Original Article

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Prognostic Accuracy of Cerebroplacental Ratio, Use as A Predictive Tool in Earlier Assessment of Adverse Perinatal Outcome

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Author`s Contribution

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ABSTRACT

Objective: To determine the prognostic accuracy of the cerebroplacental ratio (CPR) as a predictive tool for the early assessment of adverse perinatal outcomes.
Methodology: This prospective observational cohort study was conducted on pregnant women with a gestational age between 28 and 40 weeks, having singleton high-risk pregnancies in the third trimester. Participants were recruited from the outpatient department (OPD) and inpatient wards of Dr. Ruth K. M. Pfau Civil Hospital, Karachi, from June 2020 to May 2021. Doppler ultrasound assessments were performed using a high-resolution Toshiba Xario 100 ultrasound machine to estimate the pulsatility index (PI) and resistance index (RI) of the umbilical artery (UA) and middle cerebral artery (MCA). The cerebroplacental ratio was calculated as the ratio of MCA-PI to UA-PI. Doppler examinations were reviewed by two experienced radiologists, and values below the 5th percentile for gestational age (approximately <1.08–1.1) were considered abnormal.
Results: The mean age of the participants was 29.15 ± 2.03 years, and the mean gestational age was 32.23 ± 3.09 weeks. Intrauterine death (IUD) occurred in 8 cases, birth asphyxia was observed in 29 cases, and one neonatal death was reported. Abnormal MCA RI, CPR RI, and CPR PI values were observed in 28.6%, 24.6%, and 24.6% of cases, respectively. Analysis of the correlation between Doppler indices and perinatal outcomes showed that abnormal MCA RI was significantly associated with intrauterine death and birth asphyxia ($p = 0.001$). Abnormal CPR RI values were also significantly associated with birth asphyxia ($p = 0.001$), while no significant association was observed between MCA PI and adverse fetal outcomes ($p > 0.05$).
Conclusion: The cerebroplacental ratio was found to be a useful indicator for the early detection of adverse perinatal outcomes.
Keywords: Cerebroplacental ratio, MCA, CPR, IUD, Neonatal death, Birth Asphyxia

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Introduction

Adverse perinatal outcomes represent significant challenges to neonatal health and survival after birth. Global estimates indicate that approximately 75% of neonatal deaths occur during the first week of life, and in 2020 nearly 2.4 million newborns died within the first month after birth. These outcomes are particularly prevalent in low- and middle-income countries.[1,2]

Fetal growth restriction (FGR) can severely compromise neonatal health, leading to neonatal death within the first month of life and increasing the risk of intrauterine demise (IUD). Abnormal placental development is the most commonly reported pathophysiological mechanism associated with FGR.[3,4] Maternal complications such as hypertension, diabetes, and anemia may further complicate pregnancy and increase the risk of fetal growth restriction.[1,5] Despite advances in antenatal surveillance methods, adverse perinatal outcomes remain a major obstetric challenge, highlighting the need for early

identification of fetal compromise to allow timely intervention and improved outcomes.[4]

Ultrasonography is a primary non-invasive modality used for the assessment of FGR and the evaluation of perinatal risk through fetal biometry and Doppler studies. Conventional clinical assessment methods often lack adequate sensitivity for the early detection of fetal compromise that may affect normal fetal growth and development.[5]

Neonatal hypoxia, resulting from abnormal uteroplacental circulation, is also associated with poorer perinatal outcomes, such as elevated perinatal morbidity, preterm delivery, and intrauterine growth restriction (IUGR). Compromised placental perfusion can endanger fetomaternal health and survival by the involvement of adverse metabolic and cardiovascular conditions.[6] Doppler velocimetry is a reliable and non-invasive assessment of uteroplacental circulation changes in the umbilical artery (UA), fetal cerebral vessels, and middle cerebral artery (MCA) through elevated uterine artery Doppler resistance index, Gosling index, and diastolic notching. Fetal Middle Cerebral Artery (MCA) Doppler assessment serves as a more sensitive maker for fetal hypoxia detection in early stage than Umbilical Artery (UA) Doppler.[7]

Cerebroplacental ratio (CPR), which involves combined UA and MCA Doppler assessment parameters, is associated with superior prognostic values. Studies suggest significant association between abnormal CPR values and adverse perinatal outcomes, where reduced CPR values indicate placental resistance and cerebral vasodilatation, suggesting fetal compromise. CPR has a high sensitivity in detecting fetus at risk, even when individual values of UA and MCA are within normal range.[8,9] Overall expected that the use of MCA and cerebroplacental ratio indices as essential predictors of perinatal adverse outcomes; while, their diagnostic performing fluctuates across different populations and specifically very limited at local level. Consequently, this study has been planned to assess the usefulness of MCA and CPR Doppler indices in the adverse perinatal outcome estimations in our population, which may helpful to support risk stratification, encouragement obstetric interventions timely, and ultimately contribute to decreasing the perinatal adverse outcomes.

Methodology

This was a Prospective observational cohort study being conducted on pregnant patients with gestational age between 28 weeks and 40 weeks who attended the OPD and indoor wards of Dr Ruth K M Pfau Civil Hospital Karachi. The study was done during one year from June 2020 to May 2021. All the pregnant women aged 17 to 40 years with third trimester singleton high risk pregnancy, like intrauterine growth retardation, hypertension, pre-eclampsia, unhealthy obstetric history, anemia and gestational diabetes mellitus females were included in the study. However, women with twin pregnancy, intrauterine demise, morbidly adherent placenta, congenital anomalies and pregnancy with congenital anomalies were excluded.

A sample size of 174 patients was calculated by Open-epi, keeping 5% confidence interval and 95% confidence level, considering 87 % of neonatal deaths worldwide secondary to birth asphyxia, preterm birth and infections. The informed consent was obtained in the local language from each case and their care takers. The demographic maternal, clinical, and fetal information were collected using a structured proforma. The assessment of the fetus was including biometric parameters like estimated weight of fetus, circumference of the head and abdominal, index of amniotic fluid and femur length. The assessments were performed by Doppler ultrasound during gestational age of 34 to 41 weeks, if possible within seven days prior to birth, via a high-resolution machine of ultrasound Toshiba xario 100 ultrasound with transducer frequency of 3.5 MHz, with pulsed wave Doppler option, also enabling real-time and color-coded imaging. The ultrasound was conducted by the senior radiologist having minimum experience of five years following standardized protocols to estimate the umbilical artery (UA) and middle cerebral artery (MCA) pulsatility indices (PI), and the resistance index (RI).

Additionally, the ratio of cerebroplacental was estimated as the ratio of MCA-PI to UA-PI. Doppler examinations were reviewed by two experienced radiologist and below the 5th percentile values for age of gestation (around <1.08–1.1) was taken as abnormal. Collected data was entered and Statistical analyses were carried out on SPSS version 20.

Results

The mean age of the participants was 29.15 +2.03 years and abdominal circumference had a mean of 27.88+3.46 units. The mean gestational age was 32.23+3.09 months, indicating that, on average, the participants were in the third trimester of their pregnancies. Hypertensive cases were 34.9%, diabetics were 18.9% and anemia was

identified in 10.3% of the women. Out of total 175 cases, Intrauterine death (IUD) occurred in 8 (4.6%) cases, birth asphyxia was in 29 (16.6%) neonates, and only 1 (0.6%) case of neonatal death was noted, suggesting overall moderate prevalence of adverse perinatal outcomes. Figure 1

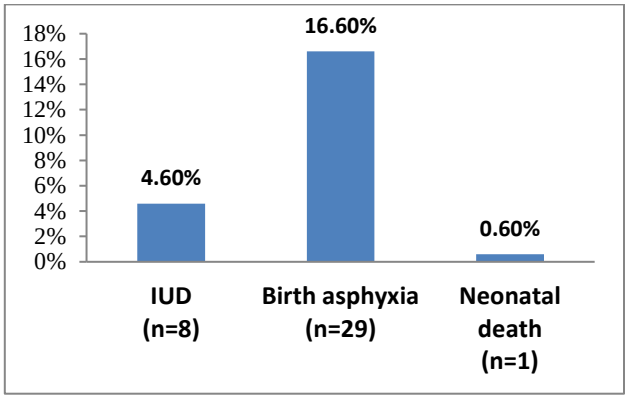

Figure 1. Adverse perinatal outcomes among patients.

Out of all, 50 participants (28.6%) had abnormal MCARI values, and (71.4%) had a normal MCARI, while overall mean of MCA RI was 0.73+ 0.102, and the mean MCA PI was 1.60+0.526. according to the cerebroplacental ratio, CPR RI mean was 1.14 ± 0.23, with third-quarters of the cases (75.4%) had normal values, while 24.6% categorized as abnormal. Likewise, the CPR PI average was 1.49 ± 0.657, and the most of the cases (75.4%) had normal, whereas around one-quarter (24.6%) had abnormal CPR PI values. Generally, findings showed that the majority of the cases had normal Doppler indices, with abnormalities more commonly detected in MCA RI and CPR PI. Table I

Table I: Doppler indices average and categorical values.

Doppler indices		Statistics
MCA RI	Overall mean	0.73±0.102
	Abnormal	50 (28.6%)
	Normal	125 (71.4%)
MCA PI	Overall mean	1.60±0.526
	Abnormal	57 (32.6%)
	Normal	118 (67.4%)
CPR RI	Overall mean	1.14 ±0.235
	Abnormal	43 (24.6%)
	Normal	132 (75.4%)
CPR PI	Overall mean	1.49±0.657
	Abnormal	43(24.6%)
	Normal	132(75.4%)

According to the correlation between Doppler indices and perinatal outcomes the abnormal MCA RI was significantly linked to the IUD and birth asphyxia, with higher proportions of IUD (14% vs 0.8%, p=0.001) and birth asphyxia (30% vs 11.2%, p=0.003) among patients with abnormal and normal values of MCA RI, respectively. While no significant link was noted between MCA RI and fetal outcomes P>0.05. Moreover, the CPR RI, abnormal values were not significantly associated with IUD and neonatal death (p>0.05) while significantly were associated birth asphyxia, where a greater proportion of asphyxia was noted in patients with abnormal CPR RI (39.5% vs 9.1%) p=0.001). Overall indicated that the abnormal MCA RI and CPR RI were useful indicators for forecasting birth asphyxia, while MCA RI also showed the significant link with IUD, while MCA PI did not show strong association with adverse outcomes. Table II

Discussion

Latest advances in obstetric Doppler ultrasonography have recognized fetal hemodynamic assessment as a key component in the surveillance of high-risk pregnancies, facilitating the early detection of fetuses at risk for adverse perinatal outcomes. In the present study, 175 patients were included, with an overall mean age of 29.15 years, a mean abdominal circumference (AC) of 27.88 cm, and a mean gestational age of 32.23 weeks, indicating that most participants were in the third trimester of pregnancy. Comparable findings were reported in the study by Poojari Y et al.,[10] who documented a mean gestational age of 32.6 weeks. In our study, 19.8% of pregnant women aged below 30 years had a mean abdominal circumference (AC) of 290.4 mm (29.04 cm), while 19.7% of those aged 30 years or above had a mean AC of 278 mm (27.8 cm). Similar patient characteristics were also reported by Dall'Asta A et al.,[11] who observed a mean maternal age of 32.6 ± 5.7 years and a mean gestational age of 34.2 weeks.

Table II: Association between outcomes and Indexes.

	IUD		p-value	Birth asphyxia		p-value	Neonatal death		p-value
MCA RI	**Yes**	**No**		**Yes**	**No**		**Yes**	**No**	
Abnormal	7 (14%)	43 (86%)		15 (30%)	35 (70%)		1 (0.8%)	42 (98.2%)	
Normal	1 (0.8%)	124 (99.2%)	0.001	14 (11.2%)	111 (88.8%)	0.003	0	133 (100%)	0.999
MCA PI									
Abnormal	2 (3.5%)	55 (96.5%)		6 (10.5%)	51 (89.5%)		1 (2%)	49 (98%)	
Normal	6 (5.1%)	112 (94.9%)	0.64	23 (19.5%)	95 (80.5%)	0.135	0	125 (100%)	0.112
CPR RI									
Abnormal	2 (4.7%)	41 (95.3%)		17 (39.5%)	26 (60.5%)		1 (0.8%)	0	
Normal	6 (4.5%)	126 (95.5%)	0.999	12 (9.1%)	120 (90.9%)	0.001	56 (99.2%)	118 (100%)	0.999

In this cohort, hypertension was the most frequent morbidity in 34.9% of the study population, followed by diabetes in 18.9%, and anemia was identified in 10.3% of the participants. Aligning with our findings, similar pattern of morbidity was documented in the study of Dall'Asta A et al[11] who found hypertension in 6.0% of patients and diabetes/Gestational diabetes in 6.4% of the participants. The differences in findings can be attributed to the differences in sample size and inclusion/exclusion criteria. Comparably, Chomon FA et al[12] found comparatively higher anemia rate of 44% in their hypertensive pregnant patients than our findings

In this series, out of all, 28.6% participants had abnormal MCA-RI values and only a small proportion of cases (3.5%) were abnormal MCA PI, while overall mean of MCA RI was 0.73± 0.102, and the mean MCA PI was 1.60±0.526, indicating that the majority had normal values for MCA-RI and MCA-PI. Additionally, according to the cerebroplacental ratio (CPR), the mean RI was 1.14 ± 0.235, with very few abnormal cases (4.7%). Likewise, the average CPR PI was 1.49 ± 0.657, while around one-quarter (24.6%) had abnormal values. Generally, findings showed that the majority of the cases had normal Doppler indices, with abnormalities more commonly detected in MCA RI and CPR PI. In agreement with these findings, in the study of Vollgraff Heidweiller Schreurs et al[13] overall mean MCA PI value was 1.54±0.41 and CPR PI value was 1.80±0.56.

In this study, according to the correlation between Doppler indices and perinatal outcomes the abnormal MCA RI was significantly linked to the IUD and birth asphyxia, with higher proportions of IUD (14% vs 0.8%, p=0.001) and birth asphyxia (30% vs 11.2%, p=0.003) among patients with abnormal and normal values of MCA RI, respectively. Aligning with our findings, in the study carried out by Shahinaj R et al[14] who found that significantly more perinatal deaths occurred among mothers with abnormal values of MCA/UA PI (30.8%) compare to normal (0.23%); P<0.0001. Similarly patterns were documented in the study of Strigini FA et al[15] who found that Abnormal MCA PI was associated with perinatal death. Consistently, in the study of Kassanos D et al.,[16] MCA Doppler RI and MCA Doppler PI were significantly lower in hypoxia (decreased oxygen saturation), indicating significant correlation between hypoxia and MCA Doppler findings.

In current study, no significant link was noted between MCA RI and fetal outcomes P>0.05. Moreover, the CPR RI, abnormal values were not significantly associated with IUD and neonatal death (p>0.05) while significantly were associated birth asphyxia, where a greater proportion of asphyxia was noted in patients with abnormal CPR RI (39.5% vs 9.1%) p=0.001). Findings overall indicting that the abnormal MCA RI and CPR RI were useful indicators for forecasting birth asphyxia, while MCA RI also showed the significant link with IUD, while MCA PI did not show strong association with adverse outcomes. Corresponding to our findings, a study conducted by Agrawal S et al.[17] found no significant correlation between MCA RI and perinatal outcomes. Similarly, in the study of Mbarak,[18] it was noted that although MCA-RI along with CPI can significantly predict adverse perinatal outcomes, adverse outcomes were not significantly associated with MCA RI alone. Generally, the literature increasingly highlights the clinical value of (MCA) and (CPR) indices as important predictors of fetal adverse outcomes. In this context, the present study adds further evidence by evaluating the diagnostic performance of these parameters in the predicting these outcomes. Although this study has several limitations, which underscores the need for further larger-scale studies to validate these findings and support the routine clinical use of these indices to improve the perinatal outcomes in high risk pregnancies.

Conclusion

The cerebroplacental ratio was found to be a useful indicator for the early detection of adverse fetal perinatal outcomes. In particular, abnormal MCA RI and CPR RI were significantly associated with adverse fetal perinatal outcomes, while MCA PI did not show a strong association with adverse outcomes. However, there were a few limitations in the study; therefore, further large-scale studies are recommended to validate these findings before including these predictors in routine clinical practice for the assessment of perinatal outcomes and improved management of high-risk pregnancies.

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