

Fetal cerebroplacental ratio at term gestation in the prediction of adverse perinatal outcome

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Abstract

Introduction: Assessment of impedance to blood flow in fetal umbilical artery (UA) and middle cerebral artery (MCA) with Doppler ultrasonography is commonly used in surveillance of fetuses at high risk. Although high UA pulsatility index (PI) and low MCA PI, themselves are predictors of adverse perinatal outcome, combining these two parameters calculating the cerebroplacental ratio (CPR) further improves the predictive value.

Objective: To find the association between the cerebroplacental ratio and adverse perinatal outcome.

Methods: Prospective cohort study conducted in Teaching Hospital, Anuradhapura. 354 singleton pregnancies at 37-41 weeks gestation were included. Ultrasound scanning performed measuring fetal UAPI and MCAPI and CPR was calculated. Fetuses were followed up for intrapartum adverse outcome categorized as NNU admission, perinatal death, fetal distress, Apgar score < 7 at 5 min and any adverse outcome. Descriptive statistics and the statistical applications for diagnostic test accuracy were used for data analysis. ROC curve were plotted to analyze the predictability of CPR for each category.

Results: CPR has a significantly positive ability of predicting any type of adverse event. (AUC=0.501-0.623, 95%CI) An overall predictability is shown by the other variables used in the study such as MCAPI (AUC=0.505:95%CI=0.444-0.567) and UAPI 0.518 (95% CI=0.457-0.579). But the predictability of CPR value is more superior to the MCAPI and UAPI values. Identified best cut off value for CPR is 0.8533 for predicting adverse events with 80.3% sensitivity.

Conclusion: More reliable predictions to detect adverse perinatal outcomes can be achieved by the CPR value than the UAPI and MCAPI values.

Key words: cerebroplacental, perinatal, outcomes

Sri Lanka Journal of Obstetrics and Gynaecology 2022; **44**: 220-227

DOI: <http://doi.org/10.4038/sljog.v44i4.8051>

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Received 20th August 2022

Accepted 6th February 2023



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Introduction

Assessment of impedance to blood flow in the fetal umbilical artery (UA) and middle cerebral artery (MCA) with Doppler ultrasonography is commonly integrated in surveillance of fetuses at high risk^{1,2,3}. Raised UA pulsatility index (PI) is significantly associated with adverse perinatal outcome⁴. Although high UA PI and low MCA PI, themselves are predictors of adverse perinatal outcome, combining these two parameters by dividing MCA PI by UA PI, thus calculating the Cerebroplacental ratio (CPR) further improves the predictive value^{5,6,7,8,9}. The CPR is emerging as an important predictor of adverse perinatal outcome and its predictive value in assessing fetal well-being has been shown not only in small for gestation age (SGA) fetuses but also in fetuses that are appropriate for gestational age (AGA) close to term¹⁰.

Studies have shown that incidence of impaired placental function leading to an adverse perinatal outcome is higher in SGA fetuses than that in AGA fetuses with birth weight above 10th centile^{11,12}. Although the prevalence of SGA fetuses is far lower than AGA fetuses and overall contribution to the number of fetuses with impaired placental function leading to an adverse perinatal outcome at delivery, is mainly from AGA group^{13,14}. It could therefore be argued that, on assumption that adverse perinatal outcome is a consequence of poor placentation, which is better indicated with low CPR value than small size of fetus, optimum perinatal care to reduce adverse perinatal outcome should be directed at screening the fetuses with low CPR rather than identifying babies with low estimated fetal weight¹⁵. Some studies providing evidence in supporting this concept, report that low CPR value, irrespective of the size of the fetus is independently associated with the need for operative delivery for presumed fetal compromise, reduced neonatal blood pH and admission to neonatal unit^{1,9,14,16,17}.

Despite the clinical importance of intrapartum hypoxia, which lead to lifelong morbidity, the antenatal prospective identification of the fetuses at risk of hypoxia-related injuries during labor remains challenging¹⁸. Widespread use of intrapartum cardiotocography (CTG) has not led to a reduction in the incidence of cerebral palsy according to the current evidence¹⁹. In addition, very poor sensitivity of CTG for intrapartum fetal surveillance makes the babies at risk of undetected hypoxia and irreversible neurological damage during labour^{20,21}. Therefore a non-redundant

necessity of a sensitive test exists, which is capable of prospective identification of fetuses which will poorly tolerate the immense stress of labor. Cerebroplacental ratio has been suggested as a tool for this purpose, but the studies done on its appropriateness and validity is limited in the literature⁸.

Methodology

This was a prospective cohort study conducted at Obstetrics ward of Professorial unit of Rajarata University in Teaching Hospital Anuradhapura. 354 pregnant mothers with singleton pregnancy who admitted for confinement during the study period, at 37 week (259 days) to 41 week (287 days) period of gestation were included for the study. Dates confirmed by Crown Rump Length measurement between 11- 13+6 week gestation. Pregnancies complicated by fetal anomaly, SGA, medical disorders and elective cesarean delivery were excluded from the analysis.

Ultrasonographic fetal biometry and Doppler study were carried out for each participant following admission, only by the principal investigator, using a single ultrasound machine which was Toshiba Nemio XG SSA- 580A with Toshiba Nemio XG PVM-375AT convex transducer with 3-6 MHz frequency. Central frequency was 3.75 MHz. Field of view angle was 70°. The Doppler sample volume was 2 mm, and the wall filter was 50-100 Hz. Recommendation by the U.S. Food and Drug Administration for obstetric scanning used as a guideline and the spatial peak temporal average intensity was maintained < 94 mW/cm². Ecosonic ultrasound transmission gel was used.

Estimated fetal weight (EFW) was calculated using the formula derived by Hadlock et al²². Standards recommended by the large scale, multicenter, multinational INTERGROWTH- 21st project was used as a guidance for measurements of growth parameters²³. UA Doppler waveforms were assessed at the middle of the umbilical cord using color flow imaging. To assess MCA Doppler waveforms, a transverse image of the fetal head at the level of sphenoid bone was obtained. Circle of Willis was identified using color flow imaging and MCA Doppler was assessed 1 cm distal to its origin of from internal carotid artery. CPR was calculated using UA PI and MCA PI. CPR <1 was considered as abnormal^{24,25}. Ultrasound scanning was carried out 1st day of admission to ward, and it was repeated every 8th day if mother remain undelivered, to make sure that the Sonographic and Doppler values

were up-to-date within maximum 7 days from delivery.

Fetuses were followed up for intrapartum adverse outcome. Main outcome measure was admission to the neonatal unit (NNU) within 24 hours from delivery. Other outcomes were 5-min Apgar score <7, Perinatal mortality, Number of still births and death in 1st week of life, Cesarean section or instrumental delivery due to presumed fetal distress. By combining the above-mentioned outcome variables “Any adverse outcome” was established. Perinatal data were extracted from clinical records after birth.

Data was entered in to an electronic data base. (Microsoft Excel for Windows 10). Then the data was transferred into a SPSS 25.0 work sheet for analysis (Statistical Package for the Social Sciences; SPSS, Chicago, IL, USA). Categorical data was presented as numbers and percentage in brackets. Presence or absence of a particular outcome was compared depending on the presence or absence of the factor using the Odds Ratio. Continuous data was presented by using measures of central tendency. Receiver operator curve (ROC) was used to analyze the value of CPR which could be used as a cut off for impending poor prognosis during labor.

Results

Participants’ age was noted to range from 16 years to 41 years duration. Mean 27.22 years (SD=5.19). Majority of the participants were between 26-30 years of age group. Majority of the participants were primigravidae women (N=166:46.9%).

Height of the participants were ranged between 1.32m to 1.72m with Mean value 1.54m (SD=0.058m). Weight of the participants were ranged between 41kg to 110kg with Mean value 64.94kg (SD=10.87kg). Body Mass index of the participants were ranged between 16.85kg/m²-42.85kg/m² with Mean value 27.12 kg/m² (SD=4.11kg/m²). Majority of the participants were in the BMI range between 25-29.99 kg/m² (N=156: 44.1%).

Range of gestational age of the participants was from 37 weeks (259 days) to 41weeks (287 days). Majority of the study participants were represented the gestational age between 39 to 40 weeks. Mean 39+2 weeks (275 days) and SD = 7.18 days.

Mean EFW was 3206.3g (SD=369.4G). In majority of study participants EFW were included between 2.5kg to 3.5kg (N=264:74.6%). Amniotic Fluid Index were ranged from 4.9cm to 28.0cm. Mean AFI 13.1cm (SD=3.31).

Predictive association of SCBU admission according to the CPR value does not provide adequate information to predict SCBU admissions (Figure 1). According to the prepared ROC curve, AUC value is 0.471. ROC curve was not capable of enclosing half of the diagnostic area (95%CI=0.332:0.609).

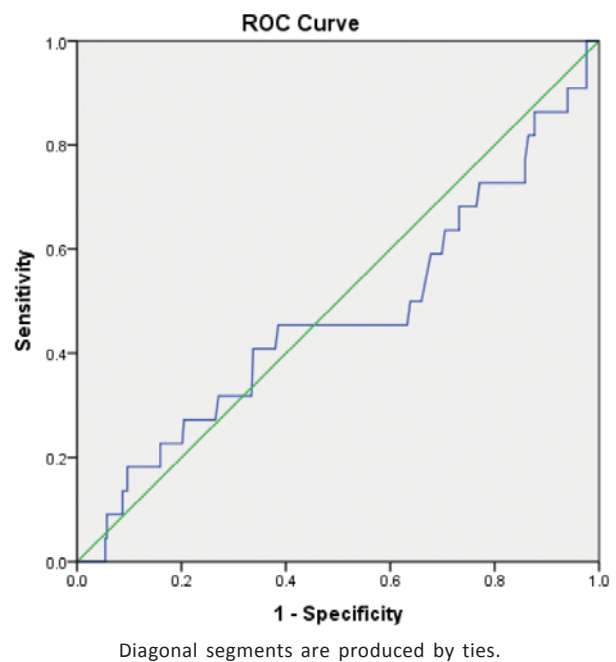


Figure 1. Predictive association of SCBU admission according to the CPR value.

ROC curve demonstrating the predictive association of Foetal distress according to the CPR value showed that AUC is merely above 0.5 and there is an ability to predict fetal distress by the CPR value. But it does not show a significant predictability (95% CI=.460-.582). As the ROC curve is distributed closer and more parallel to the central diagonal line it is not possible to detect a left uppermost point. However, 0.8483 can be calculated as a cut off value with an 80% sensitivity and there 15% specificity (Figure 2).

APGAR < 7 at five minutes after the birth can be predicted by CPR value (Figure 3). ROC curve demonstrates, AUC value is 0.712 and it shows that

reduction of APGAR score can be predicted by the CPR value. But present study findings does not give evidence to use it significantly (95%CI=0.495-0.930). Cut off value which can be used is 0.9974 and it can be used to predict reduction of the APGAR score with a 66.7% sensitivity and 48.1% predictability.

A comparison of ability to use CPR value for predicting adverse perinatal outcomes with UA PI and MCA PI indexes shows the highest predictability by the CPR value (Figure 4). Accordingly, all the pulsatile indexes

have a potency of predicting adverse perinatal outcomes. (AUC>0.5). But the highest and significant predictability is recorded by the CPR value. (95%CI = 0.501-0.623). The least predictability is revealed by the MCAPI value (AUC=0.505:95%CI=0.444-0.567) and the predictability of UAPI value is 0.518 (95% CI=0.457-0.579). Identified best cut off value for CPR is 0.8533 and by using this cut off value adverse events can be predicted with 80.3% sensitivity and there was 25.0% specificity.

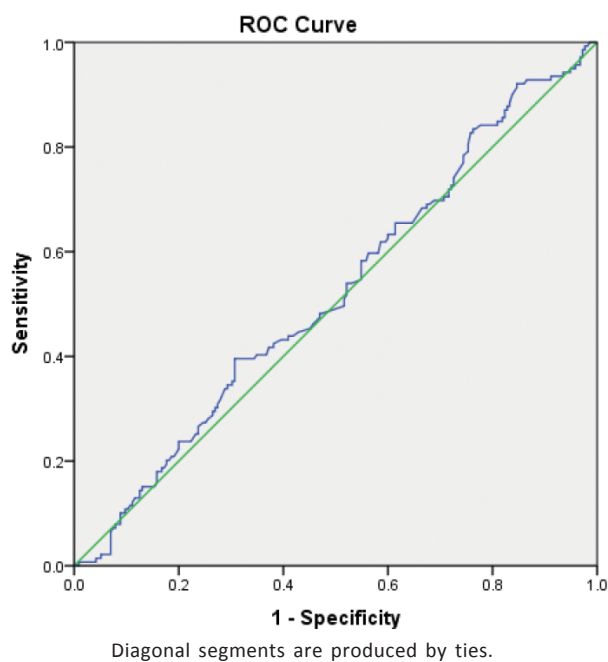


Figure 2. Predictive association of fetal distress according to the CPR value.

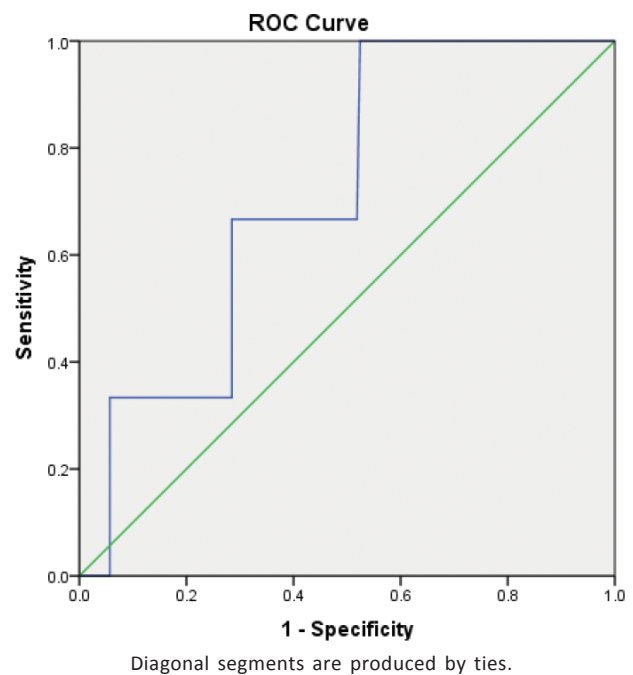


Figure 3. Predictive association of APGAR < 7 at 5min to the CPR value.

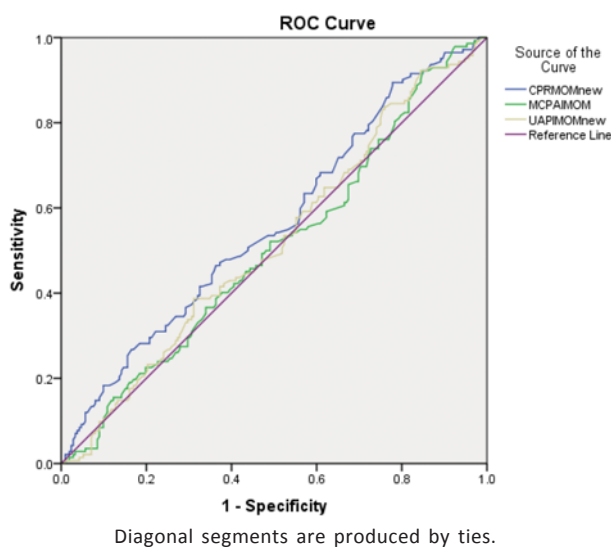


Figure 4. Comparison of CPR with other predictable variables.

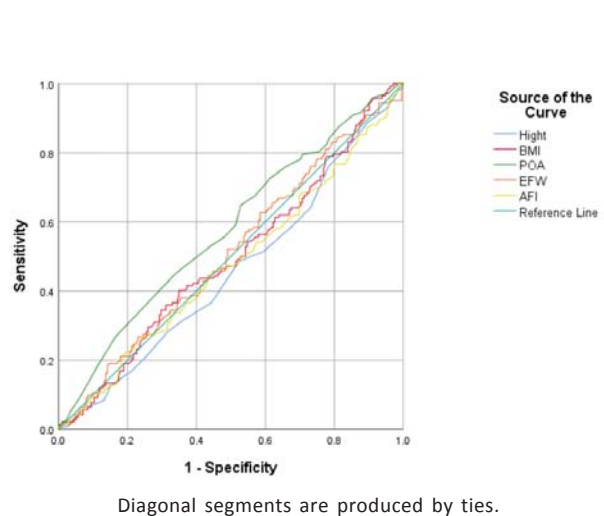


Figure 5. Any adverse event prediction by selected variables.

Table 1. ROC curve characteristics for predicting any adverse event

Test result variable	Area	P value	95% Confidence interval	
			Lower bound	Upper bound
Height	.456	.162	.395	.517
BMI	.495	.886	.434	.557
POA	.576	.016	.515	.636
EFW	.510	.753	.448	.571
AFI	.476	.448	.414	.538

BMI=Body mass Index, POA=Period of amenorrhea, EFW=Estimated foetal weight, AFI=Amniotic fluid index

The association between selected exposure variables with any adverse perinatal outcome was analysed (Figure 5, Table 1). Gestational age showed the significant predictable association with any adverse outcome (AUC=0.576;95% CI=0.515-.636). EFW showed positive association with any adverse outcomes but it does not show significant predictability (AUC=0.510;95%CI=.448-.571). Maternal anthropometric measurements and Amniotic fluid index showed poor associations with any adverse outcomes (AUC<0.5;p>0,05).

Discussion

Different studies defined the threshold value of CPR in the prediction of adverse perinatal outcome in a different manner. Some studies^{24,25} considered abnormal CPR as <1, while Gramellini et al²⁶ assumed CPR as abnormal when it is <1.08. Cut-off value of CPR <1 result in 66% sensitivity and 85% specificity²⁷.

Role of CPR in the detection of fetuses at risk of adverse outcome in Appropriate for gestational age (AGA) fetuses had been a subject of several studies. Prior et al⁹ evaluated 400 AGA fetuses prospectively. Of those who underwent cesarean section due to presumed fetal distress 36.4% had low CPR. They reported that fetuses with CPR less than 10th percentile were 6 times more likely to be delivered by cesarean section due to fetal distress. (OR 6.1. 95% C.I 3.03-12.75). It was concluded that CPR is an accurate predictor of intrapartum fetal compromise.

Similar results have been obtained in 2015, by Morales-

Rosello et al¹⁰ by retrospectively analyzing 2927 patients to determine whether SGA and AGA term fetuses with a low CPR have worse neonatal acid-base status. They found a significant association between AGA fetuses with low CPR and umbilical cord low pH. It was concluded that assessment of CPR in term AGA fetuses can be used as a predictor of intrapartum fetal compromise requiring cesarean delivery or academia at birth.

Similar kind of association was observed in a study reported by Khalil et al¹² who retrospectively compared CPR and estimated fetal weight (EFW) at term gestation as predictors on NNU admission, found that irrespective of EFW percentile, the CPR appeared to be a better predictor of NNU admission.

Khalil et al¹³ in a different study found that there's a significant association between low CPR and need for operative delivery due to presumed fetal compromise and NNU admission. Other two prospective studies by Cruz-Martinez et al²⁸ and Figueras et al²⁹ reported low CPR has a good predictive value on emergency cesarean section and adverse perinatal outcome respectively.

Raised Umbilical artery (UA) pulsatility index (PI) is associated with adverse perinatal outcome¹. Most of the studies have recognized a better predictive value in CPR than UA PI or MCA PI alone^{28,9,11,12,13}. In contrast Figueras et al²⁹ in a study explained that UA PI and Uterine artery PI (UtA PI) are better predictors than CPR.

Fundamental intent of the present study was to identify the feasibility of several relevant variables to predict adverse perinatal outcomes. Rapid identification of adverse perinatal events is an effective strategy which can be used to minimize perinatal mortality and morbidity. In Sri Lanka 99% of the child births occur around healthcare institutions and recorded non-institutional child births are less than 1%. Antenatal care coverage in Sri Lanka is above 90% and as a result the opportunity to detect adverse events is higher. This condition permits minimization of effects due to adverse perinatal outcomes.

CPR can be easily calculated by performing ultrasonography by a trained ordinary medical officer. Therefore, it is obvious that it is feasible to use CPR as a low-cost diagnostic method. At Term gestation, there is a possibility of easily motivating the mothers to perform ultrasonography as concerns regarding childbirth is higher around this period. On the other hand, CPR calculation procedure is entirely non-invasive. Therefore, there is a higher possibility of becoming popular and it could be more feasible to include this procedure to national antenatal management guidelines.

If there were distinct parameters to predict perinatal adverse events, high risk mothers could be prepared beforehand for safe deliveries. They can be admitted to suitable healthcare institutions with adequate facilities, such as continuous electronic fetal monitoring, facilities to perform emergency caesarean section and optimum neonatal care. And they can be categorised as having low threshold for caesarean section when they go into labour or else they can be offered the choice of elective caesarean section. Implementing these strategies are more practical with the manner of establishment of the Sri Lankan healthcare system. It is more feasible to be attentive with these predictions and as CPR calculation is simple, non-invasive and there is minimum utilization of additional resources. Therefore, there could be less obstacles with introduction of this new procedure.

However, a cause effect relationship is not described by the study finding between UAPI and MCAPI which were used to calculate the CPR values. Although it is possible to statistically confirm the usage of these values as predictors, they cannot be introduced as biological causative factors. This aspect should be further studied with a compulsory larger sample size.

Conclusions

It is possible to predict adverse perinatal outcomes by the CPR values which are calculated by using UA PI and MCA PI. More reliable predictions to detect adverse perinatal outcomes can be achieved by the CPR value than the UA PI and MCA PI values. More than predicting an exact adverse event or events, it is possible to assess the probability of expecting an adverse perinatal outcome by using the ultra sound scan done at the 37-41 weeks of gestation. Further studies should be conducted to confirm any cause effect relationship between MCA PI, UA PI and CPR values and adverse perinatal outcomes.

Should pay attention on including a method to predict adverse perinatal outcomes to the clinical management guidelines by using the arterial pulsatile indexes calculated during the antenatal period.

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