Original Research Article

Prospective study of role of cerebro placental ratio in predicting perinatal outcome in appropriate for gestation age (AGA) babies at 35- 37 weeks

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Abstract

Background: The fetal cerebropla cental ratio (CPR) emerging as an important predictor of adverse pregnancy outcome, and this has implications for the assessment of well-being in fetuses diagnosed as small for gestational age (SGA) and those appropriate for gestational age (AGA) close to term. **Aim:** To evaluate the usefulness of the ratio of pulsatility index (pi) of the foetal middle cerebral artery (mca) to pulsatility index (pi) of umbilical artery (UA) i.e cerebro placental ratio (CPR) in predicting the adverse perinatal outcome. **Materials and Methods:** Totally 239 singleton pregnant women with a cephalic presentation at 35 – 37 weeks gestation Who are Attending the Out-Patient Ward Of Madras Medical Mission Hospital, Chennai, between 2017-2018 were Included in The Study. **Results:** Umbilical artery PI measured during ultrasound scanning and range between 0.4 to 1. Maximum saw within 0.4 to 1.Middle cerebral artery PI was measured during ultrasound scanning and range between 0.4 to 1.8. Maximum seen within 0.4 to 1.6. Cerebroplacental ratio (CPR) was calculated after measuring the PI of UA and MCA. Maximum were above 1. 91% of babies have APGAR score > 7 in 1 minute and 8 % babies have APGAR score < 7 in 1 minute in a study group. **Conclusion:** It is a common consensus that doppler should be done only in IUGR babies. However, our paper clearly indicates that we can prevent stillbirth for babies with deranged doppler in AGA babies. In conclusion, lower CPR at term was independently associated with an increased need for operative delivery for presumed fetal compromise and admission to the NICU. The rate of operative delivery for presumed fetal compromise was higher in AGA fetuses with low CPR.

Key Words: CPR (Cerebro- Placental Ratio) Umbilical, Artery Pulsatility Index, Umbilical Artery Resistive Index, Doppler Investigation.

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Received Date: 21/05/2019 Revised Date: 08/06/2019 Accepted Date: 19/07/2019
DOI: https://doi.org/10.26611/10081124

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 08 August 2019

INTRODUCTION

The incidence of impaired placentation and adverse perinatal events is higher in SGA than in appropriate- for-gestational- age (AGA) foetuses with a birth weight above the 10th percentile. However, a study of 30780 singleton pregnancies examined at 30- 34 weeks gestation reported that the majority of cases for each adverse outcome were in the AGA group[1], including about 70% of stillbirth , 80% of cases of Caesarean section for foetal distress, those with venous cord blood pH≤7.1, 5 min Apgar score < 7 and admission to the neonatal unit (NNU) or neonatal intensive care unit (NICU) and 85%

How to cite this article: G Yuvabalakumaran, K Ranjeeta. Prospective study of role of cerebro placental ratio in predicting perinatal outcome in appropriate for gestation age (AGA) babies at 35- 37 weeks. *MedPulse – International Journal of Radiology.* August 2019; 11(2): 55-60. http://www.medpulse.in/Radio%20Diagnosis/

of those with arterial cord blood pH≤7.0.[2] It could therefore be argued that, if adverse outcome is the consequences of impaired placentation , prenatal care should be directed at identifying hypoxemic rather than small foetuses and consequently, screening should focus on the detection of pregnancies with low CPR rather than those with low estimated foetal weight. Some evidence in favour of such a concept was provided by studies reporting that low CPR, regardless of foetal size is associated independently with the need for operative delivery for presumed foetal compromise, low neonatal blood pH and NNU admission.[3] However, a major screening study at 32 weeks gestation reported that the performance of low CPR in screening for adverse perinatal outcomes is poor, with detection rates of 5-11%, at false positive rate (FPR) of about 5%.[4] The study reported that the prediction of adverse outcome by low CPR was better if the time interval between assessment and delivery was ≤ 2 weeks rather than > 2 weeks and consequently , suggested that the performance of screening by CPR at 36 weeks may be superior to that at 32 weeks .[5]The cerebroplacental ratio (CPR) is emerging as an important predictor of adverse pregnancy outcome and this has implications for the assessment of foetal well – being in foetuses diagnosed as small – for-gestation – age (SGA) and those appropriate–for–gestational – age (AGA) close to term.[6] Interest in this assessment tool has been rekindled because of recent reports associating an abnormal ratio with adverse perinatal events and associated postnatal neurological outcome.[7] Foetuses with an abnormal CPR that are appropriate – for – gestational – age or have late onset SGA (> 34 weeks of gestation)have a higher incidence of foetal distress in labour requiring emergency Cesarean delivery, a lower cordpH , and an increased admission rate to the newborn intensive care unit (NICU) when compared with foetuses with a normal CPR. Foetuses with early – onset SGA (<34 weeks of gestation) with an abnormal CPR have a higher incidence of the following when compared with foetuses with a normal CPR : (1) lower gestational age at birth,[2] lower mean birthweight,[3] lower birthweight centile,[4] birthweight less than the 10th centile,[5] higher rate of Cesarean delivery for foetal distress in labour,[6] higher rate of Apgar scores less than 7 at 5 minute,[7] an increased rate of neonatal acidosis,[8] an increase rate of newborn intensive care unit (NICU) admission,[9] higher rate of adverse neonatal outcome, and[10] a greater incidence of perinatal death.[8] The CPR is also an earlier predictor of adverse outcome than the biophysical profile, umbilical artery, or middle cerebral artery. In conclusion, the CPR should be considered as an assessment tool in foetuses undergoing third – trimester ultrasound examination, irrespective of the findings of the individual umbilical artery and middle cerebral artery measurement .[9,10]

MATERIALS AND METHODS

Totally 239 singleton pregnant women with cephalic presentation at 35 – 37 weeks gestation Who are Attending the Out Patient Ward Of Madras Medical Mission Hospital, Chennai Were Included in The Study. An obstetric ultrasound scan (U/S) was carried out on request by the clinician on all selected patients at 35 -37 weeks gestation and coded for foetal presentation , placental position , foetal heart rate (FHR) , approximate ultrasonoFigureic age , BPPS , umbilical artery (UA) PI , RI and S/D and middle cerebral artery (MCA) PI , RI and S/D. The ultrasound machine used were real time machines. The transducer frequency was 3.5 – 5.0 MHz, the Doppler sample volume was 2mm and the wall filter was 50 – 100 Hz. The examination was performed with the mother in a semi – recumbent position during relative foetal inactivity and apnea. This is because the end diastolic flow (EDF) decreases with decreasing foetal heart rate and foetal breathing movements increase variability in the Doppler measurements. The study population included singleton pregnant women with cephalic presentation at 35 – 37 weeks gestation. The study arms were defined as Group 0 : Mothers with singleton cephalic presentation at 35 – 37 weeks and with a Doppler ultrasound indicative of an abnormal cerebral / placental ratio (CPR < 1.0) .Group 1 : Mothers with singleton cephalic presentation at 35 – 37 weeks with a Doppler ultrasound indicative of a normal cerebral / placental ratio (CPR > 1.0) .

INCLUSION CRITERIA

1. Gravid women at 35 – 37 weeks Gestation
2. Singleton pregnancy
3. Cephalic presentation
4. Normal fetal anatomic survey

EXCLUSION CRITERIA

1. Multiple pregnancy
2. Foetuses with malpresentation
3. Foetuses with congenital malformation
4. Intrauterine foetal death

METHODOLOGY

An obstetric ultrasound scan (U/S) was carried out on request by the clinician on all selected patients at 35 -37 weeks gestation and coded for foetal presentation, placental position , foetal heart rate (FHR) , approximate ultrasono Figureic age, BPPS, umbilical artery (UA) PI, RI and S/D and middle cerebral artery (MCA) PI, RI and S/D. The ultrasound machine used were real-time machines. The transducer frequency was 3.5 –5.0 MHz, the Doppler sample volume was 2mm and the wall filter

was 50 – 100 Hz The examination was performed with the mother in a semi-recumbent position during relative foetal inactivity and apnea. This is because the end-diastolic flow (EDF) decreases with decreasing foetal heart rate and foetal breathing movements increase variability in the Doppler measurements. The umbilical artery (UA) was sampled at the middle of a free loop of umbilical cord . This is because the EDF is higher near the umbilical cord insertion into the foetal abdomen than near the placental insertion and vice versa at the placental end. It could also be assessed at the level of the foetal bladder. For middle cerebral artery (MCA), a transverse image of the foetal head was obtained at the level of the sphenoid bones. Colour flow imaging was used to display the circle of Willis. The MCA in the near field was insonated about 1 cm distal to its origin from the internal carotid artery. By using the optimal spectral trace from each artery, the Pulsatility index (PI) was calculated from the of a minimum of five consecutive waveforms on a frozen image. A series of three readings were taken for each artery to avoid errors. The cerebral / placental ratio (CPR) was calculated from the MCA PI and UA PI. A CPR of > 1.08 are considered normal and a CPR of < 1.08 abnormal. U/S foetal heart rate, biometric measurements, BPPS and MCA / UA Doppler results were used to determine management. The pregnancies will be followed and the final perinatal outcome of each will be assessed by various intrapartum and neonatal indicators like Cesarean section for foetal distress, low birth weight (LBW), Apgar score < 7 in 5 min, intensive care unit admission (NICU), stillbirth (SB) or perinatal death . Perinatal outcome will be considered as adverse by presence of one or more of these indicative outcome.

STASTICAL ANALYSIS

Statistical analysis is conducted based on sufficiently large sample size and comparison is done with various characters. 2 way and 3 way classification Figures are adopted to present the data. Significance of the study is ascertained by means of Chi square test, Student t- test and Normality test at 5% level of significance. Also, the confidence interval at 90% or 95% is used to express the variation of the data.

RESULTS

A total of 239 singleton pregnant women in the cephalic presentation were prospectively examined. MCA PI and UA PI are measured in all pregnant women at 35 – 37 weeks gestation and CPR were calculated. The pregnancies will be followed and the final perinatal outcome of each will be assessed by various intrapartum and neonatal indicators like Cesarean section for fetal distress, APGAR score < 7 in 5 minutes, low birth weight, NICU admission, stillbirth or perinatal death. The perinatal outcome will be considered as adverse by the presence of one or more of the indicative outcomes.

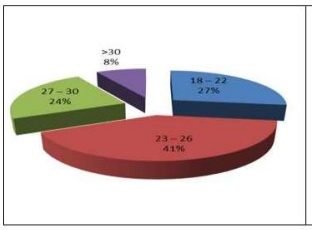

Figure 1: Age Distribution

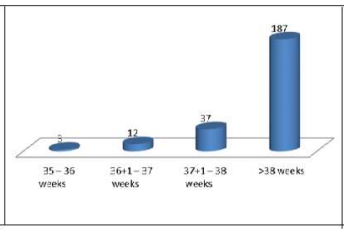

Figure 2: GA In Weeks At Termination

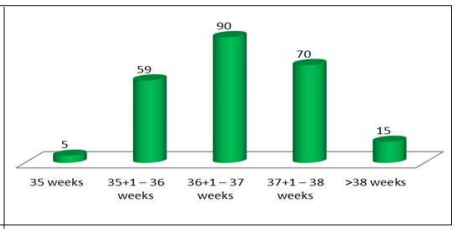

Figure 3: GA in weeks during USG

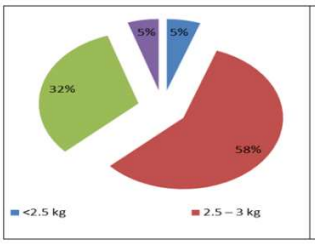

Figure 4: ESTIMATED FOETAL WEIGHT

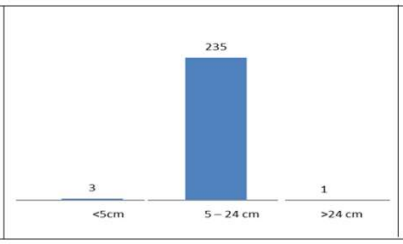

Figure 5: AMNIOTIC FLUID INDEX

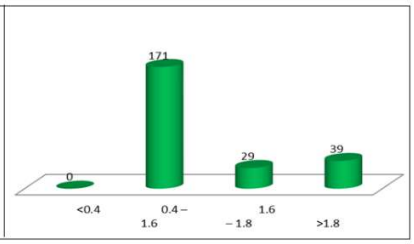

Figure 6: UMBILICAL ARTERY PI

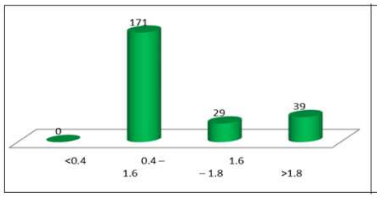

Figure 7: MIDDLE CEREBRAL ARTERY PI

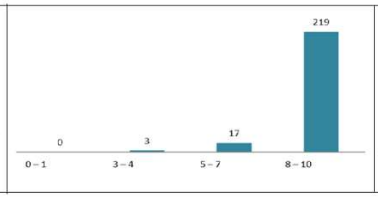

Figure 8: APGAR SCORE IN 1 MINUTE

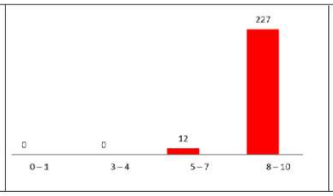

Figure 9: APGAR SCORE IN 5 MINUTE

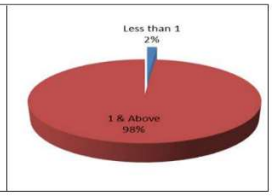

Figure 10: CEREBRO PLACENTAL RATIO (CPR)

Figure: 1 shows the age group ranged from 18 years to as much as> 30 years, the maximum women being in the age group 22 – 26 years. Figure 2: Women between 35 to 41 weeks gestation were included in the study, 35 – 36 weeks 1.26 %, 36 – 37 weeks 5.02 %, 37 – 38 weeks 15.48% and > 38 weeks 78.24%. Figure 3: Women between 35 to 38 weeks gestation were included in the study. 35 weeks 2.09%, 35 – 36 weeks 24.69%, 36 – 37 weeks 37.66%, 37 – 38 weeks 29.29% and > 38 weeks 6.28%. Figure 4: The estimated fetal weight (EFW) range from 2.5 to 3.5 kg, the maximum weight is within 2.5 to 3 kg. Figure: 5 Amniotic fluid index (AFI) were measured during ultrasound scanning. Maximum was within 5 to 24 cm. Figure 6:- Umbilical artery PI measured during ultrasound scanning and range between 0.4 to 1. Maximum seen within 0.4 to 1. Figure 7: Middle cerebral artery PI were measured during ultrasound scanning and range between 0.4 to1.8. Maximum seen within 0.4 to 1.6. Figure8.0:- 91% babies have APGAR score > 7 in 1 minute and 8 % babies have APGAR score < 7 in 1 minute in a study group. Figure 9 :- 94% babies have APGAR score > 7 in 5 minute and 5 % babies have APGAR score < 7 in 5 minute in a study group. Figure :10 Cerebroplacental ratio (CPR) was calculated after measuring PI of UA and MCA. Maximum were above 1. There were 85 (27%) adverse neonatal outcomes (composite outcome defined as pHa.

DISCUSSION

The CPR incorporates data of both the placental status using the umbilical artery and the foetal response using the middle cerebral artery as the brain is a vital structure in the prediction of adverse outcomes .[11] In this study , thevarious characteristics were compared with categorical threshold of the CPR < / □ 1 . I found that 60.7% of study population to be primigravida which is keeping with Dr. Abdalla Mohammed *et al* showing that 60% were primigravida.[12] Women between 35 to 41 weeks gestation at the time of termination in the study population. 35 – 36 weeks (1.26%) , 36 – 37 weeks (5.02%) , 37 – 38 weeks (15.48%) and > 38 weeks are 78.24% .The median gestation was > 34 weeks which is a gestation where the foetus has achieved a good health and lung maturity . CPR was calculated between 35 to 38 weeks gestation. 35 – 36 weeks (24.29%) , 36 – 37 weeks (37.66%), 37 – 38 weeks (29.29%) and > 38 weeks (6.28%)[13] Robert Quirko *et al* have found that the best predictors for identifying SGA foetuses at risk for emergency Caesarean delivery in labour were the following: (1) an abnormal low CPR, (2) an estimated foetal weight less than the third centile and (3) an elevated PI of the uterine arteries . Amniotic fluid index (AFI) was measured during ultrasound scanning and did not show much variation and maximum between 5cm to 24cm . <5cm (1.26%) , 5 – 24cm (98.33%) and > 24cm (0.42%) AFI shows the chronic hypoxic status of the foetus so as CPR but CPR is better than AFI in predicting adverse perinatal outcome . CPR also decide on proper timing and method of management so as to reduce on perinatal morbidity and mortality. Longitudinal studies in early onset FGR foetuses have shown that the AFI progressively decreases and 20 – 30% of cases have oligohydramnios.[14] There is limited evidence on the role of AFI to predict perinatal complication. Umbilical artery (UA) PI measured during USG scanning and value range between 0.4 to 1. < 0.4 (0%) , 0.4 – 1 (91.63%) and > 1 (8.37%).[15] In normal pregnancy, pulsatility index (PI) decreases with advancing gestation in Umbilical artery . But in uteroplacental insufficiency there is decreased diastolic flow in the Umbilical artery due to increase in the resistance that occurs in small arteries and arterioles of terminal villi.[16] As the placental insufficiency worsen , the diastolic flow decreases , then become absent and later reverses Francesc Figueras *et al*, Middle cerebral artery PI also measured during USG scanning and value range between 0.4 to 1.8. < 0.4 (0%), 0.4 – 1.6 (71.55%), 1.6 – 1.8 (12.13%) and > 1.8 (16.32%) Foetal Middle cerebral artery (MCA) is a high resistance circulation with minimal antegrade flow in foetal diastole throughout pregnancies and accounts for 7% of cardiac output . Increase in diastolic flow with decreased pulsatility index shows the brain sparing taking place in foetuses with placental insufficiency.[17] The ratio of PI of MCA/UA is more sensitive than MCA PI alone in predicting adverse neonatal outcome Cerebro Placental Ratio were calculated after getting values of UA PI and MCA PI. The CPR is calculated by dividing the Doppler indices of Middle cerebral artery PI by Umbilical artery PI (MCA PI / UA PI). It should be > 1 then it is normal. < 1 (1.67%) and 1 (98.33%) (Figure1). In my study CPR <1 were found with pregnancies with other comorbidities like pre – eclampsia, IUGR, oligoamnios and GDM. In these pregnancies, neonates had APGAR score < 7 in 5minute and shifted to NICU. MCA/UA ratio reflects not only the circulatory insufficiency of the Umbilical velocimetry of the placenta , manifested by alteration in the Umbilical S/D ratio but also the adaptive changes resulting in modification of the Middle cerebral S/D ratio [18] Several studies have reported higher sensitivities and specificities for Middle cerebral Artery , Umbilical Artery (MCA/UA) Doppler ratio compared with Umbilical velocimetry alone for prediction of foetal prognosis .As a result of impaired uteroplacental blood flow, manifestations of pre – eclampsia may be seen in the foetal placental unit . These include intrauterine growth restriction (IUGR), oligoamnios, placental abruption and non – reassuring

foetal status found on antepartum surveillance by Doppler.[19] In my study group, CPR was most common indication for Caesarean section (7.1%) and foetal distress (6.7%) We have checked association of CPR value with CS rate (Figure 3) . t – Test showed p – value 70.7%. Since p – value is not less than 5% (p – value = 0.05), the assumption of equality of CPR in CS and non – CS category accepted which means CPR value does not affect the CS rate. In my study population, out of 239 4 cases showed CPR less than 1. In these 4 cases 2 had emergency Caesarean section for foetal distress (Figure 3) Prior *et al* prospectively evaluated 400 AGA foetuses at term and reported an abnormal CPR in 11%.[20] Of those who underwent Caesarean delivery for foetal distress, 36.4% had an abnormal CPR compared with 10.1% (p < .001) that had a normal CPR.[21] An abnormal CPR was a better predictor for an emergency Caesarean delivery than an abnormal UA or MCA. Even though the association was not studied here , a total of 6.7% were found to have foetal distress for which some intervention have taken like instrumental delivery or Caesarean section .91% babies had APGAR score >7 in 1 minute and 8% babies had APGAR score < 7 in 1 minute in a study population .94% had APGAR score > 7 in 5 minute and 5% had APGAR score< 7 in 5 minute.[22] Kibaru JG *et al* 2015, multivariable regression analysis demonstrated that an abnormal CPR has significant contribution to predict of a 5 minute APGAR score <7 was provided by onset of labour and method of delivery.[23] Arias F *et al* 2014, evaluated 509 foetuses with late – onset SGA and found 39.3% to have an abnormal CPR. There is a higher rate of NICU admission in foetuses with an abnormal CPR[24] kovanci E *et al* 2015, by using multivariate logistic regression analysis, they found a significant association between an abnormal CPR and NICU admission in both AGA and SGA babies. No still birth and perinatal death were recorded during my study period in my study population.[25]

CONCULSION

It is a common consensus that doppler should be done only in IUGR babies. However our paper clearly indicates that we can prevent stillbirth for babies with deranged doppler in AGA babies. In conclusion, lower CPR at term was independently associated with increased need for operative delivery for presumed fetal compromise and admission to the NICU. The rate of operative delivery for presumed fetal compromise was higher in AGA fetuses with low CPR. Our results suggest that the categorization of the at-risk fetus according to size alone is inadequate.

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Source of Support: None Declared
Conflict of Interest: None Declared