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Antepartum cerebroplacental ratio in low risk pregnancy and its relationship with adverse perinatal outcome: a prospective cohort study

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Abstract

Objectives: To assess the relationship of cerebroplacental ratio (CPR) with non-reassuring/abnormal cardiotocography (CTG) tracing and perinatal outcomes like operative delivery, birth weight, NICU admission, meconium-stained liquor, and APGAR score in low-risk pregnancy.

Methods: This was a prospective cohort study at tertiary center in western India which included low risk singleton pregnancies between 35 and 37+6 weeks with cephalic presentation. Ultrasound was done between 35 and 37+6 weeks gestation including fetal biometry and Doppler for CPR calculation. Patients were divided into two groups, with normal CPR (>10th centile) and abnormal CPR (≤10th centile), and maternal and neonatal outcomes were compared.

Results: Out of 172 cases enrolled, CPR was abnormal in 55 (31.97 %) patients and normal in 117 (68.02 %) patients. In abnormal CPR group, CTG tracing was reassuring in 61.81 %, non-reassuring in 18.18 %, and abnormal in 20 %. While in normal CPR group, CTG tracing was reassuring in 81.19 %, non-reassuring in 11.11 %, and abnormal in 7.69 %. This was significant difference between the two groups (p=0.027). Cesarean and operative vaginal delivery rates were comparable in both groups, (p value=0.63, 0.33). Lower birth weight was observed in 45.45 % of women in the abnormal CPR group, while 21.36 % of women had low birth weight in the normal CPR group (p value=0.006). No significant difference was found in APGAR score and NICU admissions between the two groups (p-value-0.94, 0.87).

Conclusions: We conclude that CPR measurement has good negative predictive value for fetal outcome in low risk pregnancy.

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Keywords: cerebroplacental ratio; cardiotocography; fetal growth restriction; AGA (appropriate for gestational age); antepartum Doppler

Introduction

Fetal growth restriction (FGR) is becoming a common obstetrical complication owing to uteroplacental insufficiency resulting in birth asphyxia and fetal morbidity and mortality. The need of the hour is to early identify FGR, adequate fetomaternal surveillance, and plan the timing of delivery [1]. Doppler has been known as a good modality for assessing fetal circulation and it can be used for surveillance of high-risk pregnancy [2]. It can also identify appropriate for gestational age (AGA) pregnancies which are complicated by placental insufficiency [3]. Primary tools for fetal assessment in FGR are fetal biometry, fetal growth velocity, doppler velocimetry, biophysical profile scoring, cardiotocography with short-term variation and placental Biomarkers [4].

Dynamic fetal variables like tone, gross body movement, breathing movement, amniotic fluid volume (AFI), and fetal heart rate by non-stress test (NST) are included in the biophysical profile score (BPS). Doppler ultrasound describes vascular resistance in umbilical arteries and preferential blood flow to middle cerebral artery [5]. Growth restricted fetuses demonstrate a significant progression to decreased placental circulation (Umbilical Artery [UA]), brain sparing effect (middle cerebral aretry [MCA]), and direct cardiac decompensation (Ductus venosus [DV] changes) before a change in BPS [6].

Fetus with appropriate EFWt (estimated fetal weight) but uteroplacental insufficiency is not detected by routine ultrasound [1]. Doppler indices should be done to detect placental flow abnormalities thereby identifying women who are at high risk for fetal distress and operative delivery in labor. For this, cerebroplacental ratio (CPR) is defined, which is calculated by dividing middle cerebral artery (MCA) pulsatility index (PI) and umbilical artery (UA) PI [1, 7]. This ratio includes both maternal (placental flow) and fetal factors (MCA flow) so it has better prognostic capability than MCA or UA doppler alone [8]. Abnormal CPR has been found

to be associated with increased operative delivery, abnormal fetal heart rate pattern, NICU admissions, low APGAR scores, low birth weight, meconium-stained amniotic fluid, stillbirth, neonatal death, and respiratory distress. In this study, we have compared fetal distress by CTG (cardiotocography) monitoring and perinatal outcomes in abnormal and normal CPR groups in labor in low risk patients (AGA fetuses) and used CPR cut-off as 10th centile.

Materials and methods

This study was a prospective cohort study conducted on women with low risk pregnancies undergoing ultrasound with Doppler and biometry at 35 to 37 + 6 weeks gestation and delivering at our center over a period of 18 months from March 2021 to November 2022, after the approval of the Ethics Committee of the Institute. A total of 172 women were finally included in the analysis, patients were divided into two groups according to ultrasonography findings done earlier. Out of this, 55 women had low CPR group I (≤10th centile) and 117 women had normal CPR group II (>10th centile). All women were followed till delivery, CTG tracings were observed and adverse perinatal and neonatal outcomes were compared between the two groups. The composite adverse perinatal outcome included 5' APGAR scores, birth weight, meconium stained liquor, NICU admissions were compared between the two groups.

Inclusion criteria

All women of age group 18–35 years with singleton pregnancy in cephalic presentation between 35 and 37 + 6 weeks POG with no major prenatally diagnosed fetal anomalies were included in the study.

Exclusion criteria

Women with any comorbidities like diabetes mellitus and hypertension, fever, IVF pregnancy (*in vitro* fertilization), premature rupture of membranes, chronic diseases, malpresentation, multiple pregnancies, planned cesarean delivery, fetal demise, major fetal anomalies. Pregnancy with diagnosed FGR before 35 weeks, early onset FGR and small for gestational age FGR determined by fetal growth curves in previous examinations to distinguish from AGA fetus were also excluded from the study. All subjects fulfilling the criteria and willing to participate were approached for enrollment into the study. Patients were counseled and informed written consent was taken. The patient's baseline characteristics with history and examination were assessed for anemia, fever, routine blood pressure, and GDM screening, and other antenatal investigations were performed as per the existing protocol and according to the individual case. Ultrasonography was performed with a 5 Hz logic S8 GE pulse wave Doppler in the Department of Diagnostic and Interventional Radiology for three consecutive waveforms; angle of insonation should be <30°. MCA-PI was measured at the origin of MCA from ICA (internal carotid artery) after identifying the circle of Willis. At the free loop of the umbilical cord, UA-PI was measured and CPR was calculated.

Fetal biometry, amniotic fluid index (AFI), and Doppler indices were recorded and the CPR ratio was calculated using Barcelona growth chart calculator. Gestational age at delivery, on-reassuring/ abnormal fetal CTG (cardiotocography) tracing during labor was noted and classified according to NICE guidelines 2017 (Table 1). Managing clinicians were not aware of CPR results, labor was managed according to the institute protocols.

Patients undergoing cesarean section or operative vaginal delivery due to fetal distress, meconium-stained amniotic fluid, birth weight, APGAR score at 1' and 5' and NICU admission were observed in both the groups.

Statistical analysis

The expected incidence of abnormal CPR in low-risk pregnancy is ~15 % (13.2 %) [3] Flatley et al. [2], sample size for the study is calculated as 172. The quantitative variables were compared between the two groups by using an independent t-test and if the data did not follow a normal distribution, then a non-parametric test Mann-Whitney *U* test was used for comparison. The qualitative data was compared by using Chi-square test. Data analysis was done using SPSS version 23.0. A p-value <0.05 was taken as statistically significant.

Results

We compared the demographic variables in two groups in terms of age, education, occupation, socioeconomic status, address, gestational age at USG and rate of induction of labor. The mean age of patients in our study was 26.3 ± 3.9 years and the rate of induction of labor was also comparable (40 vs. 44 %). The two groups were equally matched in terms of baseline characteristics (Table 2).

CPR was abnormal in 55 (31.9 %) patients and normal in 117(68.02 %) patients. Thus the incidence of abnormal

Table 1: CTG classification NICE guidelines 2017.

Description	Baseline (beats/minute)	Baseline variability (beats/minute)	Decelerations
Reassuring	110 to 160	5 to 25	None or early Variable decelerations with no concerning characteristics[a] for less than 90 min
Non-reassuring	100–109[b] OR 161 to 180	Less than 5 for 30–50 minOR more than 25 for 15–25 min	Variable decelerations with no concerning characteristics[a] for 90 min or more OR variable decelerations with any concerning characteristics[a] in up to 50 % of contractions for 30 min or more OR variable decelerations with any concerning characteristics[a] in over 50 % of contractions for less than 30 min OR late decelerations in over 50 % of contractions for less than 30 min, with no maternal or fetal clinical risk factors such as vaginal bleeding or significant meconium
Abnormal	Below 100 OR above 180	Less than 5 for more than 50 min OR more than 25 for more than 25 min OR sinusoidal	Variable decelerations with any concerning characteristics[a] in over 50 % of contractions for 30 min or less if any maternal or fetal clinical risk factors OR late decelerations for 30 min (or less if any maternal or fetal clinical risk factors) OR acute bradycardia, or a single prolonged deceleration lasting 3 min or more

CTG, cardiotocography. [a]Regarding the following as concerning characteristics of variable decelerations: lasting more than 60 s; reduced baseline variability within the deceleration; failure to return to baseline; biphasic (W) shape; no shouldering. [b]Although a baseline fetal heart rate between 100 and 109 beats/minute is a non-reassuring feature, continue usual care if there is normal baseline variability and no variable or late decelerations.

cerebroplacental ratio (CPR) in low risk pregnancy was 31.9 % given below. A significantly higher number of women 11 (20 %) with abnormal CPR had abnormal CTG pattern as compared to 9 (7.69 %) women with normal CPR (p=0.027) [Table 3]. Normal delivery was higher in normal CPR group II but no significant difference was seen.

Another significant finding of the study was birth weight. It was classified into two groups of >2.5 kg, low birth weight <2.5 kg as standardised low birthweight has been defined by the World Health Organization (WHO) as less than 2,500 g often consistent with 10th percentile for that gestation. This is based on epidemiological observations that infants weighing less than 2,500 g are approximately 20 times more likely to die than heavier babies [9].

In our study, the upper and lower extremes of birth weight were 1,340 g and 4,210 g, respectively. Seventy one

Table 2: Baseline characteristics of patients.

Variable	Group I (<10th Centile) Mean ± SD	Group II (>10th Centile) Mean ± SD	p-Value
Mean age	25.64 ± 3.5	26.62 ± 4.05	0.126
BMI	22.75 ± 3.09	23.15 ± 2.89	0.57
Gestational age at USG	35.98 ± 0.93	36.08 ± 0.93	0.503
Education (Graduate)[a]	19(34.54 %)	37(31.6 %)	0.76
Occupation (Housewife)[a]	41(74.54 %)	92(78.63 %)	0.8
Socioeconomic status (lower middle class)[a]	34(61.8 %)	86(73.5 %)	0.37
Residential status (urban)[a]	23(41.8 %)	45(38.46 %)	0.6
Gestational age at delivery	38.18 ± 1.27	38.49 ± 1.38	0.536
Parity – nulliparous[a]	31(56 %)	60(51 %)	
Multiparous[a]	24(43 %)	57(48 %)	0.53

[a]n(%); used *t*-test; used Chi square test; p<0.05 – statistically significant.

Table 3: CTG tracings and perinatal outcomes.

Parameters	Group I (≤10th centile) n=55(%)	Group II (>10th centile) n=117(%)	p-Value
Normal CTG tracings	34(61.81 %)	95(81.19 %)	0.173
Non-reassuring CTG tracings	10(18.18 %)	13(11.11 %)	0.245
Abnormal CTG tracings	11(20 %)	9(7.69 %)	0.027
Normal delivery rate	27(49.09 %)	67(57.26 %)	0.47
Cesarean section rate	25(45.45 %)	47(40.17 %)	0.63
Operative vaginal delivery rate	3(5.45 %)	3(2.56 %)	0.33
Cesarean section due to fetal distress	10(40 %)	14(29.78 %)	0.38
APGAR at 5' </=7	3(5.45 %)	6(5.12 %)	0.94
Mean birth weight[a]	2,587 ± 454	2,873 ± 431	<0.0001
Meconium stained liquor	4(7.27 %)	10(8.54 %)	0.77
NICU admission	2 (3.63 %)	5(4.27 %)	0.87
Adverse perinatal outcome	5(9 %)	3(2.5 %)	0.057

[a]Mean ± SD; p<0.05 – statistically significant.

percent of babies had a birth weight >2.5 kg while 29 % had a low birth weight (<2.5 kg).

In normal CPR group II, 92 (78.6 %) had normal birth weight only 21.3 % had low birth weight (p value 0.08). In abnormal CPR group I, 54.5 % of babies had normal birth weight and 45.45 % were born with low birth weight (p value 0.006) which was quite significant.

Rest all perinatal outcomes like APGAR at 5', NICU admission, meconium stained liquor composing adverse perinatal outcomes and cesarean section due to fetal distress were comparable and not significant (p>0.05). The CTG tracings and other perinatal outcomes are summarized in Table 3.

We also calculated the odds ratio of CPR ≤10th centile for non-reassuring and abnormal CTG which is 2.61. The positive predictive value of CPR<10th centile in predicting Abnormal and non-reassuring fetal status during labor is 20 % and 18.18 % respectively, while the negative predictive value is 81.19 %

Discussion

Most of the studies done earlier have compared perinatal outcomes in small for gestational age (SGA) fetuses with normal and abnormal CPR on Doppler. There are few studies done in low risk pregnancy with AGA fetuses like Rial-Crestelo et al. [10] and Buca et al. [11] which also compared perinatal outcomes by means of CPR in low risk term or AGA pregnancies.

The demographic profile of the patients in the present study was comparable to the previous studies. The mean period of gestation (POG) at ultrasound which was also the POG at enrollment was around 38–41 weeks in most previous studies. Khalil et al. [3] included patients with USG within 2 weeks of delivery so most previous studies included term patients. We enrolled patients at a fixed POG (35–37+6 weeks). The definition of abnormal or low CPR was different in various studies considered to be <5th in Rial-Crestelo et al. [10] centile and <1st centile in Chainarong et al. [12], <1.08, <0.6765 MoM in Khalil et al. [3], presently in our study we have used ≤10th centile as cut off which was also similar to Prior et al., Figueras et al. and Dall'Asta et al. [13–15].

The incidence of abnormal Doppler was compared in various studies and our study had a higher incidence of abnormal CPR (32 %) because we have increased the cut off to 10 centile and our institute being tertiary care center as compared to Chainarong et al. [12] which was 52 (13.5 %) and Rial-Crestelo et al. (5.35 %) [10].

We have compared fetal distress in patients with normal and abnormal groups by using CTG tracings (abnormal and non-reassuring CTG tracings) as a tool. It was not comparable to previous studies due to less sample size, but p value was significant in all studies as shown in Table 4. Our study had a lower incidence of abnormal CTG tracings in both groups as we included only low risk patients while in other studies high risk patients with preeclampsia, diabetes [12], or previously diagnosed SGA were also included [13].

Table 4: Abnormal CTG tracings as compared to literature.

Studies	Abnormal CPR, n(%)	Normal CPR, n(%)	p-Value
Chainarong et al. [12]	28(53.8 %)	93(28 %)	<0.01
Prior et al. [13]	86 %	31 %	< 0.001
Present study	11(20 %)	9(7.69 %)	0.027

The mean period of gestation at delivery was around 38–40 weeks in previous studies and was comparable to the index study (38 weeks).

In the index study, the incidence of operative delivery was higher in the abnormal CPR group as compared to the normal CPR group but was not significant (p-0.38) as compared to Dall'Asta et al. in which obstetric intervention for suspected fetal distress was >3 times higher among reduced CPR MoM ([16.7 %] vs. [5.5 %]; p= 0.004) [15].

The difference can be explained by the cohort included in various studies which did not exclude high risk pregnancies likewise only SGA or patients with increased risk of SGA were recruited in Karlson et al. [16] (Table 5).

Meconium staining during delivery observed in our study was comparable to Chainarong et al. [12] in the abnormal CPR group and was not significantly different in previous studies (p>0.05) [8, 12, 13].

APGAR score was calculated in previous studies at 5 min only with a low APGAR cut-off of ≤7. It was found to be equal in both groups p=0.9 which was similar to Chainarong et al. and Dall'Asta et al. [12, 15].

NICU admission was compared in various studies, it was observed that admission was more in Khalil et al. [3] and Flood et al. [17] with statistical significance. However, in our study, NICU admissions were comparable to Chainarong et al. and Dall'Asta et al. which was not significant [12, 15]. The cause of lesser NICU admission is due to lower sample size, NICU facilities at various centers, and exclusion of high-risk pregnancies.

Mean birth weights were compared in all studies and found to be significantly different in both groups in the majority of previous studies, while some studies compared birth weight centiles (≤10th centile) [12, 14, 15, 17]. Mean birth weight was lower in abnormal CPR groups, as compared to the normal CPR group in our study as well.

Table 5: Operative delivery due to fetal distress in various studies.

Studies	Abnormal CPR, n(%)	Normal CPR, n(%)	p-Value
Chainarong et al. [12]	10(19.2 %)	43(12.9 %)	0.31
Khalil et al. [3]	13.1 %	9.4 %	<0.01
Karlsen et al. [16]	31(52 %)	17(12 %)	0.032
Figueras et al. [14]	79.1 %	10.7 %	<0.001
Prior et al. [13]	36.4 %	10.1 %	<0.001
Dall'Asta et al. [15]	16.7 %	5.5 %	0.004
Present study	10(40 %)	14(29.78 %)	0.38

CPR for predicting perinatal outcomes was compared in previous studies using positive predictive value (PPV) and negative predictive value (NPV) [8, 12, 13, 15]. In our study, CPR ≤10th centile has a negative predictive value of reassuring CTG was 81.19 % which was slightly lower than other studies as previous studies have taken high risk pregnancies. Hence, it indicates that normal CPR reasonably excludes fetal distress in labor especially in low risk pregnancy. Najam et al. [8] and Karlsen et al. [16], have higher positive predictive value as they included high risk pregnancies and patients with already diagnosed SGA or at risk of SGA respectively while Dall'Asta et al. has lower PPV (18.0 %) but relatively higher NPV (>90 %) [15].

Previous studies like Dall'Asta et al. also compared the use of uterine artery (UtA), umbilical artery (UA) middle cerebral artery (MCA) or CPR alone to predict perinatal outcomes [11, 18]. If CPR can be used in addition to UA or EFWt there was no extra benefit as compared to UA alone. The majority of studies observed that CPR has good negative predictive value which can be used in the future.

The strength of study was that it was a prospective cohort study and one of the few studies done in western India. No previous study has analyzed the outcomes in AGA fetuses not in labor. We excluded chronic illness and major fetal malformations which are responsible for FGR, which were included in most of the previous studies. The patients were properly followed up till delivery and postnatal period of hospital stay.

Limitations of the study

We used centiles for CPR and not actual values, using the 10th centile attributed to a higher incidence of abnormal CPR. APGAR was based on pediatrician perception and was a subjective finding with interobserver variations. Neonatal acid-base status was not evaluated in our study as compared to Dall'Asta et al. and Rial-Crestelo et al. [10, 15]. We have focused on other outcomes, such as maternal and neonatal complications, which are comparable. and obtaining umbilical cord blood samples might be considered an unnecessary invasive procedure, especially in healthy newborns in low risk population.

Longer follow-up may be required regarding fetal outcomes like neurodevelopment sequelae, feeding problems, and immune dysfunction. Lastly, the lower rate of adverse perinatal outcomes in our study can be attributed to the fact that the study was done in a tertiary care center with all the facilities for the prevention of perinatal asphyxia.

Conclusions

It is concluded from our study that there is an increased rate of fetal distress as reflected by CTG tracings and higher incidence of low birth weight in patients with abnormal CPR. Hence, abnormal antepartum CPR in low risk pregnancy can predict fetal distress during labor and also low birth weight despite normal fetal biometry on ultrasound. Additionally, CPR measurement has a good negative predictive value so it can help to stratify women who will be benefited from CTG monitoring.

Concurrent use of CPR with cardiotocography may be used for labor triage, and intrapartum monitoring of patients and can plan timing and mode of delivery but merits further trials.

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Research ethics: Ethical Approval number: (AIIMS/IEC/2021/3320) approved by Ethical Committee, AIIMS Jodhpur. Authors state that this study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Informed consent: Informed consent was obtained from all individuals included in this study, or their legal guardians or wards.

Author contributions: NR contributed to study planning, design, data collection and analysis, and writing of manuscript. MG contributed to study planning, data analysis, and editing of the manuscript. TY helped in the data collection process. PS and SS contributed to study planning, supervision of the data collection process, and reviewing the manuscript critically. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

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