth were present in group with abnormal CPR (p<0.0001). When we assessed the cord blood ABG, we found that blood pH<7.3 was found to be higher in patients with abnormal CPR (p<0.0001). In case of relationship of perinatal outcomes with CPR we find that significantly higher percentage of perinatal asphyxia and NICU admission in abnormal CPR group (p<0.00077 and p<0.0001 respectively). There was no significant association seen in meconium-stained liquor and mortality in abnormal CPR group (Table 4).

When we study the performance of CPR in the prediction of adverse outcomes in study population (n=140) on basis of CPR, amongst the patients with CPR <1 sensitivity, specificity, PPV and NPV of the test is 58.82%, 94.38%, 85.71%, 80.00% (Table 5). Diagnostic accuracy of the test to detect the perinatal outcome on the basis of CPR is 81.43%. This implies that when CPR is within the normal range, it provides confidence to clinicians about the wellbeing of the fetus. Its impressive specificity of 94.38% and low false positive rate of 5.62% help avoid unnecessary tests and interventions. Conversely, strong positive predictive value of CPR (85.71%) indicates that pregnancies with the abnormal CPR values face heightened risk of adverse perinatal outcomes and should be delivered at a facility equipped for thorough monitoring.

#### Table 1: Clinico-demographic profile, (n=140).

Parameters		N (%)	
Age (In years)	≤25	63 (45)	
	26-30	67 (48)	
	31-35	7 (5)	
	≥35	3 (2)	
	Upper middle	8 (6)	
Socioeconomic	Lower middle	71 (51)	
status	Upper lower	49 (35)	
	Lower	12 (8)	
Parity	<b>P</b> <sub>0</sub>	82 (58.57)	
	<b>P</b> <sub>1</sub>	45 (32.14)	
	P <sub>2-4</sub>	13 (9.28)	
	37-37W6D	99 (71)	
Period of	38-38W6D	21 (15)	
gestation	39-39W6D	16 (11)	
	40-41W	4 (3)	
Cerebro-	<1	35 (25)	
placental ratio	≥1	105 (75)	

#### Table 2: Correlation of CTG tracing with CPR and perinatal outcome, (n=140).

Variables		Normal CTG	Abnormal CTG (Pathological and indeterminate CTG)	P value
CPR	CPR<1 CPR>1	10 101	25 4	<0.0001
Perinatal	Adverse outcome	26	25	< 0.0001
outcome	Normal outcome	85	4	<0.0001

Table 3: Correlation of CPR tracing with mode of delivery, (n=140).

Mada of dolinom	CPR<1	CPR<1		CPR≥1		0/	P value
Mode of delivery	Ν	%	Ν	%	Total	%	r value
LSCS							
Assuring CTG	3	8.5	20	19.04	40	25	< 0.0001
Pathological CTG	20	57.1	6	5.71	- 49	35	
Instrumental							
Forceps	3	8.5	2	1.9	7	E	0.043907
Ventouse	1	2.8	1	0.95		3	
NVD	8	22.8	76	72.38	84	60	< 0.0001

Variables		CPR<1	CPR≥1	P value
Perinatal outcome	MSL	8	14	0.179998
	Asphyxia	6	2	0.00077
	NICU admission	15	4	< 0.0001
	Mortality	1	1	0.410854
	No adverse outcome	5	84	< 0.0001
APGAR at 1 min	≥7	5	84	
	4-6	28	20	< 0.0001
	<4	2	1	
APGAR at 5 min	≥7	5	84	
	4-6	29	20	< 0.0001
	<4	1	1	
Cord blood pH	<7.3	30	21	<0.0001
	≥7.3	5	84	<0.0001

Table 4: Correlation of CPR with perinatal outcome, APGAR at 1 and 5 min, and cord blood pH, (n=140).

 Table 5: Performance of CPR in the prediction of adverse outcome in study population, (n=140).

CPR levels	Adverse outcome, (n=51)		Normal outcon	Normal outcome, (n=89)		
CDD $<1(n-25)$	30	30		5		
CPR <1 (n=35)	(True positive)		(False positive)	(False positive)		
CDD > 1 (n - 105)	21		84			
CPR ≥1 (n=105)	(False negative)		(True negative)			
Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy		
58.82%	94.38%	85.71%	80.00%	81.43%		

### DISCUSSION

Identifying pregnancies with insufficient placental function to support optimal fetal growth and a higher risk of adverse perinatal outcomes is challenging. Therefore, there is a requirement for a predictive tool to anticipate these adverse perinatal outcomes in advance. The standalone use of CPR holds significant importance in predicting intrapartum fetal distress, neonatal intensive care unit admission at term, stillbirth, perinatal mortality, and neonatal morbidity.

In our study, the percentage of patients with abnormal CPR was found to be significantly higher in the patient with lower socioeconomic status (upper lower and lower). Esther et al conducted a study in, which yielded similar findings.<sup>5</sup> They investigated the CPR ratio's role as a predictor of adverse perinatal outcomes and discovered a significant association in patients with lower socioeconomic status. When the demography was compared in two group divided according to CPR cut off, we had found no significant difference between the two group with respect to age and parity. Similar study done by Prior et al also noted no difference in age, ethnicity, habitat, literacy status between different CPR/CU ratio percentile group.<sup>6</sup> The rate of abnormal (pathological) CTG and indeterminate were significantly high in group with low CPR and 86.2% of the patients with abnormal CTG have adverse outcomes. Lesiak et al in their study also reported a higher percentage of CTG abnormalities.<sup>7</sup> In a study led by Maitrayee et al they explored CTG as an

early predictor of adverse neonatal outcomes, and their research yielded similar results.

The rate of caesarean and instrumental delivery for intrapartum fetal compromise was significantly higher in abnormal CPR group. Similar results were also observed in the study done by Figueras et al, Ashraf et al and Khalil et al.<sup>8,9,13</sup> in which he described that emergency caesarean section were higher in patients with abnormal CPR and CTG. While looking for association between fetal CPR and low APGAR scores, we found significant higher number of babies born with APGAR<7 at 1 min and 5 min of birth were present in group with abnormal CPR. Prior et al and Gramellini et al had reported a greater proportion of babies with poor Apgar score in abnormal CPR group.<sup>6,15</sup> Ropacka et al reported that the prevalence of adverse neonatal outcome values of 1- and 5-minutes Apgar score <7 was significantly higher in study group.<sup>7</sup> In our study, the patients with abnormal CPR value had blood pH<7.3. Ashraf et al found that women with a CPR  $\geq 0.67$  multiples of the median had significantly lower pH levels (< 7.2) compared to women with a CPR <0.67 multiples of the median. Also, pO<sub>2</sub> levels<50 and pCO<sub>2</sub> levels >45 was seen to be significantly higher in patients with CPR<1 as compared to patients with CPR $\geq$ 1.<sup>6</sup> In study conducted by Mariola et al and Rabei et al demonstrated significantly higher prevalence of adverse neonatal outcomes and small for gestational age newborns (SGA), in patients with abnormal parameters including 1- and 5-minute Apgar scores <7, pO<sub>2</sub><15 mm Hg, pCO<sub>2</sub>>45 mm Hg, pH<7.2, and BE<12 mEq/l.<sup>7,14</sup> These findings collectively emphasize the importance of CPR as a predictor of adverse perinatal outcomes. In the case of relationship of perinatal outcomes with CPR we find that significantly higher percentage of perinatal asphyxia and NICU admission in abnormal CPR group. In study done by Mohamed et al, it was noted that neonates with a CPR of  $\leq 1.1$  had notably higher rates of NICU admission compared to those with a CPR exceeding 1.1.<sup>10</sup>

Nearly all studies conducted to date, including our own research, have consistently shown that abnormal CPR measurements at term are linked to unfavorable perinatal outcomes. Our research contributes to the expanding body of evidence indicating that abnormal CPR serves as a predictor for heightened obstetric interventions and adverse perinatal outcomes. Using CPR to stratify pregnancy risks before labor can enable the delivery of pregnancies with abnormal CPR at centers equipped with fetal surveillance, emergency caesarean deliveries, and neonatal intensive care units.

#### Clinical significance

CPR can assist in stratifying at risk pregnancies, subsequently influencing decisions regarding the mode and place of delivery. It is a non-invasive technique that yield immediate results and does not require continuous monitoring unlike cardiotocographic monitoring. Given the high specificity and positive predictive value of CPR, individuals with a normal CPR are likely to have a significantly lower risk of adverse perinatal outcomes. Consequently, their deliveries can be managed at peripheral centers. Conversely, those with a low CPR should be promptly referred to higher-level facilities equipped for comprehensive fetal monitoring during labor, with access to neonatal intensive care units.

#### CONCLUSION

Cerebroplacental ratio can be used as a non-invasive tool to detect fetal compromise in apparently normal pregnancies. We found that cases with CPR<1 there was a higher incidence of adverse perinatal outcomes if labor was allowed to progress normally. Thus, cases with CPR<1 can be categorized as high risk for more frequent fetal monitoring and progress of labor. By integrating CPR measurement in routine prenatal ultrasounds, healthcare providers can identify fetal distress early and take prompt action to prevent adverse outcomes. The widespread adoption of this tool in prenatal care has the potential to improve the outcomes of high-risk pregnancies and ensure that all fetuses receive the best possible care.

However, since the number of cases in our study were small, so there is need for further studies to validate the importance of CPR to predict the perinatal outcomes.

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