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Correlation of Fetal Cerebroplacental Ratio with Adverse Perinatal Outcome in Clinically Suspected Intrauterine Growth Restriction

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Key words:
Intrauterine growth restriction (IUGR), cerebro-placental ratio, perinatal adverse outcome.

Abstract

Background: *Intrauterine growth restriction is defined as a fetus's development rate being slower than normal, given the fetus's growth potential (for that particular gestational age). Intrauterine growth restriction (IUGR), as one of the primary causes of prenatal death and morbidity, has enormous ramifications for children's short- and long-term growth. The fo the study to correlate cerebroplacental ratio with adverse perinatal outcomes in intrauterine growth restriction.* ***Methods:*** *A total of 60 females with singleton pregnancies between 30-40 weeks of gestation with IUGR were subjected to an obstetric Doppler ultrasonogram. The middle cerebral artery pulsatility index (MCA-PI) and umbilical artery pulsatility index (UA-PI) were recorded, and the cerebroplacental ratio (CPR) was calculated. All patients underwent serial sonographic evaluation of fetal weight and the above-mentioned Doppler indices at two-week intervals until delivery.* ***Results:*** *The validity of emergency caesarean section (CS) for evaluating suspected IUGR pregnancies correlated by CPR, calculating sensitivity 84.4%, specificity 71.4%, accuracy 78.3%, positive predictive value 77.1% and negative predictive value 80.0%. The validity of low birth weight for evaluating suspected IUGR pregnancies correlated by CPR calculating sensitivity 89.2%, specificity 91.3%, accuracy 90.0%, positive predictive value 94.3% and negative predictive value 84.0%. The validity of low APGAR score for evaluating suspected IUGR pregnancies is correlated by CPR calculating sensitivity 90.6%, specificity 100%, accuracy 94.4%, positive predictive value 100% and negative predictive value 88.0%. The validity of NICU admission for evaluating suspected IUGR pregnancies correlated by CPR, calculating sensitivity 89.5%, specificity 56.1%, accuracy 66.7%, positive predictive value (PPV) 48.6% and negative predictive value (NPV) 92.0%.* ***Conclusion:*** *A better indicator of poor prenatal outcomes would be cerebroplacental ratio (CPR) measurement and Doppler evaluation, which are non-invasive tools for clinical practice. Cerebroplacental ratio should be taken into consideration as a sign of placental under-perfusion and placental reserve and may prove to be a valuable indicator to pinpoint fetuses that are more likely to experience hemodynamic disturbances prior to delivery.*

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Introduction:

Intrauterine growth restriction (IUGR) birth is defend as a fetal growth rate below its genetically determined potential size per race and gender and is associated with a higher risk of cardiovascular morbidity, mortality and long-term neurological adverse outcome.[1]

The terms IUGR and Small for Gestational Age (SGA) are often used alternatively to describe the same problem, although there exist subtle differences between the two. IUGR may be defined as grow that the 10th or less percentile for weight of all fetuses at that gestational age. The burden of IUGR is concentrated mainly in Asia which accounts for nearly 75% of all affected infants.[2]

Intrauterine growth restriction is associated with an increased risk of perinatal mortality and morbidity. It has long been recognized that impaired feto-placental perfusion is associated with intrauterine growth retardation. Ultrasonography with Color Doppler has provided a new tool for this purpose.[3] Color Doppler evaluation of MCA and UAP l ratio is a useful modality in diagnosis of IUGR and prediction of adverse perinatal outcome.[4]

The correct detection of the compromised intrauterine growth retardation fetus to allow for timely intervention is a main objective of antenatal care. Umbilical artery (UA) and middle cerebral artery (MCA) Doppler velocimetry was the most rigorous evaluation test among the noninvasive tests of fetal wellbeing.[5]. Previous study reported that among the Doppler indices, the CPR was a better predictor of SGA fetuses and adverse perinatal outcome than either the UA-PI or the MCA-PI alone, with a high specificity and PPV.[6]

A color Doppler apparatus may be used to assess the blood flow velocity profiles in the umbilical arteries to determine if complications associated with impaired trophoblastic invasion of the placental bed could be predicted by this measurement. Therefore, the purpose of this study was to assess the efficacy of CPR to predict IUGR in clinically suspected IUGR cases and its correlation with perinatal outcome. There is inadequate data available regarding the role of CPR to predict adverse perinatal outcome in clinically suspected IUGR cases in Bangladesh. Therefore, present study may be helpful to assess the efficacy of CPR to predict IUGR in clinically suspected IUGR cases and its correlation with adverse perinatal outcome.

Methods:

Prospective longitudinal observational study was carried out Department of Radiology & Imaging at Dhaka Medical College Hospital, Dhaka during From July 2019 to June 2021. A total of 60 females with singleton pregnancies between 30-40 weeks of gestation with IUGR were subjected to obstetric Doppler ultrasonogram. The MCA-PI and UA-PI were recorded, and CPR was calculated. All patients underwent serial sonographic evaluation of fetal weight and the abovementioned Doppler indices at two weeks intervals until delivery. These data were not available for the obstetrical team and hence, could not influence management decisions. Emergency cesarean section for fetal distress, APGAR scores at 5 minutes < 7, neonatal intensive care admission and stillbirths were recorded as primary perinatal outcomes. Statistical analyses were carried out by using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA) as well as Statistical and data analysis libraries of the programming language Python, where necessary. A descriptive analysis was performed for all data. The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies. For the validity of study outcome, sensitivity, specificity, accuracy, positive predictive value and negative predictive value of color Doppler study in the diagnosis of clinically suspected IUGR pregnancies were calculated. A “p” value <0.05 was considered as significant.

Results:

Table I: *Maternal demographic characteristics of the study subjects (N=60)*

	Frequency	Percentage
Age(years)		
18-20	2	3.3
21-25	19	31.7
26-30	28	46.7
31-37	11	18.3
Mean ± SD	27.4 ± 4.2	
Parity		
Primi	21	35.0
Multi	39	65.0
Gestational age at Doppler examination		
32-34 weeks	43	71.7
35-36 weeks	17	28.3
Risk factors		
Anemia	9	15.0
GDM	4	6.7
Pre-eclampsia (PE)	17	28.3
PE + anemia	25	41.7
Nil	5	8.3
Gestational age at delivery		
Preterm	37	61.7
Term	23	38.3
Mode of delivery		
Elective caesarean section	3	5.0
Emergency caesarean section (for fetal distress)	32	53.3
Normal vaginal delivery (Induced/Assisted)	6	10.0
Normal vaginal delivery (Spontaneous)	19	31.7

Table I shows that the majority 28(46.7%) patients belonged to the age group 25-30 years with mean age was 27.4±4.2 years. Almost two third (65.0%) patients were multi para, 43(71.7%) patients were gestational age 32-34 weeks at Doppler examination, 25(41.7%) patients had PE + anemia, 37(61.7%) patients had preterm delivery and 32(53.3%) patients had an emergency caesarean section for fetal distress.

Table II shows that 29(48.3%) patients with MCA-PI level <1.5 among them 20(62.5%) had adverse perinatal outcomes. 48(80.0%) patients were UA-PI level <1.5 among them 20(62.5%) had adverse perinatal outcomes. 35(58.3%) patients had CPR < 1.0 among them 29(90.6%) had adverse perinatal outcomes. The differences were statistically significant ($p<0.05$) between the two groups.

Table III shows that 35 study subjects had CPR<1; among them, the majority, 27(77.1%), had emergency caesarean section for fetal distress, 12(34.3%) had low APGAR scores (<7 at 5 minutes), 17(48.6%) needed NICU admission, and 6(17.1%) were stillborn babies. Whereas in the 25 study subjects having CPR ≥1, only 5(20%) had emergency caesarean section for fetal distress, 1(4%) had low APGAR scores (<7 at 5 minutes), 2(8%) needed NICU admission, and no babies were stillborn.

Table II: Doppler indices of the study subjects (N=60) and its association with perinatal adverse outcome.

Frequency	Percentage	Outcome			P value
		Yes (n = 32) n (%)	No (n = 28) n (%)		
MCA-PI					
0.709-1.49	29	48.3	20 (62.5)	9 (32.1)	0.023[s]
1.50-2.24	31	51.7	12 (37.5)	19 (67.9)	
UA-PI					
0.56-1.49	48	80.0	20 (62.5)	28 (100.0)	0.001[s]
1.5-6.57	12	20.0	12 (37.5)	0 (0.0)	
Cerebroplacental ratio					
0.51-0.99	35	58.3	29 (90.6)	6 (21.4)	0.001[s]
1.00-2.73	25	41.7	3 (9.3)	22 (78.6)	

s=significant; P value reached from Chi square test

Table III: Distribution of study subjects by CPR and perinatal adverse outcomes (N=60)

Perinatal adverse outcomes	CPR <1 (n=35)	CPR ≤1 (n=25)
Still birth	6(17.1%)	0(0.0%)
Emergency caesarean section	27(77.1%)	5(20.0%)
Low APGAR score	12(34.3%)	1(4.0%)
NICU admission	17(48.6%)	2(8.0%)

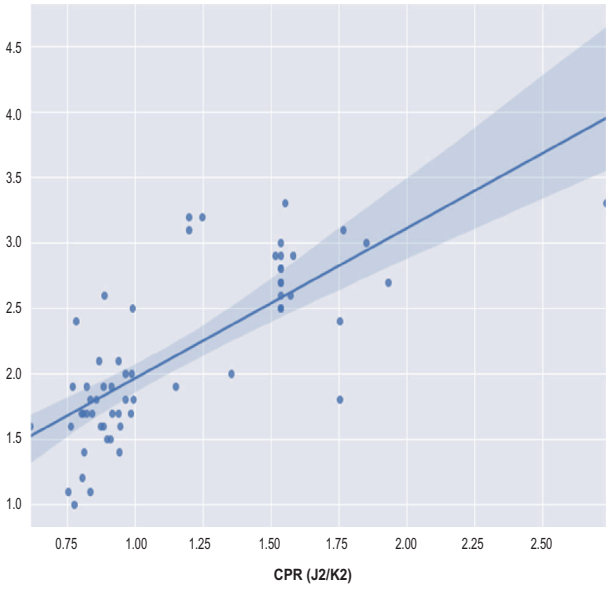

Figure 1: Scatter diagram showing positive significant correlation (r = 0.750; p = 0.001) between birth weight with CPR.

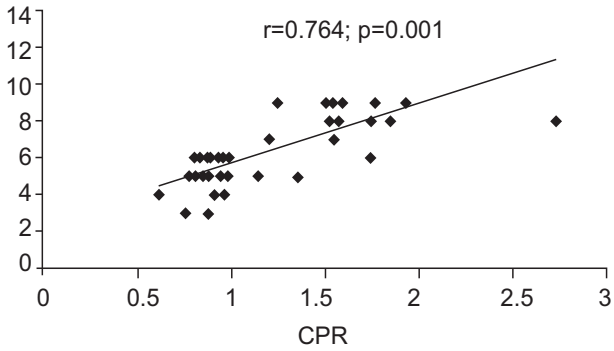

Figure 2: *Scatter diagram showing positive significant correlation*

(r = 0.764; p = 0.001) between low APGAR score (< 7 at 5minute) with CPR.

Table IV: Sensitivity, specificity, accuracy, positive and negative predictive values of the emergency CS, birth weight, APGAR score, NICU admission evaluation of suspected IUGR pregnancies

Validity test	Emergency Caesarean Section	Low birth weight	Low APGAR score	NICU admission
Sensitivity	84.4	89.2	90.6	89.5
Specificity	71.4	91.3	100.0	56.1
Accuracy	78.3	90.0	94.4	66.7
PPV	77.1	94.3	100.0	48.6
NPV	80.0	84.0	88.0	92.0

Table IV shows that for evaluating suspected IUGR pregnancies correlated by CPR, the sensitivity for emergency CS 84.4%, the sensitivity for low birth weight 89.2%, the sensitivity for low APGAR score 90.6%, the sensitivity for NICU admission 89.5%.

Discussion:

This prospective longitudinal observational study was carried out with an aim to correlate cerebroplacental ratio with adverse perinatal outcomes in intrauterine growth restriction. Fetal cerebroplacental ratio by color Doppler study was used to predict adverse perinatal outcomes in clinically suspected and/or biometrically diagnosed IUGR pregnancies.

This study showed that the majority, 28(46.7%) patients, belonged to the age group of 25-30 years with a mean age of 27.4±4.2 years. Khadija et al.[7] also revealed a similar observation where the mean age was found 26.13±4.63 years. In the current study, almost two third (65.0%) patients were multipara and 21(35.0%) were primi para. Sing et al.[8] reported 62% of patients were primi gravida and 38% were multigravida. Kuber et al.[9] observed primipara (n=29) constituted 58% and multipara (n= 21) constituted 42 %. In their study multiparous patients were marginally less than the primi group.

In this study, it was observed that at Doppler examination the majority 43(71.7%) patients were of gestational age 32-34 weeks. Kuber et al.[9] reported that the gestational age at the time of Doppler examination ranged between 31 to 39 weeks.

Regarding mode of delivery more than half (53.3%) patients had emergency caesarean section for fetal

distress followed by 19(31.7%) had spontaneous normal vaginal delivery (NVD-SP), 6(10.0%) had induced or assisted vaginal delivery (VD-I/A) and 3(5.0%) had elective caesarean section. Page et al.[10] reported 29 patients (9%) underwent operative delivery (instrumental delivery or cesarean section) for presumed fetal compromise. Deora and Gara[11] vaginal delivery was 96 cases and caesarean section 74 cases.

Regarding mode of delivery more than half (53.3%) patients had emergency caesarean section for fetal distress followed by 19(31.7%) had spontaneous normal vaginal delivery (NVD-SP), 6(10.0%) had induced or assisted vaginal delivery (VD-I/A) and 3(5.0%) had elective caesarean section. Page et al.[10]reported 29 patients (9%) underwent operative delivery (instrumental delivery or cesarean section) for presumed fetal compromise. Deora and Gara[11] vaginal delivery was 96 cases and caesarean section 74 cases.

This study showed that 29(48.3%) patients had MCA-PI <1.5 and 31(51.7%) had MCA-PI e"1.5. Bhattacharjee et al.[12] reported 38% of the study population had an MCA PI value <1.5, while 62 % had a value ≥1.5. Kuber et al.[9]observed low MCA PI in 72 %. In this study, 12(20.0%) patients had UA-PI ≥1.5 and 48(80.0%) had UA-PI <1.5. Bhatta charjee et al.[12] reported 24% of the study population had an abnormal UA PI >1.42(12 cases). The current study showed that 35(58.3%) had CPR <1.0 and 25(41.7%) patients had CPR e"1.0. Bhatta charjee et al.[12] reported the mean CPR of the present study population was 1.42±0.55. The range of CPR values of the patients with 0.34 to 2.75.

Present study observed that 35 study subjects had CPR<1, among them the majority 27(77.1%) had emergency caesarean section for fetal distress, 12(34.3%) had low APGAR scores (<7 at 5 minutes), 17(48.6%) needed NICU admission and 6(17.1%) were stillborn babies. Whereas in 25 study subjects having CPR ≥1 only 5(20%) had emergency caesarean section for fetal distress, 1(4%) had low APGAR scores (<7 at 5 minutes), 2(8%) needed NICU admission and no babies were stillborn. Sing et al.[8] reported that most of the cases with CPR<1.08 had a birth weight <2.5 kg (n=12) which comprised of 75% of the study population having abnormal CPR while 63.6% of the group with CPR>1.08 were found to have a birth weight >2.5 kg.

In this study it was observed that twenty-nine (29) patients were with MCA-PI <1.5, among them 20(62.5%) had adverse perinatal outcomes. Thirty one (31) patients had MCA-PI level ≥1.5, out of which 12(37.5%) had adverse perinatal outcomes. The difference was statistically significant (p<0.05) between two groups. Kuber et al.[9] reported 66% (33 cases) cases were associated with adverse perinatal outcomes. The fall in Doppler indices was the fetus's adaptive mechanism to hypoxemia mentioned in literature as "brain sparing effect". Bano et al.[6] reported the 90 pregnancies showed abnormal MCA PI and all four (100%) fetuses were SGA and all (100%) had adverse perinatal outcomes.

In this study observed that 48 patients were UA-PI <1.5, among them 20(62.5%) had adverse perinatal outcomes. Twelve (12) patients were UA-PI level ≥1.5, out of which 12(37.5%) had adverse perinatal outcomes. The difference was statistically significant (p<0.05) between two groups. Bhatta charjee et al.[12] only 55.6% of the study group had an abnormal UA PI>1.42(n=5) who had adverse perinatal outcome while 44.4% of women having normal UA PI also had poor outcome (n=4) which was not statistically significant.

In this study observed that 35 patients were CPR <1.0 among them 29(90.6%) had adverse perinatal outcomes. Twenty-five (25) patients had CPR ≥1.0, out of which 3(9.3%) had adverse perinatal outcomes. The difference was statistically significant (p<0.05) between two groups. Kuber et al.[9] reported considering Doppler parameters of umbilical artery and middle cerebral artery separately, 68.7% showed elevated umbilical artery PI and 56.2% cases showed low MCA PI values. Thus, highlighting that CPR is a better indicator of predicting adverse perinatal outcome than either umbilical artery PI or MCA PI alone.

In this study the validity of CPR for evaluating IUGR pregnancies was correlated by emergency CS calculating sensitivity 84.4%, specificity 71.4%, accuracy 78.3%, positive predictive value 77.1% and negative predictive value 80.0%. The validity of CPR for evaluating IUGR pregnancies was correlated by low birth weight calculating sensitivity 89.2%, specificity 91.3%, accuracy 90.0%, positive predictive value 94.3% and negative predictive value 84.0%. The validity of CPR for

evaluating IUGR pregnancies was correlated by low APGAR score calculating sensitivity 90.6%, specificity 100%, accuracy 94.4%, positive predictive value 100% and negative predictive value 88.0%. The validity of CPR for evaluating IUGR pregnancies was correlated by NICU admission calculating sensitivity 89.5%, specificity 56.1%, accuracy 66.7%, positive predictive value 48.6% and negative predictive value 92.0%. Munikumari et al.[13]reported cerebroplacental ratio (MCA/UA PI Ratio) was the most sensitive (sensitivity 95.8%). It was more sensitive than either UA PI (sensitivity 91%) or MCA PI (sensitivity 87.5%) alone in predicting any adverse outcome. Cerebroplacental Ratio and UA PI were equally specific (Specificity= 84.6%) and MCA PI had comparably low specificity (specificity=46%). Cerebroplacental Ratio had the highest Positive Predictive Value (PPV=85%) followed by UAPI (PPV=84%) and MCA PI (PPV=60%). Negative Predictive Value of Cerebroplacental Ratio was 95% when compared to 91% for UA PI and 80% for MCA. Diagnostic accuracy of Cerebroplacental ratio (Accuracy=90%) was better than UA PI (Accuracy=88%) and MCA PI (Accuracy=66%) in predicting adverse outcomes. Nimmagadda et al.[14] reported Low EFW shows 83% sensitivity and 85% specificity, 38% positive predictive value and 97% negative predictive value for estimation of IUGR. Cerebroplacental ratio (CPR) less than one is seen in 90% of IUGR cases with positive predictive value 66% in the present study. Deora and Gara[11] reported that UA/MCA PI index ratio was the best test when compared with MCA, UA, and RA PI indices (sensitivity 89%, specificity 94%). Sing et al.[8] study, sensitivity and specificity of cerebro-placental ratio was 93.2% and 89% respectively which was more than sensitivity and specificity of UA PI and MCA PI. The diagnostic accuracy in prediction of adverse perinatal outcomes in clinically suspected IUGR cases Cerebroplacental ratio has the diagnostic accuracy of 91.6%, and MCA PI was 72.6% and UA PI was 79.6%. Gupta et al.[5] the diagnostic accuracy of MCA-PI:UA-PI or CPR was 72% for SGA while 96% for adverse perinatal outcome. Bano et al.[6] reported 72.2% diagnostic accuracy of MCA-PI:UA-PI or CPR for SGA while 95.6% for adverse perinatal outcome. In their study the diagnostic accuracy of UA PI was 70% for SGA while 78% for adverse perinatal outcome which was correlating with the study of Gramillini et al.[15] being 65.5% and 83.3% respectively. The diagnostic accuracy of MCA PI was 54% for SGA while 78% for adverse perinatal outcome in their study which is also correlating with the study of Bano et al.[6] being 54.4% and 77.8% respectively.

Conclusion:

In conclusion, a non-invasive method for clinical practice called Doppler evaluation and measurement of cerebroplacental ratio (CPR) would be a better indicator of unfavorable perinatal outcomes. The cerebroplacental ratio should be taken into consideration as a measure of placental underperfusion and placental reserve in order to help identify fetuses who are more likely to experience hemodynamic disturbances prior to delivery.

Limitations:

Single-center and the relatively short study duration might limit validity. Future multi-center studies with longer follow-up periods will provide more comprehensive insights.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

The authors stated that there was no conflict of interest in this study.

Funding:

This research received no external funding.

Ethical consideration:

The study was approved by the Ethical Review Committee of Dhaka Medical College, Dhaka, Bangladesh. Informed consent was obtained from each participant or caregivers of the patients.

Author Contributions:

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; had agreed on the journal to which the article had been submitted; and

agreed to be account able for all aspects of the work.

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