

STUDY OF CEREBROPLACENTAL RATIO IN FETAL GROWTH RESTRICTED CASES AND ITS RELATION TO ADVERSE PERINATAL OUTCOMES.

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AIMS AND OBJECTIVES-

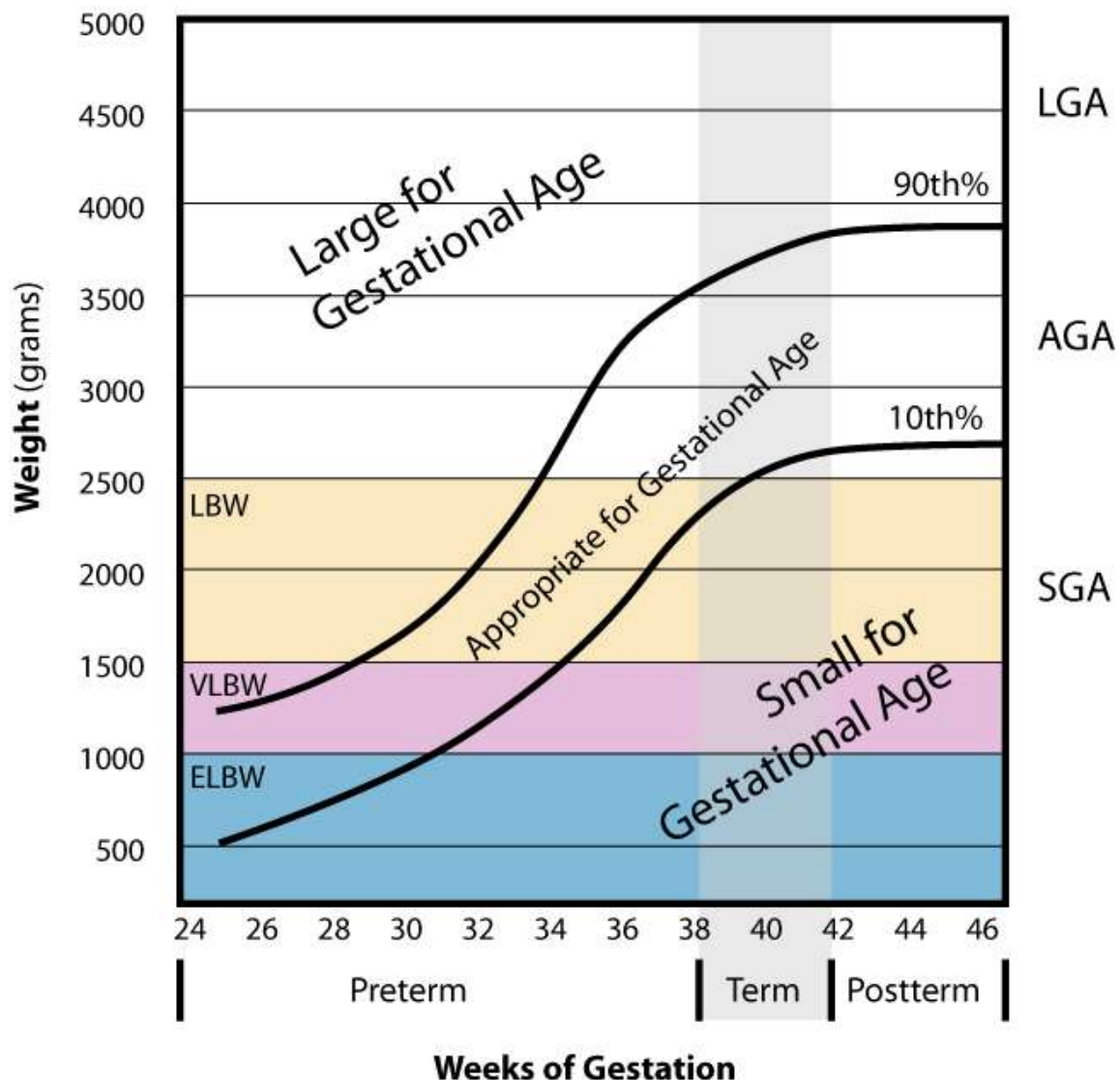
Following are the objectives of this study:

1. To study serial Doppler imaging of singleton pregnancies with clinically and radiologically diagnosed FGR, who come for check up or follow up at 34 weeks or beyond.
2. It aims to record the Doppler indices of Fetal Umbilical arteries and Middle Cerebral arteries in FGR pregnancies, calculate their pulsatility index ratio, i.e. the cerebroplacental ratio and to correlate the findings with the perinatal outcome.
3. USG measurement of
 - A) Biparietal diameter (BPD)
 - B) Head circumference (HC)
 - C) Abdominal circumference (AC)
 - D) Femur length (FL)
 - G) Estimated Fetal Weight (EFW)
4. Doppler measurement of
 - A) Umbilical artery indices (SDR, RI, PI)
 - B) Middle cerebral artery indices (SDR, RI, PI)
 - C) Cerebroplacental ratio (CPR).
5. To study if cerebroplacental ratio can predict adverse fetal outcomes in FGR cases.

INTRODUCTION:

DEFINITION: As per *ISUOG (International Society of Ultrasound in Obstetrics and Gynecology) Practice Guidelines 2020*, Fetal growth restriction (FGR) is described as

- a) Sonographic estimated fetal weight or abdominal circumference of less than 3rd percentile of the average for gestational age.
- b) EFW or AC < 10th percentile with abnormal doppler (maternal or fetal)



c) A drop of > 2 quartiles in AC or EFW centile in serial USG.

Graph showing estimated fetal weight (EFW) as per gestational age.

Fetal Growth Restriction (FGR) is a serious obstetric complication affecting 5–10% of pregnancies worldwide ¹. Fetal Growth Restriction (FGR), otherwise known as Intrauterine Growth Restriction (IUGR) is defined as a pathologic decrease in the rate of fetal growth. Here the fetus does not achieve its inherent growth potential, thereby increasing perinatal morbidity and mortality.

It is associated with an increased risk of adverse perinatal outcome, such as premature birth, fetal hypoxia, neonatal acidosis, low APGAR score or intrauterine death ^{2,3}. There are multiple causes for FGR—they can be of fetal, placental or maternal origin such as preeclampsia. Ultimately, they lead to the same endpoint: insufficient uteroplacental perfusion and restricted fetal nutrition which is reflected by abnormal Doppler parameters ⁴.

FGR incidence is between 3% and 7% of the total population with round figure of 5.13% with a progressively higher incidence during the last decade ⁵. In India, the prevalence of LBW has been reported as 26% while the proportion of FGR has been found to be 54% ⁶.

Fetal biometry and Doppler are the mainstay of investigation and diagnosis of IUGR than clinical measurement of fetal growth and abnormality as cited by **M Alberry and P Soothill in 2007.7**

Doppler velocimetry is a rapid non invasive test that provides information about hemodynamic situation of fetus & is efficient diagnostic test of fetal jeopardy & is one of the most important achievements of modern obstetrics.

The present study was conducted to evaluate the accuracy of doppler indices like Cerebroplacental ratio in predicting adverse fetal outcome in already diagnosed FGR cases.

MATERIALS AND METHODS:

PLACE OF STUDY: Department of Obstetrics & Gynaecology, VSS Institute of Medical Sciences and Research (VSSIMSAR), Burla

PERIOD OF STUDY: 24 Months (Jan 2021 - Dec 2022).

STUDY POPULATION: The subjects included 288 pregnant women beyond 34 weeks of gestation.

INCLUSION CRITERIA:

1. Singleton pregnant women between 18-45 years who visit VSSIMSAR O&G Department or Labour Room at or beyond 34 weeks.
2. Fundal height of uterus, on clinical evaluation, lagging behind atleast 4 weeks of expected height according to gestational age.
3. H/O previous IUGR or diagnosed as IUGR in current pregnancy before or after 34 weeks of GA.

EXCLUSION CRITERIA:

1. Multifetal gestation & congenital malformation of the foetus.
3. Mother lost to follow up or didn't deliver in our department.
4. Pregnant women whose estimated fetal weight was >2.5kg on ultrasonographic evaluation.

At booking, detailed history and thorough general examination & obstetrical examination were undertaken. All investigations were done according to proforma.

- They were assessed clinically then subjected to ultrasonographic examination at 34 weeks & >37 weeks for detection of IUGR by fetal biometry and then Doppler velocimetry was done. Foetuses who had Estimated foetal weight (EFW) < 10th percentile of the average for gestational age were classified as FGR (Fetal Growth Restriction). During the 34-40 weeks gestation, Doppler indices were measured for these cases at serial intervals. Ultrasonographic evaluation was done in the Dept. of Obstetrics and Gynaecology, VSSIMSAR, BURLA.
- They were followed till child birth and 7 days after birth.

OUTCOME MEASURES:-

Unfavourable obstetrical outcomes :

1. Need for caesarean section
2. Still birth

Unfavourable perinatal outcomes:

1. Babies who require admission to SNCU.
2. APGAR score at 5 minutes < 7
3. Meconium Aspiration Syndrome
4. Jaundice

5. Neonatal Sepsis

6. Hypoxic Ischemic Encephalopathy

Statistical analysis was done using the SPSS system to see if abnormal cerebroplacental ratio can predict poor perinatal outcome in fetal growth restricted cases.

ULTRASOUND EXAMINATION:

BPD & HC: Biparietal diameters were measured as described by Campbell 1968, at the level of thalami, third ventricle & septum pellucidum. Head circumference was measured at the same level by using (perimeter) ellipse function which averages the two diameters BPD & occipitofrontal diameter.

FL: A transverse section of fetal abdomen was found & so the transducer slid caudally until the iliac bones were visualized. At this point cross section of femur was seen. Here the transducer was rotated until the full length of femur was made from the centre of U' shape at each end of the bone.

AC: At the level of the shadow of stomach, liver, ductus venosus & fetal spine the measurement for abdominal circumference was taken.

Standard charts used for BPD, HC, FL & AC measurement was that of Hadlock et al⁷.

EFW: It was done by Hadlock's formula

$$\text{Log}_{10} \text{ EFW} = 1.3596 - 0.00386 (\text{AC} + \text{FL}) + 0.0064 (\text{HC}) + 0.00061 (\text{BPD} \times \text{AC}) + 0.0425 (\text{AC}) + 0.174 (\text{FL})$$

DOPPLER INDICES:-

The Doppler signals were recorded in 3.5 Hz frequency with a curvilinear probe.

UA-The umbilical artery (UA) waveform was obtained from free floating portion of the umbilical cord, in the lumen of the artery away from the placental and foetal cord insertion in a free loop of cord during minimal fetal activity & in the absence of fetal breathing.

MCA-Recordings from the middle cerebral artery were obtained on a transverse section of fetal head, at the level of the thalami and cavum waveform, and pulsatility index and S/D ratio was noted. Doppler sample was placed within 1 cm of origin of MCA that was easily identified as major branch running anterolateral from the circle of Willis towards the lateral edge of orbit.

The commonly used indices are

1. S/D Ratio
2. Resistance Index (RI) = S-D/S
3. Pulsatility Index (PI) = S-D/ Mean

The ultrasound machine automatically calculated above three indices by its installed software.

$\text{CPR} = \frac{\text{PI of middle cerebral artery/}}{\text{PI of umbilical artery}}$

• A single cut-off value of CPR 1 was taken, $\text{CPR} \leq 1$ is considered as abnormal while $\text{CPR} > 1$ is considered as normal.

RESULTS:**Table1:Distribution of value of cerebroplacental ratio as per gestational age in FGR cases**

CPR	≤ 1	> 1
34W-36W6D	44	38
≥ 37	122	84
Total	166	122
Percentage	58%	42%

Out of all the cases, 58 percent (no.166) cases had CPR ≤ 1 and 42% cases had CPR > 1 .

CPR	≤ 1	> 1	Total
Cesarean section	122	81	203
Vaginal delivery	44	41	85
Percentage of CS	74%	66%	70%

Table2: Mode of delivery in relation to CPR

Out of all the cases having cesarean section, 60 percent (no. 122) cases had CPR ≤ 1 (p value= 0.032, OR =1.4, significant). Thus, cesarean section is mostly associated with CPR ≤ 1 .

CPR	Still birth	Live birth
≤ 1	20	120
> 1	10	138
Total	30	258
Percentage	10%	90%

Table3: Fetal outcome as per CPR in all FGR cases

Out of all the still birth cases, 85% cases had CPR ≤ 1 (p value= 0.032, significant). Thus, still birth is more associated with CPR ≤ 1 and live birth is more associated with CPR > 1 .

SNCU Admission	Yes	No
CPR \leq 1	109	44
CPR $>$ 1	40	65
Total	149	109
Percentage	58%	42%

Table4:SNCU admission of babies within 48 hours of birth as per CPR in FGR cases.

In babies admitted to SNCU, 61% cases had CPR \leq 1 (p value= 0.021, significant, or=2) and 39% cases had CPR $>$ 1. Thus, most cases with SNCU admission were associated with CPR \leq 1.

MAS	Yes	No
CPR \leq1	123	43
CPR $>$1	34	88
Total	157	131
Percentage	55%	45%

Table5: Babies with meconium aspiration syndrome in FGR cases in relation to CPR

78% cases had CPR \leq 1 (p value= 0.023, OR =7.4) and 22% cases had CPR $>$ 1. Thus, majority of cases whose babies had meconium aspiration syndrome were associated with CPR \leq 1.

Jaundice	Yes	No
CPR \leq 1	126	40
CPR $>$ 1	28	94
Total	154	134
Percentage	53%	47%

Table6: Babies with jaundice in FGR in relation to CPR

82% cases had CPR \leq 1 (p value= 0.002, OR =1.8, significant) and 18% cases had CPR $>$ 1. Thus, majority of cases whose babies had jaundice were associated with CPR \leq 1.

HIE	Yes	No
CPR ≤ 1	100	66
CPR > 1	43	79
Total	143	145
Percentage	50%	50%

Table7: Babies with neonatal sepsis in FGR cases in relation to CPR

Out of all the cases with sepsis, 73% cases had CPR ≤ 1 (p=0.003, significant) and 27% cases had CPR > 1 . Thus, majority of cases whose babies had sepsis were associated with CPR ≤ 1 .

Table8: Babies with hypoxic ischemic encephalopathy (HIE) in FGR cases in relation to CPR

70% cases had CPR ≤ 1 (p value=0.022, OR = 2, significant) and 30% cases had CPR > 1 . Thus, majority of cases whose babies had HIE were associated with CPR ≤ 1 .

Low APGAR at 5 min	Yes	No
CPR \leq 1	120	46
CPR $>$ 1	70	52
Total	190	98
Percentage	66%	34%

Table9: Babies with low APGAR at five minutes in FGR cases in relation to CPR

63% cases had CPR \leq 1 (p value = 0.024, OR = 1.9, significant) and 37% cases had CPR $>$ 1. Thus, majority of cases whose babies had low APGAR at one minute were associated with CPR \leq 1.

Adverse Outcome	No.	CPR\leq1	%	CPR$>$1	%	P value	ODDS ratio
Cesarean section	203	122	73.40%	81	66%	0.032	1.4
Still Birth	30	20	14%	10	6%	0.003	0.42
SNCU Admission	149	109	71%	40	38%	0.038	4.02
MAS	157	123	74%	34	28%	0.023	7.4
HIE	143	100	60%	43	35%	0.022	2
Sepsis	153	122	73%	31	25%	0.001	8.1
Jaundice	154	126	76%	28	23%	0.002	1.8
APGAR $<$ 7 AT 5 minutes	190	120	72%	70	57%	0.02	1.9

Table10: The fetal adverse outcomes and their association with abnormal CPR (\leq 1)

In all the cases with CPR \leq 1, there is atleast one adverse outcome associated with it. P value in all the cases was $<$ 0.05 which is statistically significant.

Table11: The sensitivity, specificity and positive predictive value of abnormal CPR (\leq 1) in predicting different adverse outcomes as per this study

Outcome	CS (%)	Still Birth (%)	SNCU Admission (%)	MAS (%)	HIE (%)
Sensitivity	73	14	71	74	60
Specificity	34	93	61	72	64
PPV	60	67	73	78	70

Thus, the sensitivity , specificity and Positive Predictive Value of CPR ≤ 1 is more than 50 % for all the adverse perinatal outcomes.

Discussion:

In this study the maximum number of cases (70%) are delivered by caesarean section whereas 30 % of cases are delivered by vaginal delivery.

This finding is in close conjunction with a study by ERIKA F. WARNER et al (2012), 8 where 42.1% were delivered vaginally and 57.9% were delivered by caesarean section. Similar findings were found in a study by H. COENEN et al (2021)9.

Sensitivity of abnormal CPR in predicting caesarean section as a mode of delivery is 73%.
Specificity is 34%, PPV is 60%.

This finding is similar to the study by **Tran Thao Nguyen Nguyen10 (2018)**, which stated that the rate of emergency cesarean section deliveries in the CPR < 1 and CPR > 1 group were 68.75% and 39.65%, respectively (p < 0.05).

Similar findings were also found in a study by **El-Kady et al (2020),11** t (60% positive predictive value) .Study by **H. Coenen12 (2021)**, also stated that the percentage of caesarean section in abnormal CPR cases is 79.5 % with p value 0.001 which shows positive correlation.

In this study, the APGAR score at five minutes is < 7 in majority of the cases. Out of total cases 74 % of babies had APGAR score < 7 and 26 % had score ≥ 7 .

This finding is also found in a study by **COSMI et al (2011)13**.

Shahinaj et al. documented that the perinatal adverse outcome as stillbirth was highly significantly correlated with low CPR among the FGR group. the P-values of these entire outcome were = 0.001 which is similar to this study.

In a study by **Ali El-Shabrawy Ali ET AL 14 (2021)**, CPR had 100% specificity to predict stillbirth with statistically significant positive correlation as p value was < 0.001 . This finding is same as this study (specificity 93%).

Study by **Ahmed Alanwar 15 (2018)**, found that the CPR < 1 had 62.5% sensitivity and 71.43% specificity as a predictor of SNCU admission which is in close similarity to findings of this study.

The findings of this study is similar to a study by **Ashraf Jamal and Vajiheh Marsoosi (2021),16** which stated that low CPR is correlated with neonatal sepsis with p value < 0.001 .

In the study by **Tran Thao Nguyen Nguyen10, (2018)** they concluded that there was a strong correlation between CPR and adverse outcomes in fetal growth restriction cases. This finding is similar to the findings of this study.

Similar findings were found in the Study by **Singh G et al. (2018)17** where CP ratio has high sensitivity, specificity and diagnostic accuracy in predicting adverse perinatal outcome (sensitivity and specificity of cerebro-placental ratio was 93.2% and 89%).

CONCLUSION:

USG is a reliable method in diagnosing growth restriction & approximate baby weight, thus forms a valuable aid for managing high risk cases.

Fetal Doppler indices, in particular ratios obtained from umbilical and cerebral circulation, helps in the prediction of neonatal morbidity and mortality.

The present study “**Study of Cerebroplacental Ratio in Fetal Growth Restricted Cases and Its Relation to Adverse Perinatal Outcomes**” was undertaken in 288 clinically and ultrasonographically diagnosed FGR cases based on height of the uterus and fetal biometry. Fetal Doppler velocimetry of Middle Cerebral Artery (MCA) & Umbilical Artery (UA) were recorded. The cerebroplacental ratio (ratio of middle cerebral artery P.I. to umbilical artery P.I.) was calculated for each case and they were studied according to proforma . the results were then analysed.

- Sensitivity of $CPR \leq 1$ in detecting atleast one adverse outcome in FGR cases is 89%, Specificity is 85% and Positive Predictive value is 89.15% which is high as compared to normal CPR.
- Thus, this study showed that an abnormal CPR (≤ 1) has a high sensitivity, specificity and Positive predictive value in predicting most of the adverse perinatal outcomes as included in this study.
- It may be concluded from the observations of the present study that $CPR \leq 1$ is a good predictor OF adverse perinatal outcome as most of the adverse perinatal outcomes were associated to abnormal CPR in all the FGR Cases included in this study. Thus, Doppler velocimetry can be implemented in all the suspected cases of FGR for early prediction of any adverse perinatal outcomes and necessary steps can be taken according to that. In this way, fetal mortality and morbidity can be reduced.

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