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CEREBRO PLACENTAL RATIO IN GROWTH RESTRICTED FETUSES AND ITS CORRELATION WITH PERINATAL OUTCOMES

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ABSTRACT

Background: Currently, the ACOG (2021a) and the Society for Maternal-Fetal Medicine (2020) recommend defining FGR as either an EFW <10th percentile for gestational age or an AC<10th percentile for gestational age. **Aim and Objectives:** The association between the severity of FGR and cerebroplacental ratio and predictive value of CPR with relevance to perinatal outcome. **Methodology:** Prospective observational study of singleton pregnant women complicated by IUGR were enrolled during the study period from December 2021 to November 2022. 100 participants were included in the study. The chi square test was used to analyze the association between the variables. **Results and Analysis:** Out of the total 100 cases, Abnormal CPR was present in 24% of cases, out of these 79% had abnormal perinatal outcome. There were 16 neonatal deaths and 15 neonatal complications among the adverse perinatal outcomes. CPR had a 61.29%, 92.75%, 79.17%, 84.21% and 83.00% sensitivity, specificity, positive predictive value, negative predictive value and accuracy with relevance to perinatal outcomes. Neonatal sepsis, necrotizing enterocolitis and hypoxic ischemic injury was the leading cause of morbidity. **Conclusion:** CPR is a sensitive parameter and has a high Positive and Negative predictive value and Accuracy in relation to adverse perinatal outcomes.

INTRODUCTION

Currently, the ACOG (2021a) and the Society for Maternal-Fetal Medicine (2020) recommend defining FGR as either an EFW <10th percentile for gestational age or an AC<10th percentile for gestational age[1] The prevalence of FGR is 10-15%. of all pregnancies around the world.[1]

FGR also known as intrauterine growth restriction.[2] The cerebroplacental ratio (CPR)—defined as middle cerebral artery pulsatility index divided by umbilical artery pulsatility index —is a measure of this adaptation and may be abnormal in severe cases of FGR. The Cerebro placental Ratio has been studied as a potential indicator of adverse pregnancy outcomes in the setting of fetal growth restriction. It serves as a measure of fetal brain sparing. The CPR is the outcome of the interaction between increased placental resistance and increased diastolic flow to the brain brought on by hypoxia-induced cerebrovascular dilatation, which results in decreased diastolic flow of the umbilical artery. Whenever this ratio falls below the fifth percentile for gestational age, a fetus is said to have fetal brain sparing. An abnormal CPR detected at term is linked to caesarean delivery for intrapartum fetal compromise, meconium-stained amniotic fluid, low Apgar scores, neonatal acidosis, and neonatal intensive care unit admission, regardless of birth weight.[3] An abnormal CPR at term is a predictor of reduced fetal development velocity and the requirement for surgical delivery for fetal compromise.[4]

The mortality and morbidity of fetuses with FGR can be reduced if the condition is diagnosed early. Proper antepartum, intrapartum, and neonatal management are essential for a successful perinatal outcome. Intraventricular hemorrhage, periventricular leukomalacia, hypoxic ischemic encephalopathy, necrotizing enterocolitis, bronchopulmonary dysplasia, sepsis, Newborn death and stillbirth were all considered to be adverse perinatal outcomes.[5]

Objectives

To evaluate the association between the severity of FGR and cerebroplacental ratio and predictive value of CPR with relevance to perinatal outcome.

METHODS

Study type- Prospective Observational study.

Study place - Department of Radiology, Fakhruddin Ali Ahmed Medical College Hospital, Barpeta, Assam
Period of study- August 2021 to july 2022.
Selection criteria of the patient- All singleton pregnant women irrespective of age or parity complicated by FGR who met inclusion criteria selected for our study. FGR is defined as estimated fetal weights (EFW) or abdominal circumference (AC) that fall within the third percentiles, or tenth percentiles with abnormal doppler parameters.[6]

Procedures
Informed consent was taken from all patients /guardian before enrollment in our study. Based on sonographic studies, they suffered from FGR and qualified to enter the study. All singleton pregnant women of, irrespective of age or parity complicated by FGR who met inclusion criteria selected for our study. Brief history was taken for all the patients selected for our study and quick examination was performed as per the proforma given below. Estimated fetal weight or abdominal circumference (AC) that fall within the third percentiles, or tenth percentiles with abnormal doppler parameters for that gestational age were selected for our study. Doppler sonography and velocimetry including **fetus middle cerebral artery and** umbilical were registered in SAMSUNG RS80A and SONOACE R7 ultrasonography machine with a 3.5 to 5 MHz curvilinear transducer ultrasound probe **at around 32 to 37. CPR value less the** 5th percentile of standard values were considered abnormal. The pregnancies were followed up and the final perinatal outcome of each case was noted

Umbilical artery doppler
Technique:[7]
The free floating loops in mid-position were used to record flow velocity waveforms.

Middle cerebral artery doppler
Technique:[7]
A enlarged axial section of the brain was acquired, showing the thalami and the sphenoid bone wings. The Circle of Willis was mapped using colour doppler. The pulsed-wave Doppler gate was positioned in the MCA's proximal third, near to its internal carotid artery origin.

Ethical approval: The study was approved by institutional ethics committee.

Statistical analysis: The data were entered in Microsoft excel and data analysis was done using SPSS software. The chi square test was used to analyze the association between doppler parameters and perinatal outcomes. P value less than 0.05 were considered significant.

RESULTS
In this prospective study, which was conducted over a year, 100 pregnant women with FGR participated. Hence the statistical analysis was done on 100 cases. The chi-square test was used to analyze the association between the variables.

The patients were in the age group ranging from 17 to 41 years. Out of 100 women 56% belonged to age group 21-25years, 19% belonged to age group 26-30 years, 13% were < 20 years, 10% belonged to age group 31-35years and 2% were above 35 years.

Out of the total 100 participants, 29% of them were primi, and 71% were multipara.

49% belonged to class IV socio-economic status, 46% belonged to class V socio-economic status, 5% were of class III socio-economic status.

69% had weight gain between 5-10 kgs whereas 19% had weight gain of > 10 kgs **and 12% had weight gain of <5 kg.**

Out of the total 100 participants, 30% had oligohydroamios, 64% had normal liquor whereas 6% had polyhydroamnios.

7 patients underwent instrumental delivery, and 42% of those patients experienced abnormal outcomes. Out of the 59 patients who underwent LSCS delivery, 30% experienced abnormal outcomes. Out of the 34 patients who had vaginal delivery, 29% had abnormal outcomes. The modes of delivery did not significantly affect the perinatal outcome. (p value = 0. 776)

Minimum baby birth weight was 800 gm and maximum birth weight was 2.7 kg. Mean was 1.91 kg with a SD 0.31.

Mean NICU duration was 5.47 days with a SD 9.83. Minimum 0 days maximum was 41 days. Mean weeks of delivery was 37.26 days with a SD 1.88. Minimum was 32 weeks and maximum was 41 days.

In the normal group, the CPR value was 1.69 ±0.51, in the morbidity group it was 1.1 ± 0. 28, and in the mortality group it was 0.52 ±0.4.
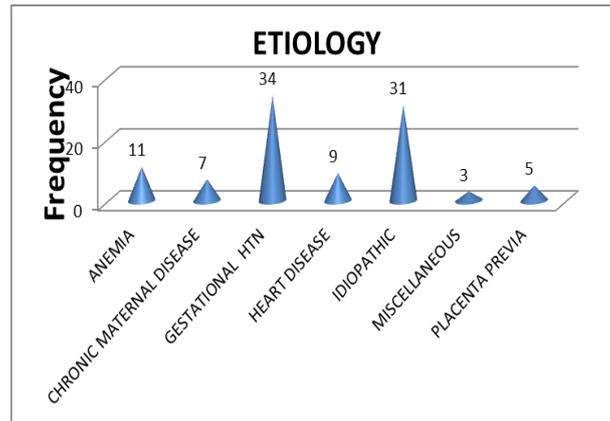P value was significant. (p= 0.001)

Fig. 1: Distribution of cases based on etiology.

Out of the total 100 women, It is seen that 34% had h/o gestational hypertension of pregnancy whereas 11% had associated anemia, 9% had heart disease.

Doppler parameters
Table 1: CPR Pattern and Perinatal outcomes.

CPR	Perinatal outcome			Chi	df	p value
	Abnormal outcome	**Normal outcome**	**Total**			
Abnormal	19	5	24			
Normal	12	64	76	34.252	2	<0.001
Total	31	69	100			

Table 2: Sensitivity specificity PPV NPV and Accuracy of CPR.

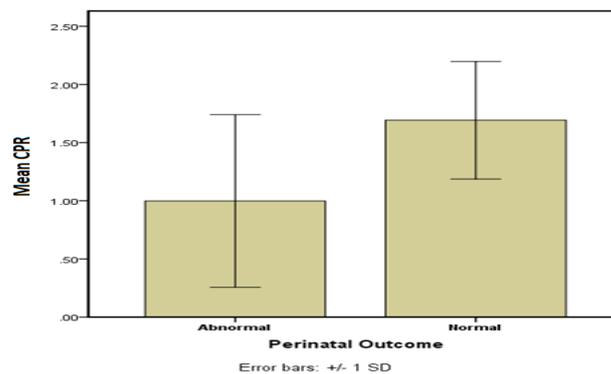| Statistic	Value	95% CI
Sensitivity	61.29%	42.19% to 78.15%
Specificity	92.75%	83.89% to 97.61%
Positive Predictive Value	79.17%	60.96% to 90.24%
Negative Predictive Value	84.21%	77.31% to 89.30%
Accuracy	83.00%	74.18% to 89.77%

Fig. 2: Mean CPR and Perinatal outcome.

Table 3: Neonatal Outcomes and Its percentage.

Neonatal outcome	Percent
Without complications	69
With complications	15
Death	16
Total	100

There were 15 neonatal complications and 16 neonatal deaths among the adverse perinatal outcomes. Neonatal sepsis and Intraventricular hemorrhage were the two leading causes of adverse neonatal outcomes followed by NEC and HIE.

Representative cases
CASE 1: 23 year old G5P3 woman showing absent diastolic flow in UA Doppler and brain sparing effect in MCA Doppler delivered at 37 weeks by CS. Baby had HIE. CPR ~ 0.5
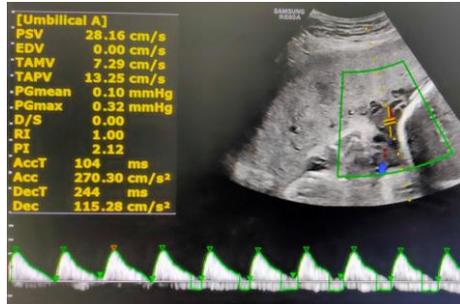

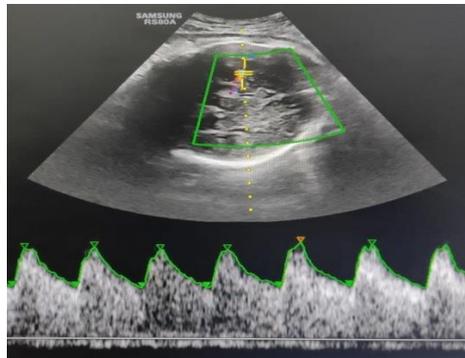**Fig. 3: UA Doppler showing absent diastolic flow.**

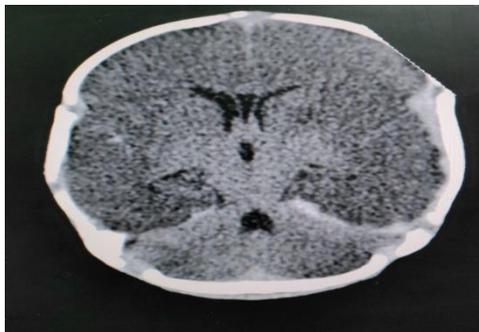**Fig. 4: MCA Doppler showing brain sparing effect.**

Fig. 5: CT brain of the neonate showing white cerebellar sign (HIE).

CASE 2: 20 year old G1P0 woman showing absent diastolic flow at 38 weeks. Baby had NEC

Fig. 6: Umbilical artery Doppler showing absent diastolic flow.

Fig. 7: XRAY of abdomen showing Pneumatosis intestinalis in FGR baby.

DISCUSSION

Prospective study included pregnant women whose pregnancy affected by fetal growth restriction. The chi square test was used to analyze the association between doppler parameters and perinatal outcomes. 69% of the patients had a normal perinatal outcome, compared to 31% of the 100 cases that had an adverse perinatal outcome.

Out of 100 cases, live births were reported in 94%, stillbirths in 4%, and IUDs in 2%. There were 16 neonatal deaths and 15 neonatal complications among the adverse perinatal outcomes. 7% patients underwent instrumental delivery, and 42% of those patients experienced abnormal outcomes. Out of the 59 patients who underwent LSCS delivery, 30% experienced abnormal outcomes. Out of the 34 patients who had

vaginal delivery, 29% had abnormal outcomes. The modes of delivery did not significantly affect the perinatal outcome. It is seen that 34% had h/o hypertension on pregnancy whereas 31% had no specific history, 11% had associated anemia, 9% had heart disease and 7 % had chronic maternal disease.

Intraventricular hemorrhage and neonatal sepsis were the two leading causes of death. Neonatal sepsis, necrotizing enterocolitis and hypoxic ischemic injury was the leading cause of morbidity. 100 patients were examined, and 24 of them had abnormal CPR.

CPR has a 61.29%, 92.75%, 79.17%, 84.21% and 83.00% sensitivity, specificity, positive predictive value, negative predictive value and accuracy for perinatal outcome.

Table 4: Comparison of UA doppler parameters with other studies.

CPR	Ozeren et al.	Najam et al.	Mohan et al.	Vollgraf et al	Our study
Sensitivity	81%	85 %	**95%**	59**%**	61.29%
Specificity	89%	89 %	87**%**	91**%**	92.75%
PPV	84%	80.7%	88**%**		7917%
NPV	86%	92%	85**%**		84.21%
Accuracy	85%		90**%**		83%

This is in line with the views expressed by Ozeren et al.[8] CPR had 81% ,89% ,84% ,86% and 85 % sensitivity, specificity, positive predictive value, negative predictive value and accuracy respectively for perinatal outcome. In Ozeren's study sensitivity was higher than our study although specificity, positive predictive value, negative predictive value and accuracy matched with our study

CPR had sensitivity, specificity, positive predictive value and negative predictive value 85%, 89%, 80.7% and 92.3% respectively in a study done by Najam et al.[9] Though sensitivity was quite higher but specificity, positive predictive value and negative predictive value matched with the current study.

In a study by Mohan et al.[10] CPR had 95% 87% 88% 85% 90% sensitivity, specificity, positive predictive

value , negative predictive value and accuracy for perinatal outcome. Sensitivity was higher than the current study but specificity, positive predictive value, negative predictive value and accuracy was consistent with the current study Vollgraf et al.[11] in their systematic review and meta-analysis the composite adverse perinatal outcome, sensitivity and specificity of CPR was 59 and 91 respectively, which similar to our study.

In the normal group, the CPR value was 1.69 ±0.51, in the morbidity group it was 1.1 ± 0. 28, and in the mortality group it was 0.52 ±0.4. Morbidity and mortality were more in low CPR value. CPR can be performed routinely in FGR setting to plan early intervention. CPR should be utilized in fetuses undergoing third-trimester ultrasound or antepartum testing.[12]

Limitations of the study

Our study has a sample size limitation, so it would be better to conduct additional research with a large sample of pregnant women, additional modalities, and also combine all Doppler indices with other tests related to FGR used in clinical care. This could increase the predictive accuracy and clinical importance of the tests.

CONCLUSION

As the impact of FGR is very detrimental, early evaluation of these patients with the available imaging modality will help in the further management of the patient and thus reducing the mortality as well as morbidity. CPR has high sensitivity, Positive and Negative predictive value and Accuracy in relation to adverse perinatal outcomes and it can be used as a routine check-up, follow-up in high risk pregnancies suspected of FGR, and to help manage and control FGR. Early assessment of the CPR should be carried out as it has a positive relationship with adverse maternal and neonatal outcomes, particularly FGR. When an abnormal Doppler finding is discovered, the obstetrician is informed of the potential difficulties that could arise, and the delivery should be scheduled at a tertiary care facility with excellent neonatal facilities.

ABBREVIATIONS
AC-Abdominal Circumference
EFW Estimated Fetal weight
AEDF-Absent End Diastolic Flow.
AFI- Amniotic Fluid Index.
FGR- Fetal growth restriction
USG-Ultrasonography
HII- Hypoxic ischemic injury
MCA – Middle Cerebral Artery
PI - Pulsatility Index
PPV- positive predictive value
NPV- negative predictive value
NEC- Necrotizing enterocolitis
RDS- Respiratory distress syndrome
IUD – Intrauterine death.

Declarations
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Conflict of interest: None
Ethical approval: The study was approved by institutional ethics committee.

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