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Comparison of the Diagnostic Accuracy of Doppler Cerebroplacental Ratio Versus Standard Fetal Biometry for Fetal Growth Restriction

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ABSTRACT

Objective: To assess the diagnostic accuracy of the Doppler Cerebroplacental ratio for fetal growth restriction keeping fetal biometry as the reference standard.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Radiology, Combined Military Hospital, Multan Pakistan, from May to Oct 2020.

Methodology: Two hundred and fifty-six-singleton pregnancies ≥ 30 weeks were included and underwent fetal biometry, including estimated fetal weight (EFW) by trans-abdominal ultrasound. The umbilical artery and middle cerebral artery resistive indices were evaluated using Doppler ultrasound, and Cerebroplacental ratio (CPR) was calculated. The presence or absence of fetal growth restriction (FGR) was noted using cut-off EFW of 10th centile and CPR of 1.0.

Results: Cerebroplacental ratio showed FGR in 145(56.64%) patients. Fetal biometry showed FGR in 141 (55.08%) patients, whereas 115(44.92%) patients revealed none. Of 145 CPR-positive patients, 127(87%) were true positive, while 18(12%) were false positive. Among 111 CPR-negative patients, 14(0.12%) were false negative, while 97(87%) were true negative. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of the Cerebroplacental ratio were 90.07%, 84.35%, 87.59%, 87.39% and 87.50%, respectively.

Conclusions: Doppler Cerebroplacental ratio is sensitive for diagnosing fetal growth restriction; however, its role as a stand-alone test needs further evaluation and may be enhanced with other tools such as estimated fetal weight.

Keywords: Cerebroplacental ratio, Doppler ultrasound, Fetal growth restriction, Sensitivity.

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INTRODUCTION

The evaluation of fetal growth is essential during antenatal care because fetal growth restriction (FGR) has a high risk of morbidity and mortality. Fetal growth restriction occurs in 5-10% of pregnancies but is the second commonest cause of perinatal mortality and is responsible for up to 30% of stillbirths.[1,2] Early onset FGR is associated with significant hypoxia but increased tolerance to hypoxia, whereas late onset is associated with a lower degree of hypoxia but less tolerance to hypoxia.[3] The diagnosis of FGR is difficult. It is also a challenge to differentiate Small for Gestational Age (SGA) babies who are constitutionally small babies with less risk of deterioration compared to FGR.[4,5] Bedside clinical techniques such as Symphysis Fundal Height (SFH) measurement were found not to have sufficient evidence to effectively diagnose FGR (intrauterine growth restriction, a term since replaced by FGR) in a Cochrane review in 2018.[6] A panel of 45 experts in 2016 derived a consensus on diagnostic criteria for FGR using the Delphi method in which solitary and contributory parameters were defined for both early and late-onset FGR. These criteria include both elements of fetal biometry as well as Doppler ultrasound parameters. 7 Of these Doppler parameters, the most promising is the cerebroplacental ratio (CPR) which is a ratio of umbilical artery (UA) and middle cerebral artery (MCA) Doppler parameters. In Pakistan, Doppler parameters have been investigated in this population, such as the MCA pulsatility index.[8] In this population, the incidence of FGR is 25%, according to a 1999 study.[7,9] Studies in this region on the cerebroplacental ratio have focused on its ability to predict the adverse perinatal outcome. This study was focused on assessing the diagnostic accuracy of the cerebroplacental ratio for fetal growth restriction by comparing it to the reference standard of fetal biometry in the local population of Pakistan.

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METHODOLOGY

The cross-sectional study was conducted at the Department of Radiology, Combined Military Hospital Multan, from February to August 2020, after approval of the Institutional Review Board (IERB Approval Letter No-13 /TRG/2022). A sample size of 256 was calculated using PASS,[11] where the incidence of FGR in

Pakistan equals 25 %,the anticipated sensitivity of CPR was 64%, and the anticipated specificity of the cerebro-placental ratio was 72%.[10] The subjects were enrolled through a non-probability, consecutive technique.

Inclusion Criteria: Antenatal cases with singleton pregnancy on ultrasound having gestational age > 30 weeks, according to LMP were included in the study.

Exclusion Criteria: Women unsure of LMP, suspected of syndromic babies on anomaly scan, and multi-fetal pregnancy were excluded**.**

Antenatal cases with singleton pregnancy in the gestational weeks of 30-41 weeks fulfilling the inclusion criteria were enrolled after written informed consent. Baseline data including age, parity, history of gestational diabetes, pregnancy-induced hypertension, and history of previous FGR pregnancies. All the patients underwent biometric profile and estimated fetal weight (EFW) assessment by trans-abdominal ultrasound using a 5 MHz convex probe by ultrasound machine Xario 100 (Canon medical systems corp.) by consultant radiologist and growth was labelled FGR if EFW was less than the 10th centile for gestational age. The Umbilical Artery Resistive index (UA-RI) and the Middle Cerebral Artery (MCA-RI) were evaluated using Doppler ultrasound, and CPR (MCA-RI/UA-RI) was calculated. Doppler waveforms were obtained from the free loop of the umbilical cord and proximal MCA immediately after its origin from the circle of Willis. The fetus was considered growth restricted if CPR was <1.[11] All the findings were recorded in the data collection proforma. In addition, the sensitivity, specificity, PPV and NPV of CPR were calculated.

Data were analysed using Statistical Package for the social sciences (SPSS) version 23.00. Quantitative variables were expressed as mean±SD and qualitative variables were expressed as frequency and percentages. The fetal biometric profile was taken as the gold standard for diagnosing FGR. The indices were compared with the gold standard using a 2x2 table to determine the sensitivity, specificity, PPV and NPV of CPR with a 95% confidence level.

RESULTS

Cerebroplacental ratio (CPR) showed FGR in 145(56.64%) patients, whereas fetal biometry revealed FGR in 141(55.08%) cases. Mean UA RI was 1.13± 0.89) and Mean MCA RI was 1.09± 0.74. The frequency table of subjects above and below the cut-off values of CPR and fetal biometry is shown in Table-I. In CPR-positive patients, 127(87%) were true positive, while 18(12%) were false positive. Among 111 CPR-negative patients, 14(0.12%) were false negative, while 97(87%) were true negative, as shown in Table-II. The age range in this study was from 18-40 years, with a mean age of 30.24 ± 4.67 years. The majority of the patients, 146 (57.03%), were between 18 to 30 years of age. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of CPR using Color Doppler in diagnosing FGR using fetal biometry as reference standard was 90.07%, 84.35%, 87.59%, 87.39% and 87.50%, respectively, as shown in Table-III.

Table-I: Frequency Distribution for Subjects Below and Above Cut off Values for CPR and Fetal Biometry (n=256)

CPR	Above 1.0	Below 1.0
(n=256)	111(43.35%)	145(56.64%)
Fetal biometry	EFW above 10th centile	EFW below 10th centile
(n=256)	115(44.92%)	141(55.08%)

Table-II: Comparison of Cerebroplacental Ratio using Colour Doppler in diagnosing FGR using Fetal Biometry as Reference Standard (n=256)

	FGR on fetal biometry	No FGR on fetal biometry
FGR on cerebroplacental ratio	127(TP)*	18(FP)***
No FGR on cerebroplacental ratio	14(FN)**	97(TN)****

-TP=True positive **-FP=False positive *-FN=False negative ****-TN=True negative*

Table-III: Validity of CPR for Fetal Growth Restriction (n=256)

Diagnostic test validity parameter	Value (%)
Sensitivity	90.07%
Specificity	84.35%
Positive Predictive Value (PPV)	87.59%
Negative Predictive Value (NPV)	87.39%
Diagnostic Accuracy	87.50%

DISCUSSION

The risk of adverse outcomes in a baby with fetal growth restriction is significant, especially in early FGR, which is 7.1% compared to 0% in late FGR. This is not a small risk, emphasising the need for precise diagnosis. This will help to preempt other morbidities such as preeclampsia which carries the risk of 35% in early FGR vs. 21.1% in late FGR.[11] Given this risk, and it is necessary to have a diagnostic tool that has a high sensitivity to rule in the diagnosis and therefore take precautions. The CPR may have some superiority to the umbilical artery Doppler as outlined in the PORTO study in which some fetuses with normal UA Doppler and abnormal CPR presented with adverse perinatal

outcomes.[12] However, as the authors point out in response to a comment, 88% of the patients with abnormal CPR also had abnormal UA Doppler (n =128/146).[13] On the whole, according to a meta-analysis, CPR was better than UA Doppler in the prediction of composite adverse fetal outcome and predicting emergency delivery for fetal distress.[14] The CPR has also been correlated with impaired fetal growth even in appropriate for gestational age infants measured by fetal biometry.[15] This, therefore, underlines the difference in sensitivity between the two markers, with fetal biometry (the current reference standard) being the lesser. The sensitivity calculated in our study was 90.07% which is high, but whether it is high enough is questionable as it implies missing 10% of true positive cases. The CPR-PI in the meta-analysis and systematic review had a sensitivity of 93% and specificity of 74% for perinatal death while having a specificity of 91% for the composite adverse perinatal outcome. The CPR-RI had a sensitivity of 84% for perinatal death and a specificity of 93% for the composite adverse perinatal outcome.[14,15] This shows the comparability of the findings of our study (focused on our local population) with other international studies. CPR is a better predictor of abnormal fetal growth, especially in small for gestational age fetuses.[16] but also able to detect reduced fetal growth velocity in AGA infants, as noted above. The challenge in a bedside clinical setting is to optimise the outcome for an individual patient using a combination of tools available such as fetal biometry to assess estimated fetal weight (EFW) and UA Doppler and CPR.[17] The GRIT trial, however, shed light on the effect of the delivery timing (i.e. early vs. as late as possible) on the outcome of death or neurodevelopmental disability at two years of age. There were no significant differences between early and deferred delivery.[18]

The discussion on FGR is only complete with a mention of the need to ensure data accuracy in resource-limited regions where the absence of an organised standardisation precludes reliable decision-making and data collection. Although the prevalence of FGR has been estimated as 25% in Pakistan, it is difficult to come to a true estimate as the rates of antenatal visits are low (only 78% had at least one antenatal visit in 2012).[19] variation in the use of centile cut off (i.e. 3rd centile vs 10th centile) and the apparent lack of population-specific standardised growth charts. The lack of population-specific growth charts may result in inaccurate diagnosis and thus affect every research effort on the subject. It is thus imperative to develop these growth charts based on the local population and come to a consensus definition of FGR.

This study contributes a set of diagnostic accuracy markers derived from the local population with sensitivity and specificity of CPR for the diagnosis of FGR comparable to other studies in the literature.

LIMITATIONS OF STUDY

The limitations of the study were the use of the resistive index instead of the pulsatility index and the lack of focus on early vs. late FGR and the non-assessment of timings for surveillance.

RECOMMENDATIONS

It is recommended that future studies focus on establishing the most useful time points for the surveillance of fetal growth restriction to improve further diagnosis of fetal growth restriction and decision-making at the bedside. In addition, the development of population-specific centile charts for fetal growth restriction is necessary for accurate comparison and decision-making.

CONCLUSION

The cerebroplacental ratio is sensitive for diagnosing fetal growth restriction; however, its role as a stand-alone test needs further evaluation and may be enhanced when used with other tools, such as estimated fetal weight.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SA:, PH: Conception, interpretation of data, drafting the manu-script, approval of the final version to be published.

MA:, YK: Study design, data analysis, drafting the manuscript, cri-tical review, approval of the final version to be published.

SAHA: Critical review, approval of the final version to be published.

MT: Data acquisition, interpretation of data, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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