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ORIGINAL ARTICLE

Study of Association of Fetal Cerebroplacental Ratio with Adverse Perinatal Outcome in Uncomplicated Term AGA Pregnancies

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Abstract

Background The cerebroplacental ratio (CPR) is emerging as a predictor for adverse perinatal outcome in term pregnancies. Earlier, it has shown a role in small for gestational age (SGA) pregnancies, but a proportion of appropriate for gestational age foetuses (AGA) despite of good size have impaired growth velocity and are thereby at risk of adverse outcome. CPR has implication for assessment of well being of SGA and AGA foetuses close to term.

Objective To investigate the association between foetal CPR and adverse perinatal outcome in uncomplicated term AGA pregnancies.

Methods This was a prospective observational study done in Department of Obstetric and Gynaecology, King George Medical University, Lucknow, over a period of one year. Women > 37 week singleton pregnancy with no known risk factor who had Doppler USG done within a week of delivery were included. CPR was calculated by dividing the Doppler indices of middle cerebral artery (MCA) by umbilical artery (MCA PI/UA PI). CPR < 1 was taken as abnormal. These patients were followed up till delivery to look for various perinatal outcomes. Results Out of 127 low-risk AGA pregnancies who went for USG colour Doppler scan, 117 patients who met our inclusion criteria were analysed; out of 117 patients 23(i.e. 19.65 %) were having CPR < 1 and 94 patients (i.e. 80.34%) were having CPR>1. Among 23 patients with CPR < 1, 22 (91.30%) had adverse outcome as compared to only 20.21% patients with CPR > 1, and this is found to be statistically significant ($p < 0.001$).

Conclusion Our study found CPR measure to be a very promising tool for optimising the identification of at risk foetus in low-risk AGA pregnancies.

Keywords Cerebroplacental ratio · Appropriate for gestational age · Small for gestational

Introduction

Identification of the fetus at risk of adverse outcome at term is a challenge to both clinician and researcher. Despite the fact that fetal growth restriction (FGR) is a known risk factor for adverse pregnancy outcome, 2/3rd of cases having adverse outcome are not small for gestational age (SGA), (a commonly use proxy for FGR) [1], so relying on fetal size alone will fail to identify fetuses at risk of adverse perinatal outcome at term.

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 [2].

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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 [3].

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. It is manifested by increased diastolic flow in middle cerebral artery(MCA) as a result of increased placental resistance. It measures the proportion of blood flow supplying the brain and the placenta.

The CPR is calculated by dividing the doppler indices of MCA by umbilical artery(MCA PI/UA PI). Although the S/D ratio, RI, and PI have been reported when computing the CPR, more recently, the PI is the computation of choice [4]. The CPR reflects mild increase in placental resistance with mild reduction in the fetal brain vascular resistance. An abnormal CPR may result from 3 types of Doppler measurement patterns. The first is when the MCA and UA PI are in lower and upper range of the normal, respectively, resulting in a low CPR. The second is when there is abnormal low MCA PI and UA PI is normal. The third pattern consists of abnormal low MCA and abnormally high UA PI resulting abnormally low CPR [3].

The CPR can detect perinatal risk in the setting of reassuring UA PI (but abnormal MCA), or even if both UA and MCA PI are within normal range.

The intrapartum period is one of the most indispensible period for the fetuses when fetoplacental circulation is challenged to the highest degree. Uterine contractions are associated with significant decline in uterine artery flow velocities leading to decrease in placental perfusion causing fetal hypoxia. Fetal hypoxia can result in neonatal squeal including neurological injury, seizure, and death. Majority of cases of intrapartum hypoxia occur in pregnancies with no antenatal risk factors, making prediction of intrapartum fetal complications difficult. Even AGA fetuses with low CPR ratio at term are at increased risk of compromise during labor leading to increase rate of obstetrics 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 Method

This was a prospective observational study done in Department of Obstetrics and Gynecology, King George medical University, Lucknow, over a period of 1 year (September 2017 to August 2018). The patients ≥ 37 week were subjected to USG plus Color Doppler scan and were followed till delivery. Pregnancies complicated by fetal anomaly, anueploidy or intra-uterine fetal demise, multiple pregnancies, women undergoing elective cesarean, women undergoing cesarean section for indication other than intrapartum fetal compromise (IFC), women with major risk factors and SGA pregnancies (EFW < 10th percentile) [8] and LGA pregnancies (EFW > 90th percentile) were excluded from the study. After recruitment, women had ultrasound plus Color Doppler performed in supine position with the head of bed elevated at 45 degree by Toshiba Xario prime USG machine with 3–7 MHz transabdominal curvilinear transducer. Gestational age was calculated on the basis of last menstrual period and whenever possible confirmed by crown lump length measurement or by earliest scan that patients had. Fetal biometry and AFI were recorded. EFW (Estimated fetal weight) was calculated using the Hadlock formula based on the combination of biparital diameter, head circumference, abdominal circumference, and femur length. Fetuses having Estimated fetal weight (EFW) < 10th percentile for gestational age were classified as SGA (small for gestational age) while fetuses having EFW between 10th and 90th percentile were classified under AGA (Appropriate for gestational age) [5].

Doppler evaluation of the umbilical artery (UA) was performed in a free loop of umbilical cord. The middle cerebral artery (MCA) evaluation was done in a cross-sectional view of the fetal head in vascular circle of Willis at approximately 1 cm after its origin from the internal carotid artery [6]. All Doppler waveforms were recorded in the absence of fetal breathing movements or uterine contractions. The angle of insonation was kept < 30 degrees. The umbilical artery (UA) and middle cerebral artery PI 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 was taken, CPR ≤ 1 was considered as abnormal while CPR > 1was considered as normal [7].

Doppler findings were not used for clinical management. Labor was then managed as per local protocols and guideline. After delivery, intrapartum and neonatal outcome data were collected from patients case notes.

Outcome measures for this study included mode of delivery, cesarean, and instrumental deliveries for IFC (intrapartum fetal compromise). Diagnosis of fetal compromise was based on CTG abnormalities, FHS irregularities, meconium stained liquor, or a combination of these. Neonatal outcome was assessed by examining the birth weight, 5 min APGAR score, admission to neonatal unit, and perinatal mortalities.

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 21.0 statistical Analysis Software.

Table 1 Demographic profile of study population, $n=117$

S. nos		CPR ≤ 1	CPR > 1
1.	Mean age of patients (yrs)	27.08 ± 3.34	26.01 ± 3.67
2.	Mean parity of patients	0.61 ± 0.84	0.44 ± 0.65
3.	Mean gestational age at the time of Doppler scan (weeks)	38.55 ± 1.33	38.21 ± 1.17
4.	Mean gestational age at the time of delivery (weeks)	38.72 ± 1.31	38.77 ± 1.14

Results

We studied 127 AGA pregnancies with no risk factor who went for USG and color Doppler examination, out of these, 10 were excluded, and finally, 117 AGA pregnancies that met the inclusion criteria were analyzed. The patients were divided according to CPR cutoff value of 1. Out of 117 total patients, 23 (i.e., 19.65%) were having CPR ≤ 1 and 94 patients (80.34%) were having CPR > 1. The demographic profile of study population was noted and was illustrated in Table 1. No difference in maternal age, parity mean gestation at delivery was observed between the two groups.

Among 23 patients with CPR ≤ 1, 22 (91.30%) had adverse outcome as compared to only 20.21% patients with CPR > 1, and this is found to be statistically significant ($p<0.001$) (Table 2). By using logistic regression analysis, we had observed that patients with CPR ≤ 1 had ninefold increase rate of cesarean section for intrapartum fetal compromise (Odd ratio (95% CI):9.65 (3.46–26.93). The rate of instrumental deliveries for fetal compromise were significantly high in group with CPR ≤ 1 (13.04% vs 1.06%; $p=0.025$). We had found a significantly higher proportion of neonatal unit admission in group with CPR ≤ 1 in comparison to those with CPR > 1 (60.86%vs 1.06; $p<0.001$).Also none of the babies born in cases with normal CPR had APGAR score < 7 at 5 min (Table 3).

For AGA pregnancies cutoff of CPR at ≤ 1 was found to be 52.5% sensitive, 97.4% specific in predicting the poor outcome. Positive predictive value and negative predictive value of cutoff value of CPR 1 was 91.3% and 79.8%, respectively. Overall diagnostic accuracy of CPR ≤ 1 was found to be 82.1%.

Discussion

There is considerable difficulty in identifying pregnancies in which placental function is inadequate to support fetal growth potential and greater risk of adverse perinatal outcome exists. This dilemma is particularly difficult in late pregnancy and during intrapartum period. Intrapartum period has always been a very crucial state, and it is very difficult to categorize these patients who will have adverse perinatal outcome. Therefore, there is a need for a tool that can predict in advance adverse perinatal outcome. Cerebroplacental ratio which incorporates data not only on placental status (UA PI) but also on fetal response (MCA PI) is emerging as a promising tool for optimizing the identification of at risk fetuses.

The result from this study demonstrates that assessment of fetal CPR measured at term in AGA pregnancies can predict adverse perinatal outcome.

In the current study, the rate of operative and instrumental deliveries for IFC was significantly high in AGA pregnancies. Khalil et al. [2] also reported increased rate of both cesarean and instrumental delivery for presumed fetal compromise in AGA pregnancies with low CPR compared to

Table 2 Association of CPR and perinatal outcome among AGA pregnancies ($n=117$)

S. nos	Outcome	CPR ≤ 1 ($n=23$)		CPR > 1($n=94$)		Total ($N=117$)	
		No.	%	No.	%	No.	%
1	Adverse outcome	21	91.3	19	20.21	40	34.18
2	Normal outcome	2	8.69	75	79.78	77	65.8

$\chi^2=41.508$; $p<0.001$

Table 3 Association of CPR with various adverse outcome among AGA pregnancies ($n=117$)

S. nos	Adverse outcome	No	CPR ≤ 1 ($n=23$)		CPR > 1 ($n=94$)		Significance of differences		Odds ratio (95% CI)
			No.	%	No.	%	χ^2	p	
1	LSCS	34	16	69.56	18	19.14	52.94	< 0.001	9.65 (3.46–26.93)
2	Instrumental	4	3	13.04	1	1.06	8.03	0.025	–
3	Apgar < 7 at 5 m	5	5	21.7	0	0.00	21.34	< 0.001	–
5	NNU admission	15	14	60.86	1	1.06	59.133800	< 0.001	–
6	No adverse outcome	77	2	8.69	75	79.78	41.51	< 0.001	0.024 (0.005–0.112)

normal CPR (11.0% vs 8.7%, $p=0.043$ and 11.2% vs 7.8%, $p=0.003$, respectively).

We observed higher rate of NNU admission, 60.86% in low CPR group as compared to 1.06% in normal CPR group had required NNU admission. Flood et al. [8] in their study also found that low or abnormal CPR was independently associated with NICU admission (69.4% vs 22%, $p<0.0001$). Prior et al. [9] also reported higher NICU (neonatal intensive care unit) admission rates among abnormal CPR cohorts, but this did not reach significance. 21.7% babies had APGAR score < 7 in low CPR group while no baby in normal CPR group had APGAR < 7 ($p=0.001$) this was consistent with the finding of Ropacka Lesiak et al. [10] who also reported a greater proportion of babies with poor Apgar score in abnormal CPR group (27.5% vs 1.3%, $p<0.001$).

These finding strongly supports that a low CPR when detected at term is associated with number of adverse perinatal outcomes regardless of birth weight.

Currently, Doppler studies are not recommended for fetuses with normal weight [11, 12]. The Cochrane Database of Systematic Reviews (2010) reported that there is still no clear evidence that a fetal Doppler examination of low risk pregnant women can reduce the prevalence of fetal mortality/morbidity [12]. The evidence for the value of fetal Doppler assessment in predicting adverse neonatal outcome has been demonstrated mainly in SGA foetuses [8].

However, recent studies [2, 4, 9] have demonstrated that AGA fetuses with abnormal CPR have a high incidence of adverse outcome. Because these AGA fetuses 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 fetuses that could suffer from placental insufficiency and fail to meet their genetic growth potential at term.

Our study adds to the growing body of evidence that abnormal CPR is predictor of increased obstetrics intervention rates and adverse perinatal outcome not only in SGA but also in AGA pregnancies.

The most appropriate cutoff value of CPR for detection of adverse perinatal outcome is still debateble. Traditionally researchers have used the absolute value (< 1 [7, 8], ≤ 1.1, or < 1.08 [10]), and more recently centiles (< 5th or 10th centile [11, 13, 14] or multiple of median (MoM) [15] have used. Flood et al. [8] had reported that the ratio had lower sensitivities but higher specificities where as centile value had high sensitivities but lower specificities. However in our opinion absolute cutoff value < 1 has good association with adverse perinatal outcome and is easy to use and remember.

Our study had shown a sensitivity of 61%, specificity of 93.4% positive predictive value 83.1%, negative predictive value 82.1%, and diagnostic accuracy 79% for CPR in prediction of adverse outcome in total study population.

In light of observation made in our study, we propose that measurement of CPR in term pregnancies can be integrated into clinical practice. CPR can be used to risk stratify pregnancies before labor so that pregnancies with abnormal CPR can be delivered at a center equipped with facilities for fetal surveillance, emergency cesarean delivery, and neonatal unit.

Limitation of Study

Doppler assessment results were not blinded, giving rise to the possibility that this knowledge could have influenced subsequent clinical intervention and a treatment effect. However, during the study period, intervention in the form of induction of labor was undertaken only by the protocol of our hospital, no decisions were taken on the basis of CPR value. Another limitation is that cord blood analysis was not done which could have correlated better with neonatal status.

Conclusions

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

With decreasing cost of USG equipment and availability of USG Doppler machine at the peripheral health center, 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 minutes 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 and timely intervention leading to improved perinatal outcome. With high specificity 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 center and those with low CPR should be timely referred to higher center where there are facilities for extensive fetal monitoring during the intrapartum period with availability of neonatal unit.

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Compliance with ethical standards

Conflict of interest They authors declare that they have no conflict of interest.

Ethical approval Institutional ethical committee clearance was obtained for study. All procedures performed in studies involving human par-

ticipants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Khalil A, Thilaganathan B. Role of uteroplacental and fetal Doppler in identifying fetal growth restriction at term. Best Pract Res Clin Obstet Gynaecol. 2017;38:38–47.
2. Khalil AA, Morales-Rosello J, Morlando M, et al. Is fetal cerebroplacental ratio an independent predictor of intrapartum fetal compromise and neonatal unit admission? Am J Obstet Gynecol. 2015;213(1):54.e1–10.
3. DeVore GR. The importance of the cerebroplacental ratio the evaluation of fetal well-being in SGA and AGA fetuses. Am J Obstet Gynecol. 2015;213(1):5–15.
4. Morales-Rosello J, Khalil A, Morlando M, et al. Changes in fetal Doppler indices as a marker of failure to reach growth potential at term. Ultrasound Obstet Gynecol. 2014;2014(43):303–10.
5. Royal College of Obstetricians and Gynaecologists. The investigations and measurement of the small for Gestational Age fetus. Green top Guidelines no.31,London:RCOG;2013.
6. Bhide A, Acharya G, Bilardo CM, et al. ISUOG practice guidelines: use of Doppler ultrasonography in obstetrics. Ultrasound Obstet Gynecol. 2013;2013(41):233–9.
7. Shaheen S, Bano I, Ahmad I, et al. Doppler cerebroplacental ratio and adverse perinatal outcome. J South Asian Feder Obst Gynae. 2014;6(1):25–7.
8. Flood K, Unterscheider J, Daly S, et al. The role of brain sparing in the prediction of adverse outcomes in intrauterine growth restriction: results of the multicenter PORTO Study. Am J Obstet Gynecol. 2014;211:88.
9. Prior T, Mullins E, Bennett P, et al. Prediction of intrapartum fetal compromise using the cerebroumbilical ratio: a prospective observational study. Am J Obstet Gynecol. 2013;208(2):124.
10. Ropacka-Lesiak M, Korbelak T, Breborowicz G, et al. Cerebroplacental ratio in prediction of adverse perinatal outcome and fetal heart rate disturbances in uncomplicated pregnancy at 40 weeks and beyond. Arch Med Sci. 2015;11(1):142–8.
11. Berkley E, Chauhan SP, Abuhamad A. Society for maternal-fetal medicine publications committee: doppler assessment of the fetus with intrauterine growth restriction. Am J Obstet Gynecol. 2012;206(4):300–8.
12. Alfirevic Z, Stampalija T, Gyte GM. Fetal and umbilical Doppler ultrasound in normal pregnancy. Cochrane Database Syst Rev. 2010:CD001450.
13. Flatley C, Kumar S. Is the fetal cerebroplacental ratio better that the estimated fetal weight in predicting adverse perinatal outcomes in a low risk cohort? J Maternal-Fetal Neonatal Med. 2018;16:1–7.
14. Bligh LN, Alsolai AA, Greer RM, et al. Cerebroplacental ratio thresholds measured within two weeks of birth and the risk of Cesarean section for intrapartum fetal compromise and adverse neonatal outcome. Ultrasound Obstet Gynecol. 2017 Jun 8.
15. Khalil A, Morales-Rosello J, Khan N, et al. Is cerebroplacental ratio a marker of impaired fetal growth velocity and adverse pregnancy outcome? Am J Obstet Gynecol. 2017;216(6):606.

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