MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.7.10.16

Study of Assessment of Cerebroplacental Ratio at 35-37 Weeks of Gestation in the Prediction of Adverse Perinatal Outcome

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Abstract

Doppler velocimetry is a rapid noninvasive test that provides valuable information about the hemodynamic situation of the fetus and is an efficient diagnostic test of fetal jeopardy that helps in management of high-risk pregnancy. Present study was aimed to assess cerebroplacental ratio at 35-37 weeks of gestation in the prediction of adverse perinatal outcome. Present study was single-center, prospective, observational study, conducted in pregnant women, >18 years of age, Singleton pregnancy, undergone a third trimester USG Doppler at 35-37 weeks. The PI ratio were measured for both UA and MCA and Cerebral placental ratio (CPR) was calculated. A low cerebroplacental ratio was defined as <1. Out of the total 283 cases studied, low cerebro-placental ratio (<1) was seen in 33.9% cases. Incidence of MSL was 55.2% in cases with low CP ratio as compared to 36.4% in cases with normal CPR, difference was statistically significant (p<0.01). There is a significant statistical association (p value <0.01) between mode of delivery and low /normal CP ratio, with higher incidence of Caeserean section in cases with low CPR ratio. Normal Doppler findings were seen in 57.2% cases with normal CP ratio as compared to only 9.4% cases with low CP ratio. Combined utero-placental and cerebro-placental insufficiency on Doppler was seen in 52.1% cases of low CP ratio as compared to 19.3% cases with normal CPR which was statistically significant (p<0.01). Overall sensitivity and specificity of CP ratio (<1) to predict adverse perinatal outcome was 53.4% and 98.1% while PPV and NPV was 97.9% and 56.1%. Overall accuracy was 70.3%. Area under ROC to predict adverse perinatal outcome was 0.734 (95% CI: 0.67-0.79, p<0.01). Cerebro-placental ratio can predict adverse perinatal outcome in uncomplicated pregnancies at term with good accuracy.

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Key Words

Cerebro-placental ratio, antenatal fetal surveillance, fetal compromise adverse neonatal outcome

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Received: 15 March 2024
Accepted: 20 April 2024
Published: 26 May 2024

Citation: Anagha Anil Jinturkar, Swati Ramchandra Gurav and Meghana Biju, 2024. Study of Assessment of Cerebroplacental Ratio at 35-37 Weeks of Gestation in the Prediction of Adverse Perinatal Outcome. Res. J. Med. Sci., 18: 10-16, doi: 10.36478/makrjms. 2024.7.10.16

INTRODUCTION

The antepartum assessment of fetal well-being has assumed a critical importance in the management of pregnancy. Doppler velocimetry is a rapid noninvasive test that provides valuable information about the hemodynamic situation of the fetus and is an efficient diagnostic test of fetal jeopardy that helps in management of high-risk pregnancy. The development of Doppler ultrasound evaluation of uteroplacental and fetoplacental circulation is one of the most important achievements of modern obstetrics[1].

Currently, assessment of the cerebroplacental ratio (CPR) is becoming widely introduced in clinical practice. The cerebroplacental ratio has been suggested as a marker of placental insufficiency and fetal compromise[2,3]. Fetuses with abnormal CPR that are appropriate for gestational age or have late onset SGA have a higher incidence of fetal distress in labour requiring emergency LSCS, low cord pH and increased admission rate in NICU.

Hence low CPR can be used as an early marker for adverse perinatal outcome and may be used to identify high risk pregnancies[4,5]. Few other studies on the clinical usefulness of CPR have reported divergent results the integration of CPR in clinical practice is thus under debate[1,6,7]. Present study was aimed to assess cerebroplacental ratio at 35-37 weeks of gestation in the prediction of adverse perinatal outcome

MATERIALS AND METHODS

Present study was single-center, prospective, observational study, conducted in department of Obstetrics and Gynaecology, B.J.G.M.C and SGH, PUNE, India. Study duration was of 2 years (January 2020-December 2021). Study approval was obtained from institutional ethical committee.

Inclusion Criteria:

- Pregnant women, >18 years of age, Singleton pregnancy, with gestational age between 35 and 37 weeks, undergone a third trimester USG Doppler, willing to participate in present study.

Exclusion Criteria:

- Women <18 years.
- Non consenting pregnant women
- Patients with preeclampsia, known cases of uteroplacental insufficiency.

Study was explained to patients in local language and written consent was taken for participation and study. A detailed clinical history was taken from all cases regarding the age of the women, socio economic status, dietary status any medical illness etc., In obstetric history, married life, number of pregnancies, mode of previous deliveries, number of abortions, various presenting complaints was noted. Menstrual history was obtained with last menstrual period.

Detailed General physical examination, Systemic examination and Obstetric examination was done in each patient. Obstetric examination includes gestational age, parity, sonographic investigations, previous mode of deliveries, uterine anomalies, AFI, any high-risk factors in mother as well as fetus etc.

All women were then subjected to Obstetric Doppler at 35-37 weeks, which was performed with 3.5-MHz curvilinear transducer (Pro Logiq 500, GE healthcare) with the patient in the supine position and the fetus in quiet and resting phase. Doppler flow velocimetries were recorded from umbilical artery-a free loop of cord equidistant from the abdominal and placental insertion point.

For MCA Doppler, a transverse image of the fetal head and colour flow imaging was used to display the circle of Willis. The MCA in the near field was insonated within 1 cm of its origin from the internal carotid artery. The PI ratio were measured for both UA and MCA. The Cerebral placental ratio (CPR) was calculated as:

CPR = MCA / UA PI

Cases were followed till delivery. The indication for elective delivery or the decision to abstain from intervention was left to the discretion of the attending obstetrician and included considerations such as gestational age, estimated fetal weight and weight gain, coexisting maternal disease, reversed end diastolic flow in umbilical arteries, abnormal fetal heart tracing, poor biophysical profile. No fetus was delivered on the basis of Doppler findings.

The prevalence of low (<1) Cerebral placental ratio was recorded and correlated with perinatal outcome like, Gestation age at birth, Mode of delivery, Low Birth weight, Low APGAR, need of resuscitation and Need of NICU admission.

All the data was noted down in a pre-designed study proforma. Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed by Chi-Square test with Continuity Correction for all 2X2 tables and Fisher's exact test for all 2X2 tables. Quantitative data was represented using Mean±SD. Analysis of Quantitative data between the two groups was done using unpaired t-test if data passed Normality test and by Mann-Whitney Test if data failed Normality test. A $p<0.05$ was taken as level of significance. Results were graphically represented where deemed necessary. SPSS Version 21.0 was used for most analysis and Microsoft Excel 2010 for graphical representation.

RESULTS AND DISCUSSIONS

A low cerebroplacental ratio was defined as <1. Out of the total 283 cases studied, low cerebro-placental ratio (<1) was seen in 33.9% cases.

Mean age of the females was 32.35 years with no difference in cases with low and normal CP ratio (p-0.56). There was no statistical correlation (p value=0.56) between age of patient and low /normal CP ratio.

Cases with low and normal CP ratio were comparable with regards to gestational age (p>0.05). There was no statistically significant association (p value=0.56) between gestational age at presentation and low /normal CP ratio.

Prevalence of low CPR was 36.4% in primigravida mothers while it was 33.7% in multi-para mothers (p-1.0). There was no statistically significant association (p-value=1.0) between parity and low /normal CP ratio. Incidence of MSL was 55.2% in cases with low CP ratio as compared to 36.4% in cases with normal CPR. The difference was statistically significant (p<0.01). There is a significant statistical association (p<0.01) between incidence of MSL and low /normal CP ratio, with higher incidence of MSL in cases with low CPR ratio.

Incidence of Caesarean section was 78.1% in cases with low CP ratio as compared to 46% in cases with normal CP ratio. The difference was statistically significant (p<0.01). There is a significant statistical association (p<0.01) between mode of delivery and low /normal CP ratio, with higher incidence of Caeserean section in cases with low CPR ratio.

Out of total 96 cases with low CP ratio, 59 cases (61.5%) had non-reactive NST while incidence of non-reactive NST was 31.6% in cases with normal CP ratio. The difference was statistically significant (p<0.01). There is a significant statistical association (p<0.01) between NST findings and low /normal CP ratio, with higher incidence of non-reactive NST in cases with low CPR ratio.

Normal Doppler findings were seen in 57.2% cases with normal CP ratio as compared to only 9.4% cases with low CP ratio. Combined utero-placental and cerebro-placental insufficiency on Doppler was seen in 52.1% cases of low CP ratio as compared to 19.3% cases with normal CPR which was statistically significant (p<0.01).

Mean birth weight was significantly low in cases with low CP ratio (1.847 vs 2.223 Kg, p<0.01). There is statistically significant association between lower mean birth weight and low CPR.

Mean APGAR score at 1 min (6.43 vs 7.54, p<0.01) and at 5 mins (7.51 vs 8.46, p<0.01) was significantly lower in cases of low CP ratio. There is significant statistical association between low APGAR score at birth with low CP ratio.

No statistically significant association was seen between low CPR and gender of the baby (males-53.4%, females-46.6%, p-0.10).

Incidence of low birth weight was observed as 89.6% in cases with low CP ratio as compared to 70.6% in cases with normal CP ratio. The difference was statistically significant (p<0.01). There is statistically significant association between low birth weight infants with low CP ratio.

Need for resuscitation was observed in 26% of cases with low CP ratio as compared to 7.5% in cases with normal CP ratio. The difference was statistically significant (p<0.01). There is statistically significant association between need for resuscitation and low CP ratio.

Incidence of NICU admission was observed as 70.8% in cases with low CP ratio as compared to 9.1% in cases with normal CP ratio. The difference was statistically significant (p<0.01). There is statistically significant association between NICU admission rate and low CP ratio

Requirement of oxygen supplementation was 82.3% in cases with low CP ratio as compared to 5.3% in cases with normal CP ratio. The difference was statistically significant (p<0.01). There is statistically significant association between need for O2 supplementation and low birth weight.

Incidence of hypoglycemia was observed as 69.8% in cases with low CP ratio as compared to 0.5% in cases with normal CP ratio. The difference was statistically significant (p<0.01). There is statistically significant association between incidence of hypoglycemia and low CP ratio.

All the cases with normal CP ratio and 99% cases with low CP ratio had normal development of neurological milestones by the end of one year (p-1.0). There is no statistically significant association between attainment of neurological milestones at age 1 and low CP ratio.

Overall sensitivity and specificity of CP ratio (<1) to predict adverse perinatal outcome was 53.4% and 98.1% while PPV and NPV was 97.9% and 56.1%.

Fig. 1: Diagonal Segments are produced by ties

Table 1. Distribution of study groups as per cerebro-placental ratio at 35-37 weeks

CPR	N	percentage
Cases (<1)	96	33.9%
Controls (>=1)	187	66.1%
Total	283	100.0%

Table 2. Comparison among cases with low and normal cerebro- placental ratio

Variables	Group		
	Cases (n=96)	Controls (n=187)	Total
Age (yrs.)	32.06 ± 6.08	32.50 ± 5.93	0.56
Gestational Age (BD)	35.86 ± 0.55	35.84 ± 0.59	0.76
Gestational Age (BS)	35.91 ± 0.62	35.90 ± 0.62	0.92

Table 3: Comparison of parity among cases with low and normal cerebro-placental ratio

	Group			
	Cases (n=96)	Controls (n=187)	Total	p-value
Parity				
Prime	8 (36.4 %)	14 (63.6 %)	22	1
Multi	88 (33.7 %)	173 (66.3 %)	261	
Incidence of Me conium stained liquor				
Absent	43 (44.8 %)	119 (63.6 %)	162 (56.9 %)	<0.01
Present	53 (55.2 %)	68 (36.4 %)	121 (43.1 %)	
Mode of Delivery				
LSCS	75 (78.1 %)	86 (46.0 %)	161 (56.9 %)	<0.01
Vaginal	21 (21.9 %)	101 (54.0 %)	122 (43.1 %)	
NST				
NR (Non- reactive)	59 (61.5 %)	59 (31.6 %)	118 (41.7 %)	<0.01
R (Reactive)	37 (38.5 %)	128 (68.4 %)	165 (58.3 %)	

Table 4: Comparison of Doppler findings

Doppler Changes	Group		
	Cases (n=96)	Controls (n=187)	Total
Normal	9 (9.4 %)	107 (57.2 %)	116 (41.0 %)
Brain Sparing Effect	28 (29.2 %)	0	28 (9.9 %)
UP Insufficiency	9 (9.4 %)	44 (23.5 %)	53 (18.7 %)
UP + FP Insufficiency	50 (52.1 %)	36 (19.3 %)	86 (30.4 %)
p-value <0.01			

Table 5: Comparison of mean birth weight and APGAR scores

Variables	Group		
	Cases (n=96)	Controls (n=187)	Total
Birth Weight (Kg)	1847.40 ± 460.50	2223.53 ± 501.67	<0.01
APGAR			
1 min	6.43 ± 2.21	7.54 ± 1.85	<0.01
5 min	7.51 ± 2.15	8.46 ±1.69	<0.01

Table 6: Gender and birth weight

	Group			
	Cases (n=96)	Controls (n=187)	Total	p-value
Gender of Baby				
Female	38 (39.6 %)	94 (50.3 %)	132 (46.6 %)	0.1
Male	58 (60.4 %)	93 (49.7 %)	151 (53.4 %)	
Birth Weight				
< 2.5 Kg	86 (89.6 %)	132 (70.6 %)	218 (77.0 %)	<0.01
>= 2.5 Kg	10 (10.4 %)	55 (29.4 %)	65 (23.0 %)	

Table 7: Neonatal outcome

	Group			
	Cases (n=96)	Controls (n=187)	Total	p-value
Resuscitation required	25 (26 %)	14 (7.5 %)	39 (13.8 %)	< 0.01
Incidence of NICU admission	68 (70.8 %)	17 (9.1 %)	85 (30 %)	< 0.01
O2 Supplementation	79 (82.3 %)	10 (5.3 %)	89 (31.4 %)	< 0.01
Hypoglycemia	67 (69.8 %)	1 (0.5 %)	68 (24.0 %)	< 0.01
>= 2.5 Kg Neurological Milestones (at 1 year)	99 (99 %)	187 (100 %)	282 (99.6 %)	1

Table 8. Efficacy of low cerebro-placental ratio to predict adverse perinatal outcome

CPR	Group			
	Cases (n=96)	Controls (n=187)	Total	p-value
<1	2 (1.9 %)	94 (53.4 %)	96 (33.9 %)	< 0.01
>1	105 (98.1 %)	82 (46.6 %)	187 (66.1 %)	

CPR	percentage
Sensitivity	53.4%
Specificity	98.1%
PPV	97.9%
NPV	56.1%
Accuracy	70.3%

Overall accuracy was 70.3%. Area under ROC to predict adverse perinatal outcome was 0.734 (95% CI: 0.67-0.79, p<0.01).

Intrapartum complications are a major contributor to adverse perinatal outcomes and significant neonatal morbidity[8]. The compromised fetuses frequently require rapid delivery by emergency operative delivery that carries considerably more maternal risk than less urgent procedures. Neonatal outcomes are also significantly poorer following emergency caesarean for fetal distress[9].

Evaluation of fetal condition is thus an integral part in the management of pregnancy. The most widely used screening method for intrapartum hypoxia is electronic fetal heart rate monitoring. It has very poor specificity and positive predictive value for hypoxia and adverse neonatal outcome[10]. The cerebroplacental ratio, a ratio of the middle cerebral artery PI and umbilical artery PI, is widely considered to be more indicative of adverse neonatal outcome than the assessment of blood flow indices individually[11,12].

In present study, out of the total 283 cases studied, low cerebro-placental ratio (<1) was seen in 33.9% cases at 35-37 weeks. In S Shaheen *et al.*[13] 21 cases had low CP ratio, prevalence of low CPR was 33.8%. In Mohamed ML *et al.*[14] study, low CP ratio was seen in 25 of these females giving a prevalence of 16.7%. Gruettner B *et al.*[14] and Bonnevier A *et al*.[15] in their respective studies observed prevalence of low CPR as 17% and 21% respectively.

Incidence of Caesarean section was 78.1% in cases with low CP ratio as compared to 46% in cases with normal CP ratio. The difference was statistically significant (p<0.01).

S Shaheen *et al.*[13] also observed high rate of caesarean section in cases with low CP ratio (47.6 5 vs 2.9%, p<0.01). Mohamed ML *et al.*[14] found a significant increase in the prevalence of cesarean sections in the group with CPR ratios <1.1 (40% vs. 25.6%). An abnormal CPR had six-fold increased odds of cesarean section for intra-partum fetal compromise. Prior *et al.*[16] reported that the CPR was an independent predictor of CS for intrapartum fetal compromise. Of those who underwent cesarean delivery for fetal distress, 36.4% had an abnormal CPR compared with 10.1% (p<.001) that had a normal CPR. Another study conducted by Bligh *et al.*[17] reported that pregnancies delivered by CS had significantly lower mean CPR than the rest of the study cohort.

Mohamed ML *et al.*[14] found that infants with an abnormal CPR ratio had a significantly higher incidence of CTG abnormalities than those with a normal CPR ratio (80%) vs (12.8%), respectively and that the likelihood of the having an abnormal FHR was increased more than twenty-seven-fold with abnormal CPR. In the line of our study Ropaka *et al.*[18] reported that the percentage of abnormal CTG records in group with abnormal CPR (62.3%) was significantly higher when compared to group with normal CPR (19.0%). Prior *et al.*[19] also reported that infants with a low CPR ratio had significantly higher rates of CTG abnormalities when compared with infants with a normal CPR ratio (82% vs 31%). Similar findings were noted in present study.

Incidence of low birth weight was observed as 89.6% in cases with low CP ratio as compared to 70.6% in cases with normal CP ratio (p<0.01). Mean APGAR score at 1 min (6.43 vs 7.54, p<0.01) and at 5 mins (7.51 vs 8.46, p<0.01) was significantly lower and requirement of NICU admission was significantly higher (70.8% vs 55.1%, p<0.01). Requirement of oxygen supplementation was (82.3% vs 62.6%) and Incidence of hypoglycemia (69.8% vs 48.7%) was also significantly higher among cases with low CPR.

S Shaheen *et al.*[13] observed high incidence of LBW babies (76.2% vs 12.2%, p<0.01), more cases with low APGAR at 5 mins (26.6% vs 2.9%, p<0.01) and high NICU admission rate (66.7% vs 17.1%, p<0.01) among cases with low CP ratio. Mohamed ML *et al.*[14] found a significant relation between CPR and low birth weight/ Apgar score. Neonates with CPR <1.1 had significantly high incidence of LBW (41% vs 16%, p<0.01) and lower Apgar score at 1 min and 5 min than those with CPR >1.1 (36% vs 11.2%, p<0.01) and (20% vs 2.4, p<0.01), respectively. In addition, the rate of NICU admission was observed to be significantly higher in neonates with CPR <1.1 than those with CPR <1.1 (32 vs. 8.8%) respectively. Similar results were also seen in the observations made by Prior *et al.*[19] and Ropacka-Lesiak *et al.*[18]

In present study, overall sensitivity and specificity of CP ratio (<1) to predict adverse perinatal outcome was 53.4% and 98.1% while PPV and NPV was 97.9% and 56.1%. Overall accuracy was 70.3%. Area under ROC to predict adverse perinatal outcome was 0.734 (95% CI: 0.67- 0.79, p<0.01).

S Shaheen *et al.*[13] observed that abnormal CPR has an overall sensitivity, specificity and positive and negative predictive values for predicting an adverse outcome as 62%, 80%, 62% and 80%, respectively. Mohamed ML *et al.*[14] on evaluation of the performance of CPR revealed that it has 63% sensitivity, 71% specificity and 70% accuracy and the positive and negative predictive values were 24% and 93% respectively.

Murata *et al.*[20] found that CPR with cut-off value of 1.1 had 62% sensitivity and 74.5% specificity to predict adverse outcome. Bonnevier A *et al.*[15] observed the ROC area under curve (AUC) as 0.65 for

CPR (95% CI-0.56-0.77, p<0.01). Vollgraff *et al.*[21] observed ROC curves for the prediction of adverse perinatal outcome of CP ratio as 0.778 (95% CI 0.715-0.831).

Thus, to summarize, present study observed that cerebro-placental ratio is a good predictor of adverse perinatal outcome in uncomplicated pregnancies. The cerebroplacental ratio index is thus useful in clinical practice as a tool for antenatal monitoring of these women in order to select those at high risk of intra- and postpartum fetal complications.

CONCLUSION

Present study concludes that cerebro-placental ratio can predict adverse perinatal outcome in uncomplicated pregnancies at term with good accuracy. The cerebroplacental ratio index is useful in clinical practice in antenatal monitoring of these women in order to select those at high risk of intra- and postpartum fetal complications.

Cerebroplacental ratio has the advantages over the other methods of antepartum fetal surveillance such as early predictor, completely non-invasive, easily available, cost effective and requires lesser expertise and has a small learning curve.

Cerebroplacental ratio can predict women at significant risk of intrapartum fetal compromise and/or adverse neonatal outcome those could be offered elective birth. This could potentially reduce the number of emergency caesarean section procedures performed and thus improving maternal and neonatal outcomes.

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