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ORIGINAL RESEARCH

Utility Of Cerebroplacental Ratio As A Useful Indicator In The Diagnosis Of Intrauterine Growth Restriction And Prediction Of Adverse Perinatal Outcome

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ABSTRACT

Aims and objectives: To evaluate the usefulness of Pulsatility Indices (PI) of the Umbilical Artery (UA), Fetal Middle Cerebral Artery (MCA) and ratio of the Middle Cerebral Artery PI to the Umbilical Artery PI (Cerebroplacental Ratio) in the diagnosis of Intrauterine Growth Restriction fetuses and in the prediction of adverse perinatal outcome. **Material and methods:** Study was performed on 100 women with singleton non-anomalous pregnancy of 31-40 weeks gestation that were clinically suspected IUGR. Fetal biometry, amniotic fluid assessment, estimated fetal weight (EFW) and Doppler indices including UA PI, MCA PI, and cerebroplacental ratio were assessed. Perinatal outcomes assessed were LSCS for fetal distress, APGAR < 7 at 5 minutes, NICU admissions and perinatal death. **Results:** Cerebroplacental ratio had a higher sensitivity (84.1%), specificity (82.1%), positive predictive value (78.7%), negative predictive value (86.7%) for the diagnosis of IUGR, than that of pulsatility indices of Middle Cerebral Artery or Umbilical Artery separately. AUROC characteristics for the diagnosis of IUGR with use of the CPR (p less than 0.0001) were statistically significant than UA PI (p less than 0.0001) and MCA PI (p 0.002). The AUROC curve for CPR, UA PI and MCA PI were 0.835, 0.811 and 0.679 respectively. For the prediction of adverse perinatal outcome, Cerebroplacental ratio had a higher sensitivity (93.3%), specificity (90.9%), positive predictive value (89.3%), negative predictive value (94.3%) than that of pulsatility indices of Middle Cerebral Artery or Umbilical Artery separately. **Conclusions:** Cerebroplacental Ratio (CPR) is a superior diagnostic tool for identifying Intrauterine Growth Restriction (IUGR) and predicting adverse perinatal outcome when compared to the Umbilical Artery Pulsatility Index (UA PI) and Middle Cerebral Artery Pulsatility Index (MCA PI)

Keywords: IUGR, Perinatal Outcome, Cerebroplacental Ratio, Umbilical Artery PI, Middle Cerebral Artery PI, Doppler

Abbreviations:

- IUGR = Intrauterine Growth Restriction
- PI = Pulsatility Index
- UA = Umbilical Artery
- MCA = Middle Cerebral Artery
- CPR = Cerebroplacental Ratio
- AUROC = Area Under Receiver Operating Characteristic
- PPV = Positive Predictive Value
- NPV = Negative Predictive Value

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INTRODUCTION

In obstetrics and perinatal medicine, assessing fetal growth and well-being is crucial for optimal outcomes for both mother and baby. Good utero-placental circulation is necessary for a successful pregnancy. Fetal surveillance is essential for detecting growth abnormalities. When the growth of the fetus is less than 10th percentile for gestational age during pregnancy, it is known as intrauterine growth retardation.[1,2] IUGR poses challenges in prenatal care and is linked to increased perinatal risks and thus timely diagnosis and intervention are crucial.

Doppler ultrasound (USG) is crucial in monitoring hemodynamic changes in placental insufficiency for high-risk pregnancies, aiding in predicting perinatal outcomes. It helps time delivery for growth-restricted fetuses and identifies those at risk using umbilical artery (UA) and middle cerebral artery (MCA) Doppler sonography. The Cerebroplacental ratio (CPR) is a novel parameter that indicates fetal well-being by assessing brain-sparing effects due to placental insufficiency. Understanding CPR's role in diagnosing intrauterine growth restriction (IUGR) and predicting adverse outcomes is essential for obstetricians to plan proper surveillance and interventions.

In IUGR, Doppler abnormalities have been observed in Umbilical Artery and Fetal Middle Cerebral Artery. 3 types of abnormalities in Umbilical Artery waveformare seen (indication of increasing resistance which correlates with fetal hypoxia): Low diastolic flow (high resistance), Absent diastolic flow and Reversed flow in diastole. A substantial increase in the vascular resistance of the fetoplacental unit leads to a decrease in end-diastolic flow velocity or its absence in the flow velocity waveform (FVW).[3]In situations of hypoxia, vascular tone is reduced in the fetal middle cerebral artery, resulting in increased diastolic velocity and reduced PI & RI values. This is known as "cerebral blood flow redistribution" to the fetal brain.[4] Early studies[5] have shown that the PI of the MCA was significantly lower and that the mean systolic velocity was higher in small for gestational age (SGA) fetuses than the respective reference ranges for normal fetuses throughout gestation. With increasing hypoxia, the fetus can become acidemic which results in cerebral edema. This causes increased cerebral resistance and diastolic flow in the MCA may be reduced or even absent which indicates poor prognosis. Demonstration of cephalization of blood flow enhances the positive predictive value of an elevated umbilical artery Doppler index for hypoxemia.

MATERIAL AND METHODS

A prospective study was done which included a total number of 100 pregnancies of 31-40 weeks' gestation period that had been clinically suspected as IUGR and referred for USG Color Doppler. After obtaining approval from the institutional ethical committee and meeting the inclusion and exclusion criteria's, Doppler USG evaluation was performed.

Imaging was done with SAMSUNG RS80A, Philips CLEAR VIEW 350 and Mindray DC-8 machines using convex probes of frequency ranging from 3 to 5 Mhz. Fetal biometry was done first, and then Doppler Waveforms of Umbilical Artery and Middle Cerebral Artery were recorded during periods of apnea and fetal inactivity. Cerebroplacental ratio was calculated by dividing the Doppler pulsatility index of Middle Cerebral Artery (MCA) by the Umbilical Artery (UA) Pulsatility Index. A single cutoff value of 1.08 was used for all cases of 31–40 weeks of gestation. Above this value, Doppler velocimetry was deemed normal and, below it, abnormal.

Doppler US results were analysed for predicting the perinatal outcome and diagnosis of IUGR. A pregnancy was considered to have an "Adverse outcome" if any of the following complications were present:Emergency CS for fetal distress, APGAR score less than 7 at 5-minutes, Admission to NICU for complications of low birth weight, or Perinatal death.Pregnancy outcome was deemed favorable or uneventful when the aforementioned complications were absent.

RESULTS

Of the 100 pregnancies studied, the mean maternal age of presentation was 27 years. The age range observed was between 18 years to 38 years. Majority of the patients were in the age group of 23-27 years (36%). Only three were more than 36 years of age.

In our study, 73 out of 100 pregnancies had Oligohydramnios, of which 37 were sonographically confirmed to be IUGR (Sensitivity = 84.1%) (*p 0.02*) and 38 had adverse perinatal outcome (Sensitivity = 84.4%) (*p* 0.02).

Out of 100 pregnancies, 41% of patients had pregnancy induced hypertension (PIH) as the risk factor. 5% pregnancies had gestational diabetes, 5% were Rh Negative pregnancies, 4% had severe anemia, 3% had heart disease complicating pregnancies. 42% cases had either no complication or one of the other complications like breech, postdates, bronchial asthma, hypothyroidism or chronic hepatitis.

44 out of 100 fetuses had an Effective Fetal Weight less than 10% thus sonographically confirming IUGR. Of these, 37 were associated with an abnormal cerebroplacental ratio (84.1%, *p 0.02*). Average birth weight at the time of delivery was 2.15kg. 64.5% (n=60) babies had a birth weight of less than 2.5kg, out of which 43 fetuses had an abnormal cerebroplacental ratio (71.7%, *p 0.01*).

45% fetuses had at least one adverse perinatal outcome, of those some (n=26) had more than one abnormal outcome. There were 4 intrauterine deaths and 96 live births. Of the 96 live births 4 neonates died in first week, 25 Neonates were admitted to NICU. 29 neonates had 5 min APGAR score of less

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than 7, and 34 babies were born by emergency caesarean section. Remaining 55 fetuses had normal perinatal outcome.

In our study, it was observed that 13 fetuses had Absent/Reversed End Diastolic Flow in Umbilical Artery, of which there were 8 IUD/perinatal deaths. Mortality rate was higher in those fetuses with reversal of EDF (100%) ($p< 0.05$) compared to Absent EDF (44.4%) ($p< 0.05$). Overall mortality rate in fetuses with Absent/Reversal of EDF was 61.5%.

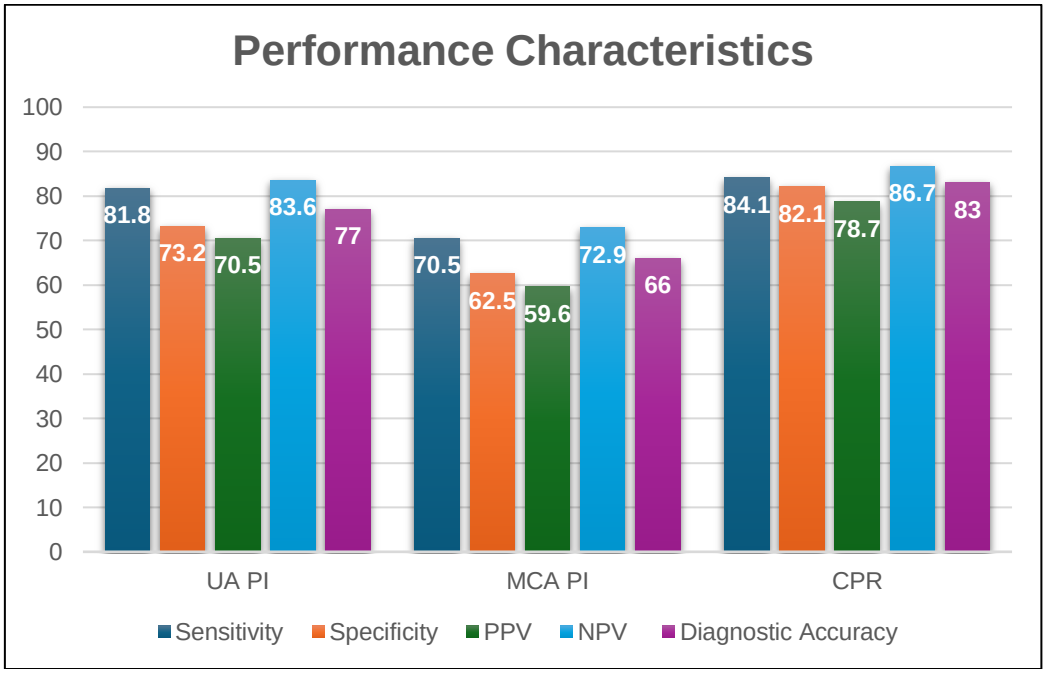
Performance Characteristics Of Doppler Indices In Diagnosing IUGR

Cerebroplacental ratio (MCA/UA PI Ratio) was most sensitive (84.1%). It was more sensitive than either UA PI (81.8%) or MCA PI (70.5%) alone in diagnosing IUGR. Cerebroplacental Ratio was most specific (82.1%) than UA PI (73.2%) or MCA PI (62.5%) alone. Cerebroplacental Ratio had highest Positive Predictive Value (PPV 78.7%) followed by UA PI (PPV 70.5%) and MCA PI (PPV 59.6%) in diagnosing IUGR. Negative Predictive Value of Cerebroplacental Ratio was 86.7% when compared to 83.6% for UA PI and 72.9% for MCA in diagnosis of IUGR. Diagnostic accuracy of Cerebroplacental ratio (Accuracy=83%) was better than UA PI (Accuracy=77%) and MCA PI (Accuracy=66%) in the diagnosis of IUGR. The areas under the ROC characteristics for the diagnosis of IUGR with use of the CPR ($p<0.0001$) were statistically significant than UA PI ($p< 0.0001$) and MCA PI (p 0.002). The ROC AUC for CPR, UA PI and MCA PI were 0.835, 0.811 and 0.679 respectively.

Performance Characteristics Of Doppler Indices In Predicting Adverse Perinatal Outcome

CPR was most sensitive (93.3%) parameter. It was more sensitive than either UA PI (91.1%) or MCA PI (77.8%) alone in predicting any adverse perinatal outcome. CPR was most specific (90.9%) than UA PI (81.8%) or MCA PI (69.1%) alone.CPR had highest Positive Predictive Value (PPV 89.3%) followed by UAPI (PPV 80.4%) and MCA PI (PPV 67.3%). Negative Predictive Value of Cerebroplacental Ratio was 94.3% when compared to 91.8% for UA PI and 79.1% for MCA. Diagnostic accuracy of Cerebroplacental ratio (92%) was better than UA PI (86%) and MCA PI (73%) in predicting adverse outcomes.The areas under the ROC characteristics for the prediction of adverse perinatal outcome with use of the CPR ($p<0.001$) were statistically significant than UA PI (p 0.0025) and MCA PI ($p< 0.0001$). The ROC AUC for CPR, UA PI and MCA PI were 0.967, 0.936 and 0.762 respectively.

In our study, the association of LSCS for fetal distress with abnormal CPR was found to be statistically significant ($p< 0.0001$) with sensitivity of 97%, specificity of 78.9%, PPV 70.2%, NPV of 98.1% and Diagnostic Accuracy of 85%. A statistically significant correlation was found between abnormal CPR and APGAR < 7 at 5 minutes, with sensitivity, specificity, PPV, NPV and diagnostic accuracy at 93.1%, 71.8%, 57.4%, 96.2% and 78% respectively. Our study also observed a statistically significant correlation between abnormal CPR and NICU admissions ($p< 0.0001$) with a sensitivity of 96%, specificity of 69.3%, PPV of 51%, NPV of 98.1% and diagnostic accuracy of 76%.



GRAPH 1: A Bar Graph Showing The Performance Characteristics Of Doppler Indices In Diagnosis Of IUGR

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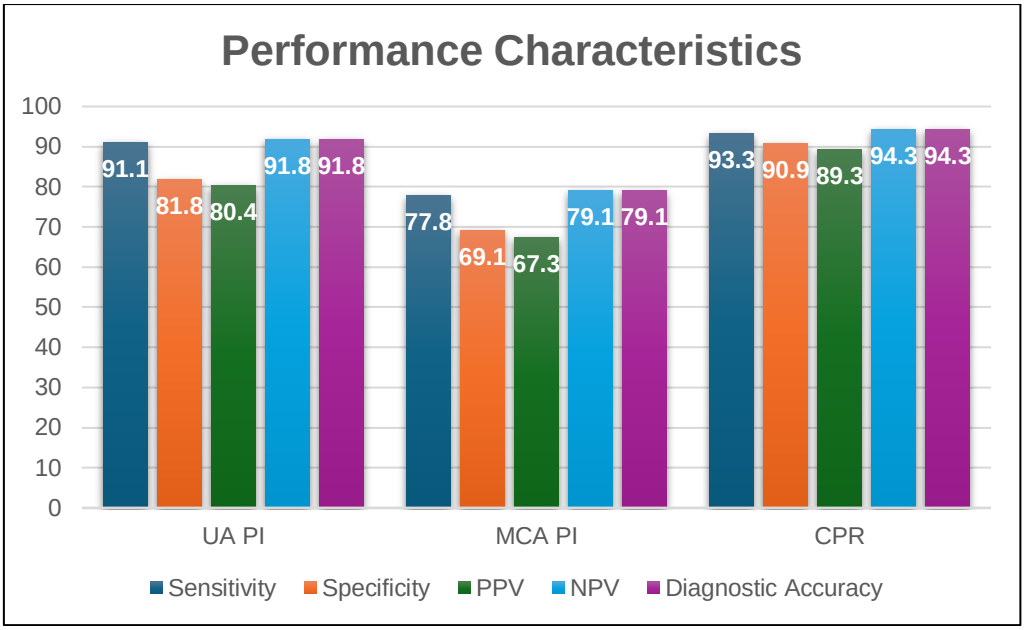

GRAPH 2: A Bar Graph Showing The Performance Characteristics Of Doppler Indices In Predicting Adverse Perinatal Outcome

DISCUSSION

Of the 100 pregnancies with clinical suspicion of IUGR studied, the mean maternal age of presentation was 27 years. The age range observed was between 18 years to 38 years. Majority of the patients were in the age group of 23-27 years (36%). Similar findings were observed in studies by Maged AM et al[6] and Simon RG et al[7].

In our study, 73 out of 100 pregnancies had Oligohydramnios, of which 37 were sonographically confirmed to be IUGR (Sensitivity = 84.1%) (*p 0.02*) and 38 had adverse perinatal outcome (Sensitivity = 84.4%) (*p* 0.02). Similar findings were observed in the studies conducted by Philipson EH et al[8] and Maged AM et al[6] where a strong association between oligohydramnios and an increased risk of IUGR was established.

44 out of 100 fetuses had an Effective Fetal Weight less than 10% thus sonographically confirming IUGR. Of these, 37 were associated with an abnormal cerebroplacental ratio (84.1%, *p 0.02*). Average birth weight at the time of delivery was 2.15kg. 64.5% (n=60) babies had a birth weight of less than 2.5kg, out of which 43 fetuses had an abnormal cerebroplacental ratio (71.7%, *p 0.01*). Thus, significant association was established between abnormal cerebroplacental ratio and Effective Fetal Weight < 10% and Birth weight <2.5kg. Our findings were in congruence with various studies performed by Lesiak MJ et al[9], Simon RG et al[7], Rosello MJ et al[10] and Gonzalez BM et al[11] whereby statistically significant association was established between abnormal cerebroplacental ratio and EFW and Low Birth Weight.

In our study, among the cases that had identified risk factors, the majority had pregnancy-induced hypertension as the risk factor (41%). This observation conformed to the studies of Albu AR et al[12] and Thekkedathu VC et al[13], which reported hypertension as the maternal risk factor of particular importance in IUGR.

In our study, it was observed that 13 fetuses had Absent/Reversed End Diastolic Flow in Umbilical Artery, of which there were 8 IUD/perinatal deaths. Mortality rate was higher in those fetuses with reversal of EDF (100%) ($p< 0.05$) compared to Absent EDF (44.4%) ($p< 0.05$). Overall mortality rate in fetuses with Absent/Reversal of EDF was 61.5%. Comparable results were found in studies by Montenegro et al[14] (mortality rate 44%), Battaglia C et al[15] (mortality rate 58%) and Ertan AK et al[16] (mortality rate 53.3%). As found in corresponding research by Hüneke B et al[17], mortality rate observed in a cohort of Absent/Reversed EDF in Umbilical Artery was 34%, which was different from the results in our study.

Cerebroplacental ratio had a higher Sensitivity (84.1%), Specificity (82.1%), PPV (78.7%), NPV (86.7%) and Diagnostic Accuracy (83%) than UA PI and MCA PI diagnosing IUGR. The areas under the ROC characteristics for the diagnosis of IUGR with use of the CPR ($p<0.0001$) were statistically significant than UA PI ($p<0.0001$) and MCA PI (p 0.002). The ROC AUC for CPR, UA PI and MCA PI were 0.835, 0.811 and 0.679 respectively. Similar results were elicited in studies performed by Vishwekar PS et al[18], Singh B et al[19], Bano S et al[20], Moawad EM et al[21] and Gramellini D et al[5].

Cerebroplacental ratio had a higher Sensitivity (93.3%), Specificity (90.9%), PPV (89.3%), NPV (94.3%) and Diagnostic Accuracy (92%) than UA PI and MCA PI for the prediction of adverse perinatal outcome. The areas under the ROC characteristics for the prediction of adverse perinatal outcome with use

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of the CPR (p<0.001) were statistically significant than UA PI (p 0.0025) and MCA PI (p<0.0001). The ROC AUC for CPR, UA PI and MCA PI were 0.967, 0.936 and 0.762 respectively. Our findings were in line with studies performed by Gramellini D et al[5], Arduini D et al[22], Singh RO et al[23], Vishwekar PS et al[18], Lesiak MR et al[9] and Moawad EM et al[21].

In our study, the association of LSCS for fetal distress with abnormal CPR was 76.7% (p< 0.0001). Similar results were observed in a study by Shahinaj R et al[24] which showed that the correlation between LSCS for fetal distress and abnormal CPR was 71.9%. In a study by Malik N et al[25], association for LSCS for fetal distress with abnormal CPR was 87.5% (p< 0.0001), which was comparable to our study.

A statistically significant correlation was also found between abnormal CPR and APGAR < 7 at 5 minutes, with sensitivity, specificity, PPV, NPV and diagnostic accuracy at 93.1%, 71.8%, 57.4%, 96.2% and 78% respectively. Comparable results were observed in a study by Alanwar A et al[26], in which abnormal CPR had good prognostic accurancy of APGAR < 7 at 5 minutes with sensitivity, specificity, PPV, NPV and diagnostic accuracy at 50%, 88.1%, 44.4%, 90.2% and 82% respectively.

Our study also observed a statistically significant correlation between abnormal CPR and NICU admissions (p< 0.0001) with a sensitivity of 96%, specificity of 69.3%, PPV of 51%, NPV of 98.1% and diagnostic accuracy of 76%. Similar results were also reported in a study by Alanwar A et al[26], who reported a statistically significant correlation between abnormal CPR and NICU admissions with 62.5% sensitivity, 71.4% specificity, 90.9% NPV and diagnostic accuracy of 70%. In a study by Nayak P et al[27], it was observed that abnormal CPR had a high sensitivity (93.3%), specificity (74.4%), PPV (53.8%) and NPV (97.2%) for prediction of NICU admissions, which are comparable to our study.

SUMMARY

The present study was undertaken to evaluate the usefulness of UA PI, MCA PI and Cerebroplacental Ratio in the diagnosis of IUGR fetuses and in the prediction of adverse perinatal outcome. 100 pregnancies with clinical suspicion of IUGR underwent Doppler evaluation, and on the basis of various observations, the conclusions drawn were:

- The mean maternal age of presentation was 27 years.
- Statistically significant association was established between abnormal CPR and EFW less than 10th percentile (p *0.02*) and birth weight less than 2.5kg (p *0.01*)
- 73 out of 100 pregnancies had Oligohydramnios. Strong association between oligohydramnios during pregnancy and an increased risk of IUGR (Sensitivity = 84.1%) *(p 0.02)* and adverse perinatal outcome (Sensitivity = 84.4%) *(p 0.02)* was established.
- In our study, most common maternal risk factor was pregnancy-induced hypertension (41%).
- Mortality rate was higher in those fetuses with reversal of EDF (100%) ($p < 0.05$) compared to Absent EDF (44.4%) ($p < 0.05$). Overall mortality rate in fetuses with Absent/Reversal of EDF was 61.5% indicating grave prognosis.
- Cerebroplacental ratio had a higher Sensitivity (84.1%), Specificity (82.1%), PPV (78.7%), NPV (86.7%) and diagnostic accuracy (83%) for the diagnosis of IUGR, than that of pulsatility indices of MCA or UA separately. The AUROC characteristics for the diagnosis of IUGR with use of the CPR (p<0.0001) were statistically significant than UA PI (p<0.0001) and MCA PI (p 0.002). The AUROC curve for CPR, UA PI and MCA PI were 0.835, 0.811 and 0.679 respectively. Our findings correlated with the results of various studies that have shown Cerebroplacental ratio to be more useful than UA PI or MCA PI in diagnosis of IUGR.
- For the prediction of adverse perinatal outcome, Cerebroplacental ratio had a higher Sensitivity (93.3%), Specificity (90.9%), PPV (89.3%), NPV (94.3%) and Diagnostic Accuracy (92%) than that of pulsatility indices of MCA or UA separately.The AUROC characteristics for the prediction of adverse perinatal outcome with use of the CPR (p<0.001) were statistically significant than UA PI (p 0.0025) and MCA PI (p< 0.0001). The AUROC curve for CPR, UA PI and MCA PI were 0.967, 0.936 and 0.762 respectively. Results were consistent with various studies indicating that the Cerebroplacental ratio is more effective in predicting adverse perinatal outcome compared to both UA PI and MCA PI.
- There was a significant association between abnormal Cerebroplacental Ratio and LSCS for fetal distress at 70.2% (p< 0.0001).
- Statistically significant correlation between abnormal CPR and APGAR < 7 at 5 minutes (p< 0.0001) was observed with sensitivity of 93.1%, specificity of 71.8%, Positive Predictive Value of 57.4%, Negative Predictive Value of 96.2%, and diagnostic accuracy of 78%.
- Significant correlation between abnormal CPR and NICU admissions was observed (p< 0.0001) with sensitivity of 96%, specificity of 69.3%, PPV of 51%, NPV of 98.1%, and diagnostic accuracy of 76%.

CONCLUSION

Present study provided compelling evidence that the Cerebroplacental Ratio (CPR) is a superior diagnostic tool for identifying Intrauterine Growth Restriction (IUGR) when compared to the Umbilical Artery Pulsatility Index and Middle Cerebral Artery Pulsatility Index. CPR demonstrated higher sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and

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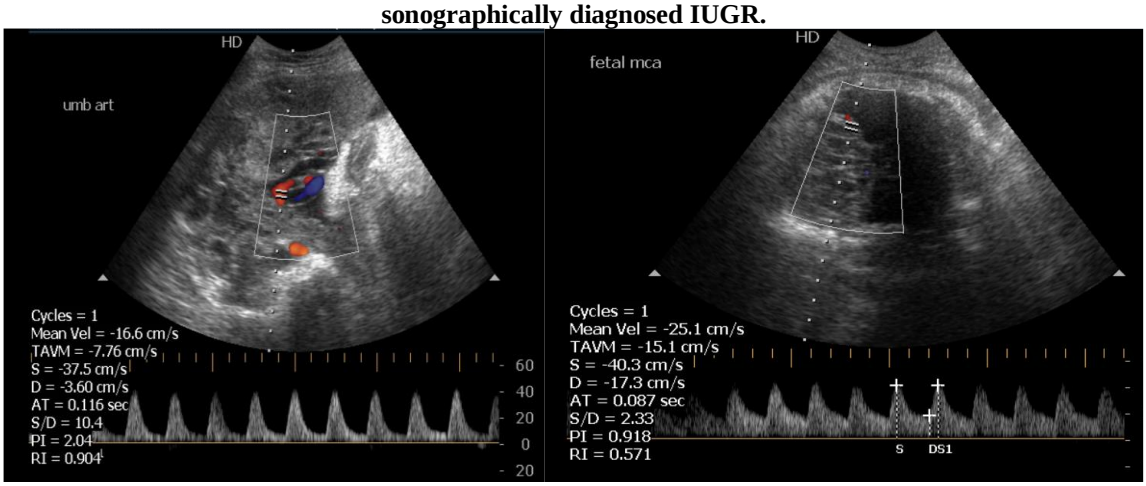
diagnostic accuracy. The statistical significance of the CPR, as reflected in the area under the ROC curve (AUC), further confirms its reliability.

Additionally, our findings highlighted the significant correlations between abnormal CPR and adverse perinatal outcomes, such as the necessity for LSCS due to fetal distress, lower APGAR scores at 5 minutes, increased NICU admissions, and higher mortality rates associated with absent or reversed end-diastolic flow in the umbilical artery. These observations were consistent with those reported in other studies, reinforcing the utility of CPR in prenatal care and its potential to improve perinatal outcomes by facilitating early and accurate diagnosis of IUGR.

Overall, the evidence strongly supports the integration of CPR into routine prenatal assessments to enhance the detection and management of IUGR, ultimately contributing to better clinical decision-making and improved neonatal health outcomes

CASES

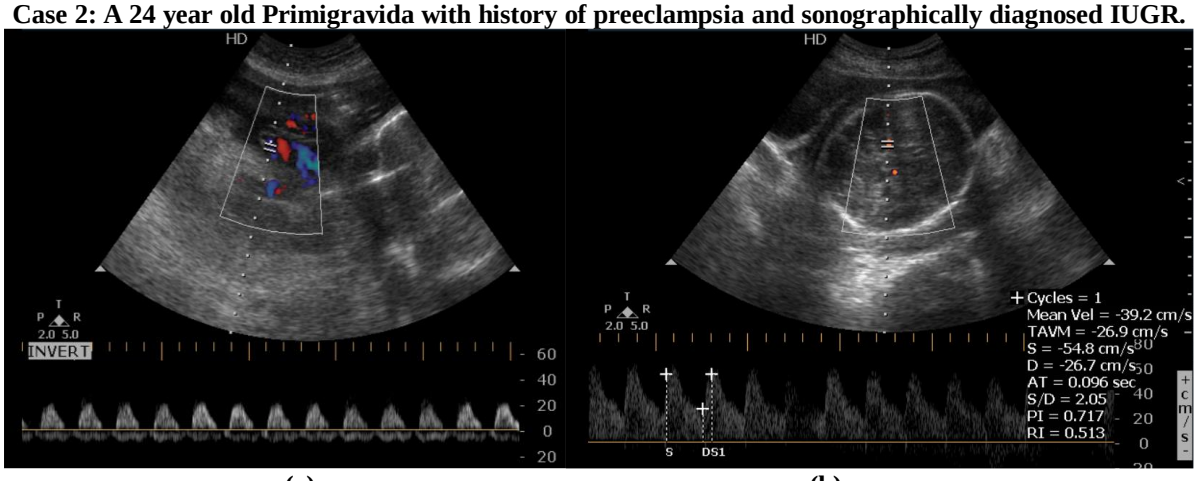
Case 1: A 35 year old G3P2A1 pregnant woman with Bad Obstetric History, preeclampsia and sonographically diagnosed IUGR.



(a) **(b)**

ColorDoppler of Umbilical Artery (a) shows reduced diastolic h diastolic flow and high Pulsatility Index. Color Doppler of the Middle Cerebral Artery (b) shows with low resistance, hig flow and reduced pulsatility index. (Brain Sparing Effect). Patient underwent LSCS for fetal distress, live birth with birthweight of 1.4kg, Low APGAR at 5 minutes and NICU admission.

Case 2: A 24 year old Primigravida with history of preeclampsia and sonographically diagnosed IUGR.



(a) **(b)**

Color Doppler of Umbilical Artery (a) shows absent diastolic flow. Color Doppler of the Middle Cerebral Artery (b) shows with low resistance, high diastolic flow and reduced pulsatility index. (Brain Sparing Effect). Patient underwent LSCS for fetal distress, live birth with birthweight of 1.7kg, Low APGAR at 5 minutes and NICU admission.

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