Cerebroplacental Ratio Infetal Growth Restriction

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Abstract
Background: The objectives of this study are (1) To assess the use of CPR in non –anomalous fetus, (2) To study the association between the severity of fetal growth restriction and abnormal CPR and to evaluate the predictive value of the same in FGR with relevance to perinatal outcome.
Materials & Methods: A Prospective observational study in 80 antenatal mothers was done in the rural area of Chidambaram, from September 2019 to August 2021.Pregnant women irrespective of age or Parity were examined with Doppler studies and relevant data was collected. All 80 singleton antenatal mothers with non-anomalous foetuses selected for this study are examined only after getting willingness to undergo study and after getting duly signed consent form and following obstetric Doppler safety guidelines as per ALARA principle. The USG machine used in our department for this research purpose is Mindray DC70 series, using curvilinear convex probes of 3.5-5 MHz.
Results: Abnormal CPR was found in 41 cases, and abnormal MCA was seen in 1 late onset term FGR fetus. CPR was abnormal in 41 cases (51.25 %), of which 12 had either normal umbilical or MCA PI individually, 28 cases were in stage 1 FGR, 1 was late onset term SGA fetus or late onset FGR fetus.
Conclusion: CPR is useful in predicting adverse perinatal outcome.

Keywords: Cerebroplacental ratio, fetal growth restriction, obstetric Doppler guidelines

Introduction

Fetal growth restriction is defined as the fetus that has not attained its growth potential[7]. The need for screening arises as there are many more cases of unexplained stillbirths. Many reviews showed that the deaths are due to unidentified risk factors and inadequate appropriate health care. Samrakshan program in India by IRIA focuses at reducing FGR and PE by various methods, of which Doppler studies play a major role.

Obstetric Doppler safety:

Though the ionisation risk is not in ultrasound, significant energy output happens during spectral doppler. so using ALARA principle, (as low as reasonably achievable), Doppler is done only for valid medical conditions. The mechanical index should be 1.0 or less. Especially in first trimester (11 weeks to 13 weeks 6 days), scanning time should be as short as possible, preferably within five to ten minutes and should not exceed sixty minutes.

Cerebroplacental ratio CPR[2,3,4,6]
Umbilical artery Doppler measurement[1,12]

Low resistance with continuous forward flow throughout the cardiac cycle is seen in normal placental vascular bed.

Doppler study of umbilical artery is done usually only after 24 weeks when the fetus has attained its

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viability. For this study, free floating/uncompressed loop of cord is sampled in view of limitations caused by fetal extremities obscuring the abdominal insertion site.

## NORMAL UMBILICAL ARTERY DOPPLER

Middle cerebral artery Doppler ultrasound:

Middle cerebral artery is a terminal of internal carotid artery. It has high resistance flow pattern producing biphasic waveform of systole and diastole .Transverse or axial section of the fetal head is taken at the level of Sphenoid bone wings with visualisation of Thalami and Cavum septum pellucidum. Circle of Willis is identified with proper angling of transducer and with the help of colour Doppler and entire length of MCS must be seen. Magnification is done such that MCA occupies more than 50% of the image. Pulsed Doppler sample volume is set at 1-2mm. Then proximal third of MCA close from its origin is sampled.

NORMAL MIDDLE CEREBRAL ARTERY DOPPLER[11]
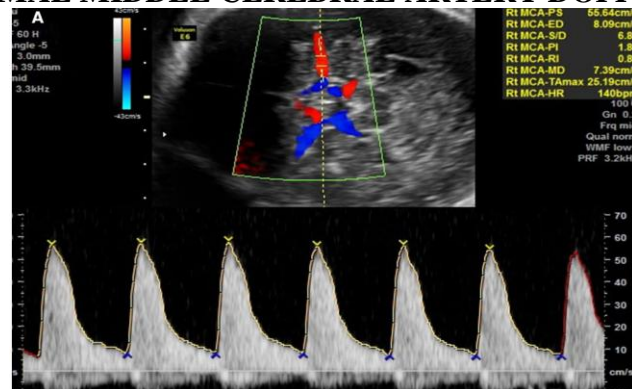
CPR is calculated by Dividing the MCA PI by the umbilical PI.

CPR = MCA PI/ UMB A. PI

This ratio is considered abnormal if it is less than fifth percentile for gestational age or more than 1.0. Increase in placental resistance causes reduced umbilical artery diastolic flow and increased diastolic flow to brain due to hypoxia induced cerebral vasodilatation. Values less than 3rd percentile has high predictive value than ratio of 1. Recent studies show that abnormal CPR is associated with high risk of emergency deliveries for fetaldistress, meconium stained amniotic fluid, low APGAR scores <7 at 1 and 5 minutes, neonatal acidosis and neonatal intensive care admissions. When CPR is used along with EFW, Uterine artery doppler in third trimester, high risk term fetuses and perinatal complications can be predicted.[10]
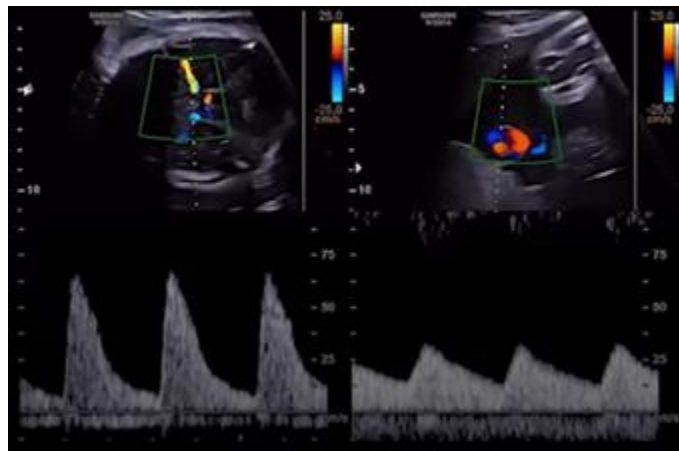
NORMAL CEREBROPLACENTAL RATIO
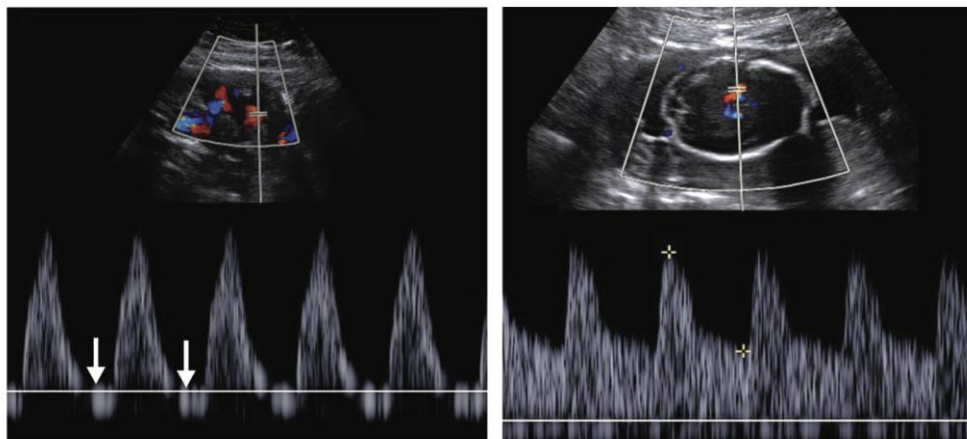
Abnormal cerebroplacental ratio. **(a)** Color Doppler duplex US image of the umbilical artery shows reversed end-diastolic flow (arrows) at 25 weeks in a fetus with severe early-onset growth restriction. **(b)** Color Doppler duplex US image shows that increased diastolic flow was present in the middle cerebral artery, indicating "head-sparing" flow and an abnormal cerebroplacental ratio. Calipers indicate peak systolic velocity (upper caliper) and end-diastolic velocity (lower caliper). The estimated fetal weight of about 350 g was such that resuscitation was unlikely to be successful if the infant were to be delivered with an emergency cesarean delivery. Intrauterine death occurred at 29 weeks; the measured fetal size was that of a fetus of 21 weeks gestation. The patient declined autopsy and placental histopathologic examination.

Greggory R. DeVore, MD The importance of the cerebroplacental ratio in the evaluation of fetal well-being in SGA and AGA fetuses http://dx.doi.org/ 10.1016/j. ajog. 2015.05.024

TABLE 1
Studies reporting the value for an abnormal cerebroplacental ratio

Study	Year	Study type	Doppler indices	Computation of ratio	Abnormal criteria
Arbeille et al[1]	1988	Cross-sectional	S-D/S	MCA/UA	Ratio <1
Arias[6]	1994	Cross-sectional	RI	MCA/UA	Ratio <1
Gramellini et al[5]	1992	Cross-sectional	PI	MCA/UA	Ratio <1.08
Bahado-Singh et al[8]	1999	Cross-sectional	PI	MCA/UA MoM	Ratio <0.05 MoM
Baschat and Gembruch[9]	2003	Cross-sectional	PI	MCA/UA	Less than fifth centile
Odibo et al[10]	2005	Cross-sectional	PI	MCA/UA	Ratio <1.08
Ebbing et al[11]	2007	Longitudinal	PI	MCA/UA	<2.5th centile
Morales et al[12]	2014	Cross-sectional	PI	MCA/UA	Less than fifth centile or MoM <0.6765

MCA, middle cerebral artery; *MoM*, multiple of the median; *PI*, pulsatility index; *RI*, resistance index; *S/D*, systolic/diastolic ratio; *UA*, umbilical artery.

DeVore. Cerebroplacental ratio in fetal well-being in SGA and AGA fetuses. Am J Obstet Gynecol 2015.
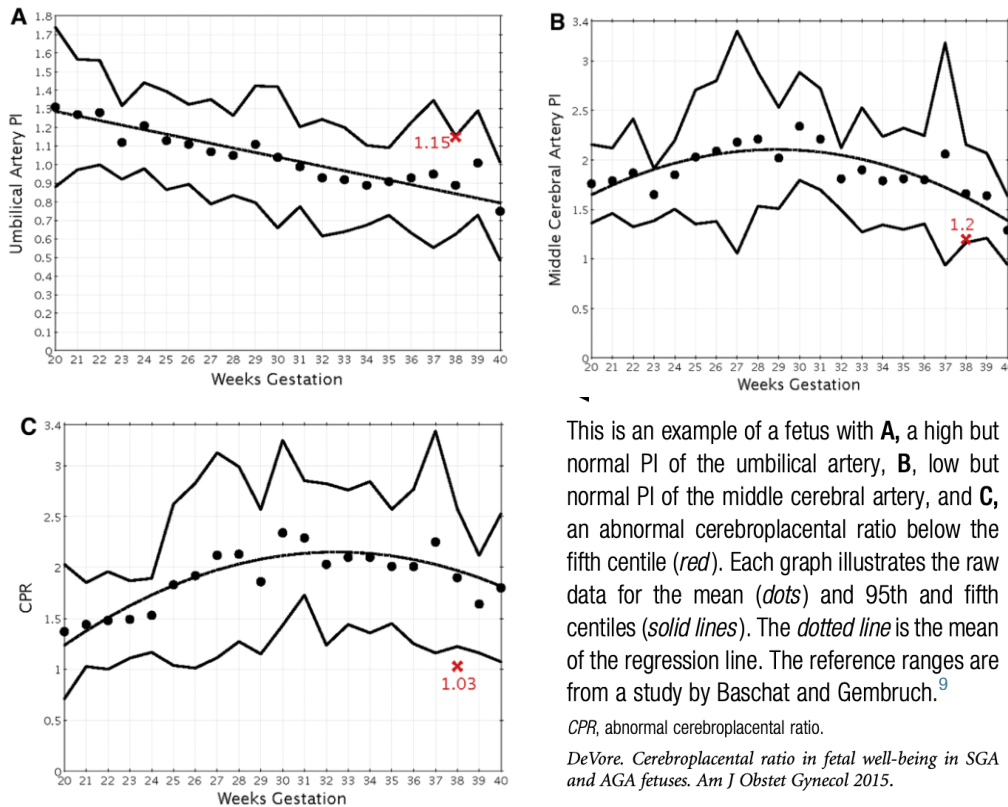
This is an example of a fetus with **A,** a high but normal PI of the umbilical artery, **B,** low but normal PI of the middle cerebral artery, and **C,** an abnormal cerebroplacental ratio below the fifth centile (*red*). Each graph illustrates the raw data for the mean (*dots*) and 95th and fifth centiles (*solid lines*). The *dotted line* is the mean of the regression line. The reference ranges are from a study by Baschat and Gembruch.[9]

CPR, abnormal cerebroplacental ratio.

DeVore. Cerebroplacental ratio in fetal well-being in SGA and AGA fetuses. Am J Obstet Gynecol 2015.

It was observed from the table that high specificity and low sensitivity was seen in the ratio, but high sensitivity and low specificity was seen when less than 5th centiles values were used.

Sensitivities, specificities, and odds ratio for CPR computations for detecting adverse perinatal outcome[a30]

Cerebroplacental ratio	Measurement standard	Sensitivity	Specificity	Odds ratio
<1	Pulsatility index	66%	85%	11.7
<1	Resistance index	66%	84%	11.8
Less than fifth centile (cross-sectional study)[9]	Centile	80%	60%	6.2
Less than fifth centile (longitudinal study)[11]	Centile	85%	41%	4.1

CPR, abnormal cerebroplacental ratio.

[a] Intraventricular hemorrhage, periventricular leukomalacia, hypoxic ischemic encephalopathy, necrotizing enterocolitis, bronchopulmonary dysplasia, sepsis, and death.

DeVore. Cerebroplacental ratio in fetal well-being in SGA and AGA fetuses. Am J Obstet Gynecol 2015.

This study shows that usg examinations in the third trimester should use CPR even if there are normal or abnormal umbilical and MCA Doppler findings' especially in late SGA ant term AGA fetuses.

When CPR is used along with EFW ,Uterine artery doppler in third trimester, high risk term fetuses and perinatal complications can be predicted .[10]

CPR is very useful in term SGA babies and post dated pregnancies fetal wellbeing

MANAGEMENT OF FETAL GROWTH RESTRICTION: [7, 8]

CPR is very useful in term SGA babies and post dated pregnancies fetal wellbeing[5]. Healthy small fetuses in the third trimester can be assessed by MCA which may show redistribution, in the presence of normal umbilcal artery, indicationg adverse perinatal outcome.[6]

RCOG guidelines suggest monitoring FGR fetuses every 14 days from 26-28 gestational weeks. If

umbilical artery shows absent or reversed EDF in preterm SGA fetuses ,unless DV become abnormal or umbilical vein showing pulsations, it is better to deliver after b32 weeks of gestation.

With the same situation of absent or reversed EDF in umbilical artery after 32 weeks, it is better to deliver later ,but not more than 37 weeks of gestation. Adverse perinatal outcome is closely related to abnormal CPR values. RCOG guidelines suggest that MCA Doppler abnormalities can be used to guide delivery in term fetuses showing normal umbilical artery Doppler, but not in preterm FGR fetuses.

Stage-based classification and management of FGR

Stage	Pathophysiological correlate	Criteria (any of)	Monitoring*	GA/mode of delivery
I	Severe smallness or mild placental insufficiency	EFW <3rd centile CPR <p5 UA PI >p95 MCA PI <p5 UtA PI >p95	Weekly	37 weeks LI
II	Severe placental insufficiency	UA AEDV Reverse AoI	Biweekly	34 weeks CS
III	Low-suspicion fetal acidosis	UA REDV DV-PI >p95	1–2 days	30 weeks CS
IV	High-suspicion fetal acidosis	DV reverse a flow cCTG <3 ms FHR decelerations	12 h	26 weeks** CS

All Doppler signs described above should be confirmed at least twice, ideally at least 12 h apart. GA = Gestational age; LI = labor induction; CS = cesarean section. * Recommended intervals in the absence of severe preeclampsia. If FGR is accompanied by this complication, strict fetal monitoring is warranted regardless of the stage. ** Lower GA threshold recommended according to current literature figures reporting at least 50% intact surviva. Threshold could be tailored according to parents' wishes or adjusted according to local statistics of intact surviva.
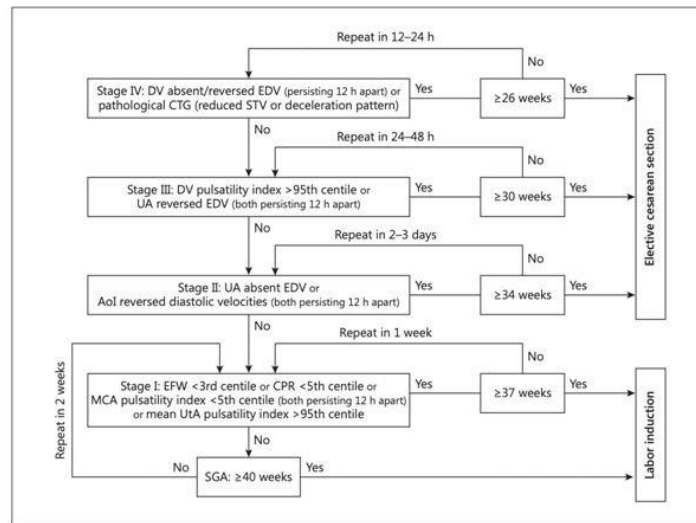
Stage-based decision algorithm for the management of FGR (see text for abbreviations).

RESULTS AND ANALYSIS:

80 Antenatal mothers were examined with obstetric Doppler and CPR was calculated using MCA and Umbilical artery PI. The results were entered in data sheet and necessary figures, tables were derived and results interpretated.

Table 1: CPR Distribution

Cerebroplacental Ratio	Number	%
Normal	46	57.5
Abnormal	34	42.5

CPR DISTRIBUTION

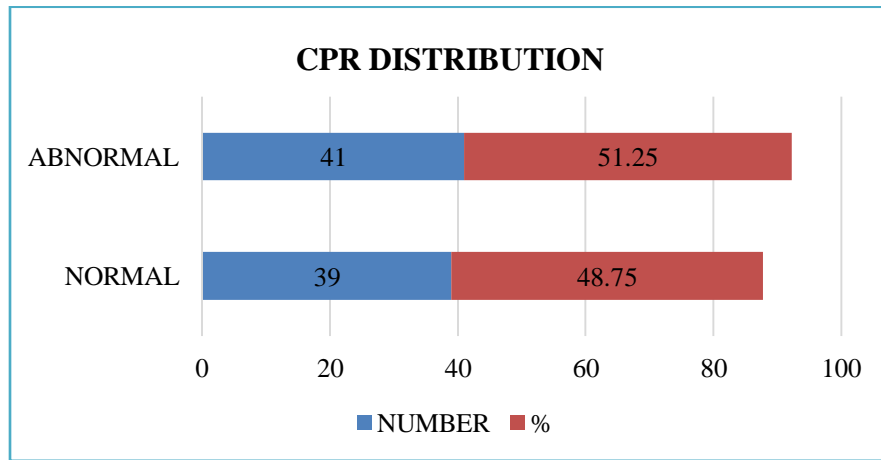|	NUMBER	%
ABNORMAL	41	51.25
NORMAL	39	48.75

Fig 1. CPR Distribution

Table 2: Less 5 min Apgar and Correlation of associated Abnormalities

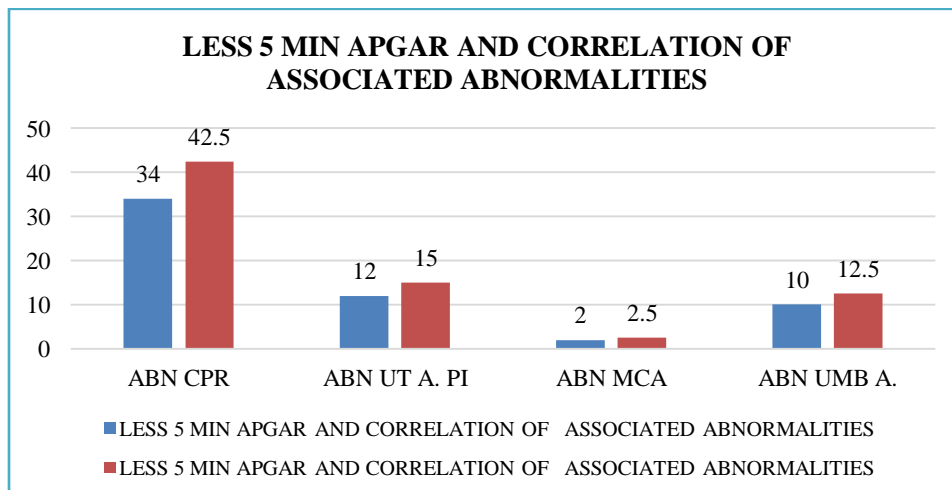| Less 5 min Apgar and correlation of associated abnormalities	Number	%
ABN CPR	34	42.5
ABN UT A. PI	12	15
ABN MCA	2	2.5
ABN UMB A.	10	12.5

LESS 5 MIN APGAR AND CORRELATION OF ASSOCIATED ABNORMALITIES

	ABN CPR	ABN UT A. PI	ABN MCA	ABN UMB A.
Number	34	12	2	10
%	42.5	15	2.5	12.5

LESS 5 MIN APGAR AND CORRELATION OF ASSOCIATED ABNORMALITIES
LESS 5 MIN APGAR AND CORRELATION OF ASSOCIATED ABNORMALITIES

Fig 2. less 5 min Apgar and correlation of associated abnormalities
Table 3: Abnormal CPR Distribution in Emergency LSCS

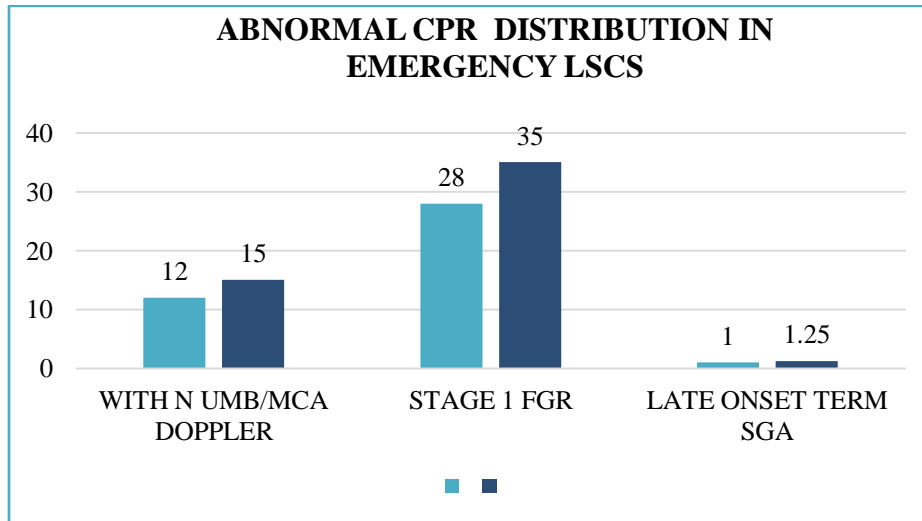| Abnormal CPR Distribution in Emergency LSCS	NUMBER	%
With N UMB/MCA Doppler	12	15
Stage 1 FGR	28	35
Late Onset Term SGA	1	1.25

Fig 3. Abnormal CPR distribution in emergency LSCS

Table 4: Emergency LSCS and associated ABN

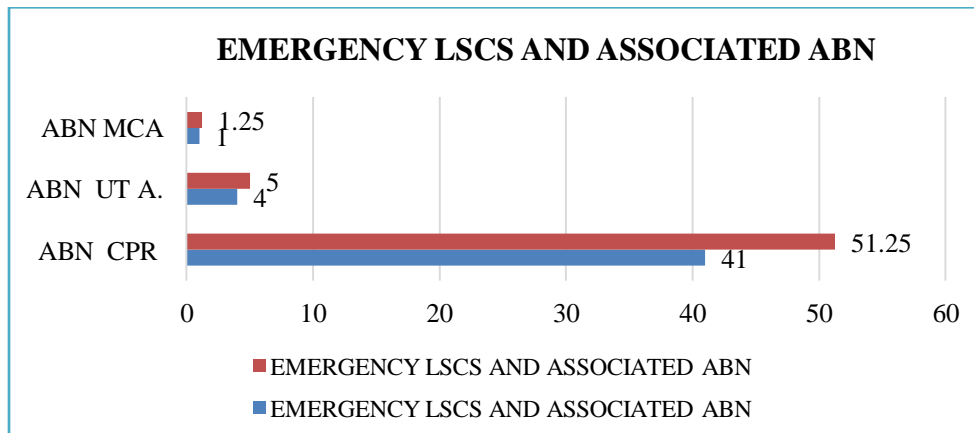| Emergency LSCS and Associated ABN		
TOTAL CASES = 45		%
ABN CPR	41	51.25
ABN UT A.	4	5
ABN MCA	1	1.25

Fig 4: Emergency LSCS and associated ABN

DISCUSSION:

80 Antenatal mothers were examined for fetal growth restriction fetus with proper antenatal history, appropriate ultrasound biometry parameters and Doppler studies. They were followed and surveillance done with appropriate Doppler studies and followed till delivery and postnatal discharge.78 was found to be FGR fetuses, of which 57 were early onset FGR fetuses and 21 late onset FGR fetuses. They were monitored till delivery, 55 LSCS and 25 vaginal deliveries were done.

Of 45 emergency LSCS done, abnormal CPR was found in 41 cases, and abnormal MCA was seen in 1 late onset term FGR fetus, CPR was abnormal in 41 cases (51.25 %), of which 12 had either normal umbilical or MCA PI individually,28 cases were in stage 1 FGR, 1 was late onset term SGA fetus or late onset FGR fetus.

48 babies had 24 abnormal CPR ratio, 2 had abnormal MCA PI with abnormal 5 min APGAR score and more than 5 days admission in NICU.

CONCLUSION:

The main goal is identification of FGR, which is a common pregnancy complication with increased risk or adverse perinatal complications. CPR is useful in predicting poor perinatal compilcations. CPR is a better predictor in emergency delivery for fetal distress.

ABBREVIATIONS USED:

CPR: Cerebroplacental ratio
FGR : Fetal growth restriction
MCA: Middle cerebral artery
PI: Pulsatility index
NICU: Neonatal intensive care unit
LSCS: Lower segment caesarean section

ANNEXURES:

Reference Centile Chart of FetalCerebroplacental Doppler from 24 to 40 Weeks Gestation in Indian Population [5]

The 5th, median and 95th reference centile chart of MCA/ UA or cerebroplacental ratio (CPR) from 24 to 40 weeks gestation

Gestational age (weeks)	MCA PI/UA–PI (CPR)			
	5th centile	10th centile	50th centile	95th centile
24–26	0.84	0.95	1.83	2.86
27–29	0.77	0.90	1.73	2.68
30–32	0.77	0.89	1.53	2.64
33–35	0.76	0.89	1.50	2.56
36–38	0.64	0.83	1.59	2.55
39–40	0.61	0.80	1.56	2.52

The mean, standard deviation, 5th, 50th and 95th centile with corresponding MOM values of middle cerebral and umbilical artery PI, RI, S/D ratio including cerebroplacental ratio or CPR across the gestational age from 24 to 40 weeks gestation

Doppler	Mean	±SD	5th centile	MOM	50th centile	MOM	95th centile	MOM
MCA (PI)	1.37	0.35	1.04	0.8	1.38	1.0	1.71	1.3
MCA (RI)	0.69	0.15	0.44	0.6	0.69	1.0	0.93	1.3
MCA (S/D)	3.37	1.33	1.18	0.4	3.03	1.0	5.56	1.8
Umbilical artery (PI)	0.93	0.31	0.59	0.7	0.83	1.0	1.56	1.8
Umbilical artery (RI)	0.58	0.14	0.36	0.6	0.56	1.0	1.48	2.6
Umbilical artery (S/D)	2.27	0.46	1.42	0.6	2.18	1.0	2.94	1.3
MCA PI/UA PI	1.60	0.58	0.71	0.4	1.57	1.0	2.52	1.6

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