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"TO STUDY THE CORRELATION OF CEREBROPLACENTAL RATIO (CPR) WITH ADVERSE PERINATAL OUTCOME IN SINGLETON UNCOMPLICATED TERM PREGNANCY"

Obstetric & Gynaecology

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ABSTRACT

Introduction: The brain sparing (BS) phenomenon is considered as an adaptive mechanism of the fetus which is activated to protect the fetal brain in adverse conditions. The current challenge is therefore to identify vulnerable fetuses at risk of hypoxic complications, particularly within an apparently low-risk cohort before the onset of labor. The cerebroplacental ratio (CPR) is emerging as an important predictor of adverse pregnancy outcome, and this has implication for assessment of well being of SGA and AGA fetuses close to term[4] . **Material And Methods:** It was a hospital based prospective observational study. After taking informed consent from the patient, she was subjected to detailed history taking and examination and underwent antenatal USG with colour Doppler for CPR calculation. **Observations And Results:** Mean age of females enrolled in the study was 25.95±3.50 years. 63.5% patients had normal vaginal delivery, 35.0% had caesarean delivery and 1.5% had instrumental delivery for intrapartum fetal compromise..Patients divided in groups on the basis of Doppler finding i.e CPR<1.08(n=50) and CPR>1.08 (n=150), adverse outcomes significantly high in group with CPR<1.08 than in group with CPR>1.08. . CPR ≤1.08 was found to be 56.25% Sensitive, 95.83 % Specific in predicting the poor outcome. **Conclusion** : With high specificity and positive predictive value of CPR it is likely that those having a normal CPR will have very less chance of adverse perinatal outcome and therefore their delivery can be conducted at peripheral centre and those with low CPR should be timely referred to higher centre where there are facilities for extensive fetal monitoring during the intrapartum period with availability of neonatal unit.

KEYWORDS

INTRODUCTION

Globally,fetal hypoxia is one of the major causes of high perinatal morbidity and mortality rates, also being a major contributor to adverse perinatal outcomes(stillbirth,hypoxic–ischaemic brain injury and various neurodevelopmental disabilities)[1] . For parents and families, the psychosocial and financial impact of these complications are profound and long lasting.

The intrapartum period is one of the most indispensible period for the fetus when fetoplacental circulation is challenged to the highest degree as it is a "asphyxia process". Uterine contractions are associated with significant decline in uterine artery flow velocities leading to decrease in placental perfusion causing fetal hypoxia as labor progresses[2] .

Fetal hypoxia activates a number of defense mechanisms, such as modification of fetal heart rate (FHR), increase in blood pressure, and redistribution of the 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 resistance index (MCA RI) values[3] .

The brain sparing (BS) phenomenon is considered as an adaptive mechanism of the fetus which is activated to protect the fetal brain in adverse conditions.

Majority of cases of intrapartum hypoxia occur in pregnancies with no antenatal risk factors, making prediction of intrapartum fetal complications difficult.

The current challenge is therefore to identify vulnerable fetuses at risk of hypoxic complications, particularly within an apparently low-risk cohort before the onset of labor.

The cerebroplacental ratio (CPR) is emerging as an important predictor of adverse pregnancy outcome, and this has implication for assessment of well being of SGA and AGA fetuses close to term[4] .

The Cerebroplacental ratio is an obstetric ultrasound tool that reflects redistribution of cardiac output to the cerebral circulation resulting from hypoxia and increased placental resistance. The CPR is calculated by dividing the doppler indices of MCA by umbilical artery(MCA PI/UA PI). Although theS/D ratio, RI, and PI have been reported when computing the CPR, more recently, the PI is the computation of choice[5] . The CPR reflects mild increase in placental resistance with mild reduction in the fetal brain vascular resistance.

It has recently been shown that a proportion of appropriate for gestational age fetuses (AGA i.e., fetuses with estimated fetal weight between 10th and 90th percentile) despite being of good size has impaired growth velocity and fail to meet their genetic growth potential and are thereby at risk of adverse pregnancy outcome[6] .

Even AGA fetuses with low CPR ratio at term are at increased risk of compromise during labor leading to increase rate of obstetrical interventions and neonatal morbidity and mortality.

The study was planned with the aim to investigate the association between fetal CPR and adverse perinatal outcome in uncomplicated term AGA pregnancies.

MATERIAL AND METHODS

It was a hospital based prospective observational study. Cases were selected from women attending Antenatal OPD and being admitted to Labour Room for delivery at Department of Obstetrics and Gynaecology at Muzaffarnagar Medical College and hospital, Muzaffarnagar, Uttar Pradesh.period of study was 18 months. Enrolled patients were 200 in accordance with the following criteria.

Inclusion Criteria

- Patient gives consent
- Term pregnancy
- Singleton gestation
- Primiparous or previous normal vaginal delivery or previous caesarean section

Exclusion Criteria

- Patient refusing to give informed consent
- Preterm
- Multiple pregnancy
- Congenital malformations
- Intra Uterine Foetal Death
- Medical illness complicating pregnancy
- Malpresentation

After taking informed consent from the patient, she was subjected to detailed history taking and examination and underwent antenatal USG with colour Doppler for CPR calculation .

Procedure For CPR Calculation

Umbilical Artery Pulsatility Index (UA PI), Middle Cerebral Artery Pulsatility Index (MCA PI) and Cerebro Placental Ratio = [(MCA PI) /

(UA PI)], was measured by a single trained practitioner with the patient lying in a semi-recumbent position.

Doppler parameters were be measured according to the recommendations by the International Society of Ultrasound in Obstetrics and Gynaecology, i.e. using an angle of insonation $< 30^0$, in the absence of maternal and foetal movements and using an automated trace of at least three consecutive waveforms. were recorded using an automated trace of at least 3 consecutive waveforms. CPR was calculated as the simple ratio between the MCA PI and the UA PI. A single cutoff value of CPR 1.08 was taken, CPR ≤ 1.08 was considered as abnormal while CPR > 1.08 was considered as normal.

Outcomes

A. Mode of delivery:

1. Instrumental deliveries for fetal compromise.
2. Caesarean section for fetal compromise

B. Neonatal outcome was assessed by

1. PRIMARY OUTCOME:
- Perinatal Outcome
- APGAR Score at 1 and 5 min

2. SECONDARY OUTCOME:
- Perinatal morbidity (NICU admission)
- Perinatal mortality

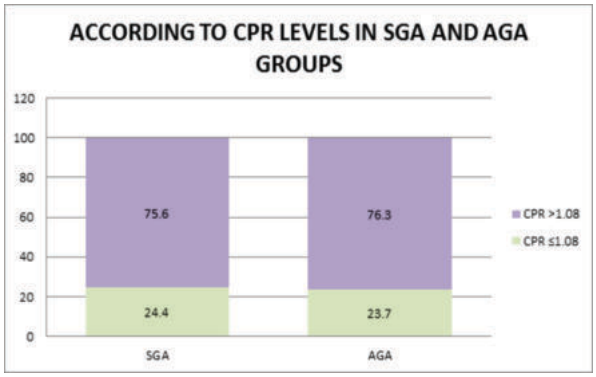
The perinatal outcomes were correlated with CPR

OBSERVATION AND RESULTS

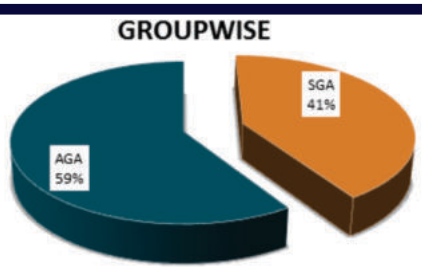
Table I: Distribution Of Cases According To Demography And Obstetrical History

SN	Age Group	No.	%
1-	≤25 years	92	46.0
2-	26-30 years	96	48.0
3-	31-35 years	10	5.0
4-	>35 years	2	1.0
	Habitat		
1-	Rural	140	70.0
2-	Urban	60	30.0
	Literacy status		
1-	Illiterate	110	55.00
2-	Literate	90	45.00
	Socio-economic Status		
1-	Upper middle(2)	01	0.50
2-	Lower middle(3)	70	35.00
3-	Upper lower (4)	103	51.50
4-	Lower (5)	26	13.00
	Parity		
1-	Nullipara (P0)	126	63.00
2-	Primipara (P1)	52	26.00
3-	Multipara (≥P2)	22	11.00

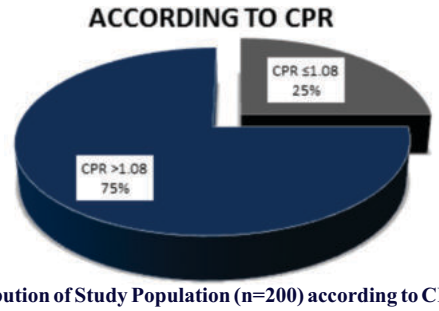
All the females enrolled in the study were between age 19-37 years. Mean age of females enrolled in the study was 25.95±3.50 years.Majority of females were from Rural areas (70.0%) 55.0% of the females enrolled in the study were Illiterate.51.50% of the females belonged to upper lower SES . Majority of the females enrolled in the study were Nullipara (63.0%) followed by Primipara (26.0%). Only 22 (11.0%) females enrolled in the study were multipara.



Distribution of cases according to CPR levels in SGA and AGA groups



Groupwise Distribution of Study Population (n=200)



Distribution of Study Population (n=200) according to CPR*

Out of 200 term pregnancies 118 (59.0%) pregnancies were AGA in which 25.00% had CPR ≤1.08 and 75.00% has CPR>1.08.Among total 82 (41.0%) SGA pregnancies 25.00% patients had CPR≤1.08 and 75.00% patients had CPR>1.08

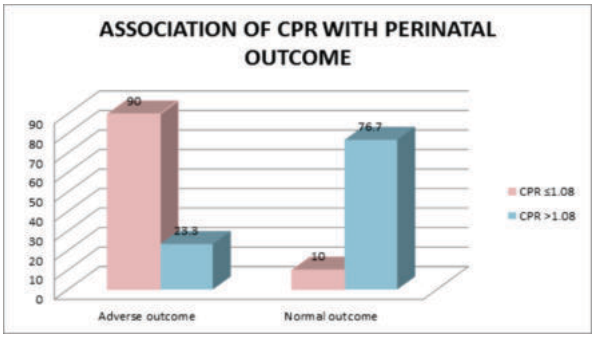
Table I: Distribution Of Cases According To Mode Of Delivery And Adverse Outcomes

SN	Mode of delivery	CPR ≤1.08 (n=50)		CPR >1.08 (n=150)		Total (N=200)		Significance of differences	
		No.	%	No.	%	No.	%	χ^2	'p'
1-	*LSCS for *IFC	36	72	34	22.7	70	35	28.763	<0.001
2-	Instrumental delivery for IFC	2	4	1	0.6	3	1.5	13.844	<0.001
3-	Normal vaginal Delivery	12	24	115	76.7	127	63.5	44.4	<0.001
	TOTAL	50	100	150	100	200	100		
SN	Adverse Outcome	No	CPR ≤1.08 (n=50)		CPR >1.08 (n=150)			Significance of differences	
			No.	%	No.	%		χ^2	P
1-	*LSCS for IFC	70	36	72	34	22.7		28.763	<0.001
2-	Instrumental for IFC	3	2	4	1	0.6		13.844	<0.001
3-	Apgar <7 at 5 m	9	9	18	0	0.0		21.193	<0.001
4-	Perinatal mortality	1	1	2	0	0.0		5.902	0.015
5-	NNU admission	28	26	52	2	0.1		62.360	<0.001
6-	No adverse outcome	120	5	10	115	76.6		64.732	<0.001
	TOTAL	231	79		152				

Out of 200 patients 63.5% patients had normal vaginal delivery, 35.0% had caesarean delivery and 1.5% had instrumental delivery for intrapartum fetal compromise.

The rate of vaginal delivery were significantly high in normal CPR group (76.7% vs 22.7%, p<0.001), while the rate of LSCS and instrumental delivery for IFC were higher in low CPR group (72 % vs 22.7 %,p<0.001 and 4 vs 0.6% ,p<0.001 respectively).

Total 200 patients when divided in two groups on the basis of Doppler finding i.e CPR≤1.08(n=50) and CPR>1.08 (n=150), adverse outcomes were found to be significantly high in group with CPR≤1.08 than in group with CPR>1.08 (90 % vs 23.3 %;p<0.001); Odds Ratio 23.54 (95% CI: 9.28-59.71). Major causes of perinatal morbidity were- hypoxic ischaemic encephalopathy, neonatal sepsis, respiratory distress syndrome, birth asphyxia.



Out of 200 total term pregnancies, 50 had CPR ≤1.08 and 150 had CPR >1.08. Proportion of patients with CPR ≤1.08 was found to be significantly higher as compared to those with CPR >1.08 for all the adverse outcomes i.e. LSCS (72 %vs.22.7 %;p<0.001), Instrumental delivery (4 % vs. 0.6%;p<0.001), Apgar <7 at 5 min (18 % vs. 0.0%;p<0.001), Intrauterine death (2 % vs. 0.00%;p=0.015) and NNU admissions (52 % vs. 0.1%;p<0.001).

Proportion of patients with no adverse outcome was found to be significantly higher among patients with CPR >1.08 as compared to those with CPR ≤1.08 (76.6 % vs. 10%, p<0.001).

Table III: Performance of CPR in the prediction of adverse outcome in Study Population (n=200)

CPR levels	Poor Outcome (n=80)		Normal outcome (n=120)	
CPR ≤1.08 (n=50)	45 (True Positive)		5 (False Positive)	
CPR >1.08 (n=150)	35 (False Negative)		115 (True Negative)	
Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
56.25	95.83	90	95.83	80

Out of total 200 term pregnant patients 50 (25%) were having CPR ≤1.08, in which 45 (90%) had poor outcome and rest 5 (10 %) had normal outcome while in rest 150 (75%) pregnant patients with CPR >1.08, 115 (76.67 %) had normal outcome and rest 35 (23.33 %) had poor outcome. CPR ≤1.08 was found to be 56.25% Sensitive, 95.83 % Specific in predicting the poor outcome. Positive predictive value and Negative predictive value of CPR was 90 % and 95.83 % respectively. Overall diagnostic accuracy of CPR ≤1.08 was found to be 80 %.

DISCUSSION

Intrapartum period has always been a very crucial state as the placental circulation is challenged to the most and it is very difficult to categorise those patients who will land up in emergency caesarean for fetal distress and who will have adverse perinatal outcomes. Therefore, there is a need for a tool that can predict, in advance, adverse perinatal outcome. Here comes the role of CPR which is emerging as a very promising tool for optimising the identification of at risk fetuses. It is also emerging as a marker of failure to reach growth potential at term.

This study was planned to find out the association of fetal CPR and perinatal outcome in term pregnancy in antenatal women.

In our study population, mean age of patients enrolled in study was 25.95±3.50 years. Age of patients ranged between 19 to 37years. Mean gestational age at the time of USG Doppler scan was 267.04 ±7.84days. Mean gestational age of delivery was 269.83 ±7.78days, The study group of 200 term pregnancies were divided into AGA and SGA on the basis of estimated fetal weight (EFW <10th percentile classified as SGA and those between 10th -90th percentile classified as AGA). Out of total 200 patients 59% were AGA and 41% were SGA. Such high prevalence of SGA was mainly because our hospital is a tertiary care referral centre and most of high risk pregnancies are referred here.

The study population were further divided in two group on the basis of Doppler velocimetry taking CPR cut-off value of 1.08, [Gramellini et al (1992)[7] and Odibo et al (2005)[8]. CPR below or equal to 1.08 was taken as abnormal or low and above was considered to be normal.

When the demography was compared in two group divided according to CPR cut off we had found no significant difference between the two group in respect to age, literacy, habitat, socioeconomic status, parity. Similar study done by Prior et al (2013)[9] also noted no difference in age, ethnicity, habitat, literacy status between different CPR/CU ratio percentile group.

In present study when the association of CPR and perinatal outcome was analysed in total study population (n=200) we found that 90 % of patients in abnormal CPR group had adverse outcome as compared to 23.3 % in normal CPR group [p=<0.001; Odds ratio 23.54 (95% CI:9.28-59.72)]. This was consistent with the finding of study done by Figueras et al (2015)[10] in which they reported that more than half of low CPR fetuses had adverse perinatal outcomes(50.7% vs 6.3%,p=<0.05).

In current study out of 200 total patients 70 (35%) patients had emergency LSCS, 3(1.5%) patients had instrumental delivery for fetal compromise and 127 (63.5%) patients had normal vaginal deliveries. The rate of normal vaginal delivery in low CPR group was significantly less compared to normal CPR group (24% vs 76.7 %,p<0.001). Prior et al (2013)[9] in their study had also observed that birth by normal vaginal delivery was up to three times more likely in the setting of normal CPR. Out of 51 patients in low CPR group only 12 (23.5%) had vaginal delivery, Out of these 6/12(50%) babies had adverse outcome. Out of these 6 babies, 2 had intrauterine fetal demise and 4(33.3%) of these babies required Neonatal unit (NNU) admission.

While looking for association between fetal CPR and low Apgar scores, we found significant higher number of babies born with Apgar <7 at 5min of birth were present in group with abnormal CPR [18% vs 0.0%, p<0.001; Odds ratio 19.73;95 % CI (2.31-168.25)]. This hold true for both SGA and AGA pregnancies (15% vs 0.0, p=0.018 and 21.4 vs 0.0,p=0.001). Prior et al (2015)[11] reported a greater proportion of babies with poor Apgar score in abnormal CPR group (27.5% vs 1.3%, p<0.001)

In the current study the rate of admission to neonatal unit were also reported to be high in group with abnormal CPR [52% vs 0.1%, p<0.001, Odds ratio-39.98; 95 % CI(11.23-142.24)] . Khalil et al (2015)[2] in their study also found that low or abnormal CPR was independently associated with NICU admission irrespective of fetal size (OR 0.55, 95% CI 0.33-0.92, P<0.021).

There was one perinatal mortality reported in our study , in SGA group with low CPR, this patient did not have any other known risk factor and she had an intrauterine fetal demise at 37wk 3day just 2 day after the Doppler scan.

No statistically significant difference was found in AGA and SGA pregnancies for perinatal mortality in low CPR and normal CPR (p=0.57 and p=0.09 respectively) as the number was very less. While comparing it perinatal mortality in total study population a significant difference was observed in group with low and normal CPR (2% vs 0.0%, p=0.015). However Arias et (1994)[12] had reported significant high perinatal death in low CPR group (18% vs 0%, p<0.05) similar to our finding.

Recent studies [Prior et (2013)[9], Morales-Rosello et al (2015)[3], Khalil et al (2015)[2] and the present study have demonstrated that AGA foetuses with abnormal CPR have a high incidence of adverse outcome. Because these AGA foetuses may not be identified using traditional clinical tools it is prudent to consider routine late third trimester evaluation of growth as well as measurement of CPR for identifying AGA foetuses that could suffer from placental insufficiency and fail to meet their genetic growth potential at term.

Our study suggests that a normal CPR assures the clinician of fetal well being. It's high specificity 95.83% and low false positive rate 5% will prevent unnecessary tests and interventions. On the other hand a good positive predictive value of CPR (90 %) suggests that pregnancies with abnormal CPR are at high risk of adverse perinatal outcome and should be delivered at a centre with good monitoring facility.

CONCLUSION

The CPR measure combining both umbilical and MCA Doppler indices appear to be a very promising tool for optimising the identification of at risk fetuses.

With decreasing cost of USG equipment and availability of USG

Doppler machine at the peripheral health centre, this measurement of CPR ratio in term pregnancies can be included as a component part of third trimester antepartum testing. These Doppler studies (UA PI and MCA PI) can be performed reliably in a few min by the doctors once they are suitably trained.

CPR thus calculated can be used to stratify at risk pregnancies which in turn will guide in decision making regarding mode and place of delivery. With high specificity and positive predictive value of CPR it is likely that those having a normal CPR will have very less chance of adverse perinatal outcome and therefore their delivery can be conducted at peripheral centre and those with low CPR should be timely referred to higher centre where there are facilities for extensive fetal monitoring during the intrapartum period with availability of neonatal unit.

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