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Original Article

Association of Cerebroplacental and Cerebrouterine Ratio with Fetal Outcome in Kashmiri Pregnant Women with Hypertension

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Abstract

Background: Doppler velocimetry is a non-invasive technique that evaluates abnormal fetal hemodynamics that take place in response to changes in placental resistance. Doppler studies of multiple fetoplacental are used to predict adverse perinatal outcome and assisting in optimal time of delivery. Cerebroplacental ratio (CPR) is calculated as the absolute ratio between the Doppler pulsatility indices of fetal middle cerebral artery (MCA) and umbilical artery (UA) or as the ratio between the corresponding multiples of the median for gestational age. CPR is reflective of fetal hypoxia and acidemia, and therefore prediction of perinatal jeopardy. A low CPR in a hypertensive pregnancy is associated with an increased risk of induction of labor, emergency cesarean section and poor perinatal outcome. CRP ratio is an established predictor of unfavorable pregnancy outcomes, while cerebrouterine (CU) ratio is fairly new ratio of vascular impedance between MCA and uterine arteries.

Objectives: The objective of the study was to study CPR as predictor of adverse fetal outcome in pregnant women with hypertension from 34 weeks of gestation, and, to evaluate the role of middle cerebral to UA blood velocity waveforms and fetal outcome in terms of fetal growth restriction, mode of delivery, neonatal intensive care unit (NICU) admission, APGAR at 5min.

Methods: This prospective study was conducted in the Postgraduate Department of Obstetrics and Gynaecology of GMC Srinagar associated Lalla Ded Hospital over a period of 1½ year. During this period on an average around 400 patients attended the outpatient department on daily basis, 50432 patients were admitted in our hospital, 34,293 deliveries were conducted. All pregnant women from 34 weeks of gestation with CPR done within 1 week of delivery, admitted or referred to Lalla Ded Hospital. The scan in these women was done within 1 week of delivery considered. CPR value was obtained from the scan. CPR is ratio of pulsatility index of the MCA by the UA pulsatility index.

Results: We observed a statistically significant correlation between abnormal CPR with caesarean section ($P < 0.001$), abnormal CPR and low for gestational age ($P < 0.001$), abnormal CPR and APGAR at 1 min ($P < 0.001$), and APGAR score at 5 min ($P < 0.001$), abnormal CPR and NICU admission. ($P < 0.001$) abnormal CPR and neonatal death was also significant ($P < 0.0008$). We observed a statistically significant association between Abnormal CU with low for gestational age ($P < 0.001$), between abnormal CU ratio and APGAR SCORE at 1 min ($P < 0.001$) and APGAR score at 5 min ($P < 0.001$), abnormal CU and NICU admission ($P < 0.001$), between abnormal CU ratio and neonatal death.($P < 0.0004$). CP ratio had higher specificity and PPV and lower sensitivity than CU ratio in predicting abnormal fetal outcome. CRU ratio had higher sensitivity and NPV and lower specificity than CP ratio in predicting abnormal fetal outcome.

Conclusion: Fetal Doppler plays a crucial role in monitoring the redistribution of blood in the fetus and the placental circulation. CPR and CUR assesses parameters on both placental side and also the fetal response.

Key words: Cerebroplacental ratio, Cerebrouterine ratio, Dopper velocimetry, Pulsality index

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INTRODUCTION

Hypertension peculiar to pregnancy (preeclampsia and gestational hypertension) is a specific syndrome characterized by reduced organ perfusion secondary to vasospasm and endothelial pathology.[1] The earliest pathology is impaired conversion of spiral arteries to

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uteroplacental arteries. As the second wave of infiltration of trophoblasts into the myometrial segments of the spiral arteries is inhibited, the blood supply to fetus is reduced.[2,3] The progression of pregnancy is marked by a number of changes and adaptations in the maternal, placental and fetal vasculatures. An inability to adapt to these changes results in the development of abnormal vascular resistance patterns, which might consecutively lead to the compromise of fetal well-being and ultimately IUGR.[4] As placental insufficiency occurs, several changes occur in fetal circulation due to fetal hypoxia which activates a number of defense mechanisms, such as modification of fetal heart rate, increase in blood pressure and redistribution of blood to the heart, brain, and adrenal glands. Low oxygen partial pressure (pO_2) leads to cerebral vasodilation and a fall in vascular resistance, which results in a decrease in middle cerebral artery (MCA) resistance index values. This is seen as Brain Sparing effect on Doppler.[5]

Accurate assessment of the fetal condition in high risk pregnancies is important if perinatal mortality, and morbidity and also unwarranted intervention in pregnancy and labor are to be reduced. Doppler ultrasound of the uteroplacental fetal circulation offers the potential to study the functional and hence physiological changes in these circulations and may help identify circulatory problems that underlie placental insufficiency and chronic fetal hypoxia.[6] The objective of fetal Doppler is to detect any hemodynamic changes at the earliest and to assess the placental dysfunction and the consequences of this on fetal growth and well-being,[6] Umbilical artery (UA) and MCA Doppler ultrasound clearly depict the information about placental resistance and the changes in the fetal hemodynamics in response to it. UA Doppler reflects the maldevelopment of the placental tertiary stem villi which increases the placental resistance.[1]

Doppler velocimetry is a non-invasive technique that evaluates abnormal fetal hemodynamics that take place in response to changes in placental resistance. Doppler studies of multiple feto-placental vessels can be used to predict adverse perinatal outcome and assisting in optimal time of delivery.[7] Cerebroplacental ratio (CPR) is calculated as the absolute ratio between the Doppler pulsatility indices (PIs) of fetal MCA and UA or as the ratio between the corresponding multiples of the median for gestational age. CPR is reflective of fetal hypoxia and acidemia, and therefore prediction of perinatal jeopardy.[1,8] A low CPR in a hypertensive pregnancy is associated with an increased risk of induction of labor, emergency cesarean section, and poor perinatal outcome. CRP ratio is an established predictor of unfavorable pregnancy outcomes, while cerebrouterine (CU) ratio is fairly new ratio of vascular impedance between MCA and uterine arteries.[6,8] CPR should be considered as an assessment tool in fetuses undergoing third-trimester ultrasound examination, irrespective of the findings of the individual UA and MCA measurements. The brain sparing phenomenon is considered as an adaptive mechanism of the fetus which is activated to protect the fetal brain in adverse conditions. Velocimetry of the uterine artery has been reported by some authors to be more accurate than is that of the UA or fetal MCA in the prediction of adverse outcome. The ratio of vascular impedance between the fetal MCA and uterine

Table 1: Patient characteristics

	Number	Percentage
Age (years)		
<20	15	2.0
20–24	209	27.9
25–29	423	56.4
30–34	57	7.6
≥35	46	6.1
Mean±SD (Range)=28.1±4.78 (18–37 years)		
Parity		
Primigravida	514	68.5
Multigravida	236	31.5
Gestational age		
<37 Weeks	348	46.4
≥37 Weeks	402	53.6
Mean±SD=37.2±3.91		
Socioeconomic status		
Upper	5	0.7
Upper middle	62	8.3
Lower middle	210	28.0
Upper lower	297	39.6
Lower	176	23.5
Mode of delivery		
NVD	343	45.7
LSCS	407	54.3
Fetal Outcome		
Live birth	730	97.3
Still birth	20	2.7
Apgar score at 1 min		
<7	207	28.4
≥7	523	71.6
Apgar score at 5 min		
<7	169	23.2
≥7	561	76.8
Birth weight		
SGA	181	24.8
AGA	549	75.2
NICU admission		
Yes	178	24.4
No	552	75.6
Neonatal mortality		
Yes	63	8.6
No	667	91.4
Cerebroplacental ratio		
Normal	507	67.6
Abnormal	243	32.4
Cerebrouterine ratio		
Normal	443	59.1
Abnormal	307	40.9

NVD: Normal vaginal delivery, LSCS: Lower segment cesarean section, NICU: Neonatal intensive care unit, SGA: Small for gestational age, AGA: Appropriate for gestational age

arteries has not yet been evaluated. Uterine artery Doppler might be expected to reflect placental perfusion, while umbilical Doppler reflects placental pathology. Uterine artery Doppler might be expected to reflect placental perfusion, while umbilical Doppler reflects placental pathology, therefore the CU ratio (CU Ratio) could have a better predictive value for unfavorable outcome.[9-11]

Aims and Objectives

Aim

The aim of the study was to study CPR as predictor of adverse fetal outcome in pregnant women with hypertension from 34 weeks of gestation.

Objectives

Tobjective of the study was to evaluate the role of middle cerebral to UA blood velocity waveforms and fetal outcome in terms of fetal growth restriction, mode of delivery, NICU admission, and APGAR at 5 min.

MATERIALS AND METHODS

This prospective study was conducted in the Post Graduate department of Obstetrics and Gynaecology of GMC Srinagar associated Lalla Ded Hospital over a period of one and a half year. During this period on an average around 400 patients attended the outpatient department on daily basis, 50,432 patients were admitted in our hospital, 34,293 deliveries were conducted. All pregnant women from 34 weeks of gestation with CPR done within 1 week of delivery, admitted or referred to Lalla Ded Hospital.

Inclusion Criteria

The following criteria were included in the study:

1. Women delivering singleton babies
2. Women who are willing to participate in the study from 34 weeks of gestation
3. All pregnant women with gestational hypertension.

Exclusion Criteria

The following criteria were excluded from the study:

1. Women who are not willing to participate in the study
2. Multiple pregnancies
3. Fetal congenital anomalies
4. Intrauterine death.

Methodology

This study was conducted in the Department of Obstetrics and Gynecology at Government Lalla Ded Hospital, Srinagar. A semi-constructed questionnaire was used to collect all relevant obstetric information (maternal age, parity, gestational age at delivery, presence, or absence of medical diseases,). Pregnant women with gestational age (34 weeks onwards) were included in the study. The scan in these women was done within 1 week of delivery considered. CPR value was obtained from the scan. CPR is ratio of pulsatility index of the MCA by the UA pulsatility index. CPR = MCA PI/UA PI.

After taking informed written consent, the recruited patients were subjected to detailed history taking and examination, routine laboratory tests as CBC, liver, and kidney function tests. Ultrasonographic scanning was done trans-abdominally using ultrasound machine equipped with 3.5 Mhz convex probe to evaluate fetal weight, biometry, and Doppler studies. SIEMENS ACUSON X 300 USG machine was used for obtaining the ultrasonogram of the patients. Umblical Artery (Um A), MCA, Uterine Artery (Ut A) was examined by Color Doppler ultrasound and Pulsed wave Doppler a single cutoff value of 1.0 for all cases. Above this value, Doppler velocimetry was considered normal and below it, abnormal. Using this cutoff value, the study population was divided into two groups - those with a normal ratio (>1.0) and those with an abnormal ratio (<1.0). Adverse fetal outcome was analyzed by above mentioned statistical method in terms of emergency cesarean section for fetal distress, low birth weight, Apgar at 5 min, NICU admission, and Neonatal death.

Chi-square test was employed for determining association of CPR and CUR with fetal outcome, in terms of still birth, birth weight, APGAR score at 1 min, APGAR score at 5 min, NICU admission, and neonatal death. Further diagnostic accuracy (Sensitivity, Specificity, PPV, and NPV) of CPR and CUR was also obtained. $P < 0.05$ was considered statistically significant.

RESULTS

The mean maternal age at presentation was 28.1 (±4.78) years with the range from 18 to 37 years. Maximum number of cases was seen between the age group of 25 and 29 years (56.4 %), followed by 20–24 years (27.9%). About 7.6% of the patients were between 30 and 34 years and 6.1% of the patients belonged to age ≥35–37 and 2% belonged to age group <20 years. About 68.5% were primigravida and 31.5% were multigravida. The parity distribution is shown in Tables 1 and 2. The gestational age was between

Table 2: Association of cerebroplacental ratio with mode of delivery

Mode of delivery	Abnormal CPR		Normal CPR		*P*-value
	No.	%age	No.	%age	
NVD	79	32.5	264	52.1	<0.001*
LSCS	164	67.5	243	47.9	
Total	243	100	507	100	

NVD: Normal vaginal delivery, LSCS: Lower segment cesarean section, CPR: Cerebroplacental ratio

Table 3: Association of cerebrouterine ratio with mode of delivery

Mode of delivery	Abnormal CPR		Normal CPR		*P*-value
	No.	%age	No.	%age	
NVD	87	28.3	256	57.8	<0.001*
LSCS	220	71.7	187	42.2	
Total	307	100	443	100	

NVD: Normal vaginal delivery, LSCS: Lower segment cesarean section, CPR: Cerebroplacental ratio

Table 4: Association of cerebroplacental ratio with fetal outcome

Fetal outcome	Abnormal CPR		Normal CPR		*P*-value
	No.	%age	No.	%age	
Still birth					
Yes	20	8.2	0	0.0	<0.001*
No	223	91.8	507	100	
SGA					
Yes	128	57.4	53	10.5	<0.001*
No	95	42.6	454	89.5	
1 min Apgar score					
<7	131	58.7	76	15.0	<0.001*
≥7	92	41.3	431	85.0	
5 min Apgar score					
<7	109	48.9	60	11.8	<0.001*
≥7	114	51.1	447	88.2	
NICU admission					
Yes	90	40.4	88	17.4	<0.001*
No	133	59.6	419	82.6	
Neonatal death					
Yes	31	13.9	32	6.3	0.0008*
No	192	86.1	475	93.7	

NICU: Neonatal intensive care unit, SGA: Small for gestational age, CPR: Cerebroplacental ratio

Table 5: Association of cerebrouterine ratio with fetal outcome

Fetal outcome	Abnormal CPR		Normal CPR		*P*-value
	No.	%age	No.	%age	
Still birth					
Yes	20	6.5	0	0.0	<0.001*
No	287	93.5	443	100	
SGA					
Yes	145	50.5	36	8.1	<0.001*
No	142	49.5	407	91.9	
1 min APGAR score					
<7	160	55.7	47	10.6	<0.001*
≥7	127	44.3	396	89.4	
5 min APGAR score					
<7	128	44.6	41	9.3	<0.001*
≥7	159	55.4	402	90.7	
NICU admission					
Yes	107	37.3	71	16.0	<0.001*
No	180	62.7	372	84.0	
Neonatal death					
Yes	38	13.2	25	5.6	0.0004*
No	249	86.8	418	94.4	

NICU: Neonatal intensive care unit, SGA: Small for gestational age, CPR: Cerebroplacental ratio

34 and 37 weeks in 348 deliveries and 402 deliveries were equal to or above 37 weeks. The mean gestational age was 37.2 ± 3.91. Majority of patients belonged to upper lower (39.6%), followed by lower middle (28%). The least number of cases belonged to upper socioeconomic class (0.7%).

Among 750 patients, majority 407 (54.3%) delivered by cesarean section and rest 343 (45.7%) delivered vaginally. About 97.3% of babies were live births, but the rest (2.7%) were still born who could not be resuscitated at birth. The 1 min APGAR score was <7 in only 28.4% while the rest had a score of 7 ≥7 (71.6). The 5 min APGAR score was <7 in only 23.2% while the rest had a score of 7 ≥7 (76.8%). Majority of the babies (75.2%) were average for gestational age; however, 24.8% were small for gestational age. Although 24.4% babies required NICU care, 75.6% did not require any NICU Admission. About 8.6% case study neonates expired. 507 (67.6%) had normal CPR, while rest 243 (32.4%) had abnormal CPR. 443 (59.1%) had normal CUR, while rest 307 (40.9%) had abnormal CUR.

Among 750 patients with abnormal CPR 67.5% had cesarean Section while rest 32.5% delivered vaginally. Among patients with Normal CUR 52.1% delivered vaginally while rest 47.9% had cesarean section. Among 750 patients with abnormal CUR 71.7% had cesarean section while rest 28.3% delivered vaginally. Among patients with normal CUR 57.8% delivered vaginally while rest 42.2% had cesarean section. About 8.2% had still-birth, 57.4% were small for gestational age, 58.7% had APGAR score <7 at 1 min, 48.9% had APGAR score, 7 at 5 min, 40.4 required NICU admission, and 13.9% neonates died. While those with normal CPR, the difference was statistically significantly for all of the above parameters. About 6.5% had stillbirth, 505.5% were small for gestational age, 55.7% had APAGAR SCORE <7 at 1 min, 44.6% had APGAR SCORE, 7 at 5 min, 37.3% required NICU admission, and 13.2% neonates died while those with normal CUR the difference was statistically significant for all of the above parameters. CP ratio had 60.4% sensitivity, 81.3% specificity, positive predictive value 56.1%, negative predictive value 73.8% and 75.3% diagnostic accuracy with statistically significant positive correlation, to predict abnormal fetal outcome. CU ratio had 68.6% sensitivity and 72.3% specificity, positive predictive value 49.5%, negative predictive value 85.3 and diagnostic accuracy of 71.2% to predict abnormal fetal outcome [Tables 3-5].

DISCUSSION

The study was held in Postgraduate Department of Obstetrics and Gynaecology, Lal Ded hospital, an associated

Hospital of GMC, Srinagar, during the period between (December 2019 and October 2021.) This study included 750 pregnant women who fulfilled the inclusion criteria. Pregnant females with age group from 18 to 37 years were included in the study and the mean patient age was 28.1 with maximum number of cases seen between the age group of 25–29 years (56.4%), followed by 20–24 years (27.9%). About 7.6% of the patients were between 30 and 35 years and 6.1% of the patients were 35–37 years 2% of the patients belonged to <20 years of age. In a study conducted by Mallick *et al*.,[12] the most common age group of the expectant mothers was 26–30 years, with 201 women (40.9%), followed by 21–25 years as seen in 176 (35.8%). 69 women (14.02%) were 31–35-years-old and 34 (6.91%) were over 35 years of age. 12 women were between 15 and 20 years of age, with most of them being 18 or 19 years. Lakhute *et al*.[13] reported the mean age among their study population as 22.31 ± 2.93 years.

Our study had maximum number of primigravida (68.5%). Primigravida is considered to have a higher risk for gestational hypertension. Konwar *et al*.[14] in their study also had maximum cases (68%) in primigravida which is comparable to our study. 46.4% patients between 34 and 37 weeks and 53.6% were equal to or above 37 weeks. In a study conducted by Mallick *et al*.[12] 10.6% were <34 weeks, 29.1% of the patients between 34 and 36 weeks and 60.4% of the patients were >37 weeks. Konwar *et al*.[14] in their study had 6% patients between 30 and 34 weeks, 24% between >34 and 37 weeks 70% >37–40 weeks. Our study had majority of patients belonging to the upper lower (39.6%), followed by lower middle socioeconomic group (28%) and the least number of cases belonging to upper socioeconomic class (0.7%). In a Study conducted by Lakhute *et al*.[13] 45% were from low class, 33% were from middle class, and 11% from upper middle class and thus concluded that socio-economic status to be an important risk factor associated with gestational hypertension. 407 (54.3%) delivered by cesarean section and rest 343 (45.7%) delivered vaginally. About 97.3% were live birth, but (2.7%) were fresh still-born who could not be resuscitated at birth. Muti *et al*.[15] observed 94.4% live birth and 5.45 still birth, and Adiga *et al*.[16] reported 95% live births and 5% still birth rate. APGAR score at 1 min was <7 in only 28.4% while it was >7 (71.6%). Muti *et al*.[15] in her study observed Apgar score of < in 8.9% and >7 in 91.1% babies. In terms of APGAR score at 5 min, 23.2% had APGAR score <7 and 76.8% had score >7. Muti *et al*.[15] in her study had 8.1% with APGAR score <7 and 91.9% with APGAR Score >7.

Majority of the babies (75.2%) were average for gestational age, however (24.8%) were small for gestational age. Lakhute *et al*.[13] found 21.2% and Mallick *et al*.[12] found 20.9% were SGA. About 24.4% babies required NICU admission and 75.6% did not require any NICU Admission. Mallick *et al*.[12] in her study reported 23.4% babies who required NICU admission. About 8.6% neonates expired in the early neonatal period. Shahinaj *et al*.[17] has also reported a neonatal mortality of 5.96% in their study. Normal CPR was observed in 67.6% fetuses, while as 32.4% fetuses had abnormal CPR. El-Guindy *et al*.[18] in his study also reported that 34.1% fetuses had abnormal CPR and 65.9% had normal CPR. Eser *et al*.[19] in their study reported 22% fetuses to have abnormal CPR. In our study, 59.1% fetuses had normal CUR, while as 40.95% had abnormal CUR. El-Guindy *et al*.[18] in his study reported 62% neonates to have normal CUR. In our study with abnormal CPR, the mode of delivery in women with abnormal CPR was LSCS in 67.5% and vaginal delivery in 32.5%. Similar finding of LSCS rate of 62.5% and vaginal delivery in 37.5% has been reported by Shahinaj *et al*.[17] In our study with Abnormal CUR mode of delivery in 28.3% was normal vaginal delivery and caesarean section in 71.7%. Eser *et al*.[19] reported 88.46% cesarean section in patients with abnormal CUR and vaginal delivery in only (11.54%). In our study of neonates with abnormal CPR, still birth rate was 8.2%. This is much less than that reported by Shahinaj *et al*.[17] who observed 17% still -births in their study. Patil *et al*.[20] observed 7.8% still birth in their study.

In neonates with abnormal CPR SGA were seen in 57.4% as per our study. This is similar to Shahinaj *et al*.[17] who reported (52.4%) babies with abnormal CPR who were small for gestational age. Sirico *et al*.[21] also observed SGA in 45.2% babies. Among abnormal CPR in our study, 58.7% babies had APGAR score <7 at 1 min and 48.9% had <7 APGAR score at 5 min. Mariam *et al*. in patients with abnormal CPR reported that 36% patients had <7 APGAR at 1 min and Shahinaj *et al*.[17] reported 61.9% babies had <7 APGAR at 5 min while El-Guindy *et al*.[18] reported APGAR SCORE<7 at 5 min in 59.5% babies. In our study, 40.4% neonates with abnormal CPR required NICU admission. About 77% babies with abnormal CPR required NICU care as reported by El-Guindy *et al*.[18] and Shahinaj[17] 77.6%. We observed neonatal death rate in 13.9% babies with abnormal CPR. This is similar to Shahinaj *et al*.[17] who reported neonatal death as 13.6% neonates with abnormal CPR. Among babies with abnormal CUR, 6.5% had still as per our study. Kanika *et al*.[22] reported 9.09% still birth in babies with abnormal CUR. In women with abnormal CUR, small for gestational age babies was found in 50.5%. Kanika *et al*.[22] reported 65 (22%) neonates with SGA in women with abnormal CUR. However, Adiga *et al*.[16] reported only 47.4% babies with SGA in women with abnormal CUR.

Among abnormal CUR in our study, 55.7% neonates had <7 APGAR score at 1 min and 44.6% had <7 APGAR score at 5 min. Kanika *et al*.[22] reported that 58.8% babies had <7 APGAR at 1 min and 41.1% babies had

<7 APGAR at 5 min in their study of women with abnormal CUR. El-Guindy *et al*.[18] reported that (68.2%) babies had APGAR <7 at 1 min, and (55.1%) babies had APGAR <7 at 5 min. Among babies with abnormal CUR in our study, 37.3% required NICU admission. Kanika *et al*.[22] reported 50% NICU admission in babies having abnormal CUR. Adiga *et al*.[16] reported 31.6% NICU admission. In our study among abnormal CUR, neonatal death rate was 13.2%. El-Guindy *et al*.[18] reported 14% neonatal death rate in babies with abnormal CUR. In the present study CP ratio had 60.4% sensitivity, 81.3% specificity, positive predictive value 56.1%, negative predictive value 73.8%, and 75.3% diagnostic accuracy with statistically significant positive correlation, to predict abnormal fetal outcome. Comparison of our results of the sensitivity, specificity, positive predictive value, and negative predictive value of MCA/UA ratio with those of the study of Gramellini *et al*.,[23] Shahinaj *et al*.,[17] El-Guindy *et al*.[18] In our study with CU ratio had 68.6% sensitivity and 72.3% specificity, positive predictive value 49.5%, negative predictive value 85.3 and diagnostic accuracy of 71.2% to predict abnormal fetal outcome. Comparison of our results of the sensitivity, specificity, positive predictive value, and negative predictive value of MCA/UA ratio with those of the study of Adiga *et al*.,[16] El-Guindy *et al*.[18]

CONCLUSION

Hypertensive disorders of pregnancy have a significant impact on the fetal outcome. Fetal Dopplerplays a crucial role in monitoring the redistribution of blood in the fetus and the placental circulation. CPR and CUR assesses parameters on both placental side and also the fetal response. They help us to identify fetuses who are at higher risk of adverse perinatal outcomes and hence intensive monitoring during labor can be done for such fetuses. This is of great help in a high risk place with high case load like our hospital, as it identifies fetuses at potential risk during labor. CUR can be used as a complementary test.

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