

## Original artery:

# Importance of cerebroplacental ratio in prediction of adverse perinatal outcome in unselected pregnancies of western Maharashtra population

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## ABSTRACT:

### Objectives -

1. To evaluate the distribution of Doppler pulsatility index (PI) measurements of the umbilical and middle cerebral arteries & Cerebroplacental ratio values in western Maharashtra population coming to tertiary care centre, Fetal Medicine unit, SKNMC, Pune.
2. To evaluate the distribution of these Doppler values with neonatal outcome.
3. To evaluate the distribution of these Doppler values with perinatal morbidity.

**Materials and methods** - A prospective observational study was performed at Fetal Medicine Unit, SKNMC, Pune, from September 2014 to August 2017. Total 4579 women were screened at routine antenatal visit during this period, out of which 400 were selected.

**Results** - Abnormal CPR values at 28 - 32 weeks, 32 - 37 weeks & 37 - 42 weeks (Figure no. 2 - 8) has shown clear cut increased in cesarean section rate, NICU admission and duration of stay in NICU, Intrauterine deaths and low birth weight. We have categorically identified that CPR values < 5<sup>th</sup> centile and > 95<sup>th</sup> centile clearly increases perinatal morbidity & mortality. We have seen that there is substantial increase in intrauterine and neonatal deaths at < 5<sup>th</sup> centile.

**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.

## INTRODUCTION

For the majority of pregnancies, the placenta provides adequate metabolic and oxygen supply to the fetus through to birth without any detrimental effects on growth or wellbeing. However, when placental function is suboptimal impaired fetal growth can supervene. Fetal hypoxia is one of the major causes of high perinatal morbidity and mortality rates [1,2]. Overall 98% of all stillbirths occur in low-income and middle-income countries; 77% in south Asia and sub-Saharan Africa(3). There is no substantial drop in cerebral palsy as the main cause is hypoxia in antenatal period in around 70 % cases. There is urgent need to answer questions like when, how and where to deliver such compromised babies. Doppler

investigation of the fetal circulation can give important clues to fetal well-being in a number of fetal conditions.

The fetal cerebroplacental ratio (CPR) is the ratio of the fetal middle cerebral artery (MCA) pulsatility index (PI) to umbilical artery (UA) PI. It is believed to be a proxy for suboptimal fetal growth given it quantifies both suboptimal placental function and subsequent fetal circulatory adaptations (4). CPR is 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. The CPR represents the interaction of alterations in blood flow to the brain as manifest by increased diastolic flow as the result of cerebrovascular dilation resulting from hypoxia and increased placental resistance, resulting in decreased diastolic flow of the umbilical artery. (5) Baschat and Gembruch developed a gestational age-based nomogram for the CPR. (4) The aim of this study was to determine the effect of using the gestational age-specific reference levels of the CPR on the prediction of adverse perinatal outcomes compared with the use of categorical thresholds.

#### **MATERIALS & METHODS**

A prospective observational study was performed at Fetal Medicine Unit, SKNMC, Pune, from September 2014 to August 2017. Total 4579 women were screened at routine antenatal visit during this period, out of which 400 were selected.

Inclusion criteria -

1. Pregnant women more than or equal to 28 weeks of gestation.
2. Women who are willing to perform the doppler study (written informed consent taken).

Exclusion criteria -

1. Pregnant women who are less than 28 weeks of gestation.
2. Multifetal pregnancies.
3. Diagnosed case of IUGR either clinically or ultrasonographically.

This visit included recording of maternal characteristics and medical history, and estimation of fetal size from transabdominal ultrasound measurement of biparietal diameter fetal head circumference, abdominal circumference and femur length. Determination of gestational age was done from menstrual history or measurement of the fetal crown-rump length at 11 weeks - 13 weeks 6 days gestation or the fetal head circumference at 19–24 weeks (6).

UA and MCA were visualised by transabdominal colour doppler. Pulsed-wave Doppler was then used to assess impedance to flow; when three similar waveforms were obtained consecutively the PI was measured (7). Doppler studies were performed using Seimens Acuson X300 Ultrasound machine by single Fetal medicine specialist using 5-MHz sector transducers with spatial peak temporal average intensities below 50 mW/cm<sup>2</sup> and the high-pass filter at 50–100 Hz. The said fetal medicine specialist had accreditation to FMF. Umbilical artery pulsatility index is measured at its midportion (4).

For measurements of the middle cerebral artery an axial view of the fetal head was obtained at the level of the cerebral peduncles at base of skull, within 2 mm of internal carotid artery origin, then the color Doppler was used to visualize the circle of Willis, and the Doppler sample volume was placed within 1 cm of the origin of the middle cerebral artery that was easily identified as a major branch running anterolateral from the circle of Willis toward the lateral edge of the orbit. The Doppler signals

were recorded with a 5 MHz curved array duplex transducer. The sample volume size was 2 mm. Angle of insonation kept as close to 0° as possible. Waveforms of good quality were collected and analyzed in the absence of fetal breathing movements. Waveform analysis was performed by measuring in the frozen display the maximum and minimum values of the velocity waveforms with the electronic calipers of the instrument (8). All images taken during this study were stored at PACS (Picture archiving and communication system) electronic database at Fetal medicine department, SKNMC, Pune.

When at least five consecutive uniform flow velocity waveforms with a high signal-to-noise ratio were obtained during periods of fetal rest and apnea the image was frozen and the waveforms were quantified using the PI. CPR was calculated with the help of Barcelona fetal medicine calculator and reported in percentile form. Their relationship with GA was explored using regression analysis. An abnormal CPR was defined as a CPR below the 5th percentile for gestational age on the basis of the nomogram by Baschat and Gembruch. (4)

Maternal parameters studied were weeks of gestation, mode of delivery (vaginal or Cesarean section), complications during pregnancy (oligohydramnios, pregnancy induced hypertension).

Neonatal parameters studied were birth weight, NICU admissions, neonatal death. Newborns were classified as small for gestational age (SGA) if their birth weight was below the 10th percentile for gestational age according to Brenner et al. (9). SGA newborns were considered growth retarded if they showed signs of malnutrition (decreased amount of subcutaneous fat, hypoglycemia, hyperbilirubinemia, hypocalcemia, hyperviscosity syndrome) in the immediate neonatal period. Preterm delivery was defined as delivery before 37 completed weeks. Neonatal morbidity was assessed by the length of stay in the neonatal intensive care unit. We have taken help of Barcelona fetal medicine calculator and perinatology calculators as derivation of MoM and percentile value is required for better prediction than mere numbers.

## RESULTS

Maternal and perinatal characteristics were evaluated and sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated.

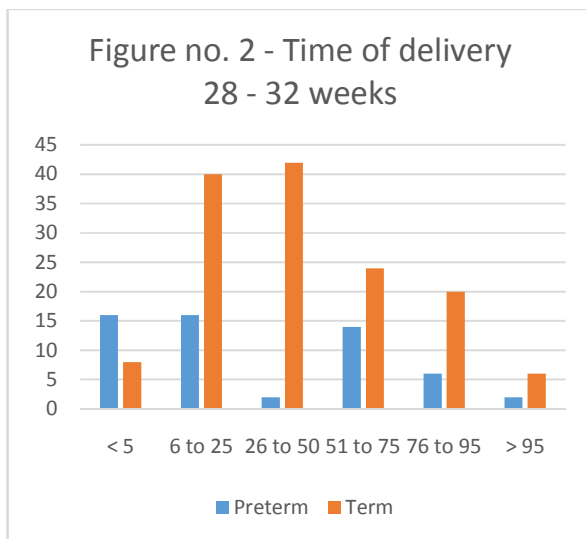
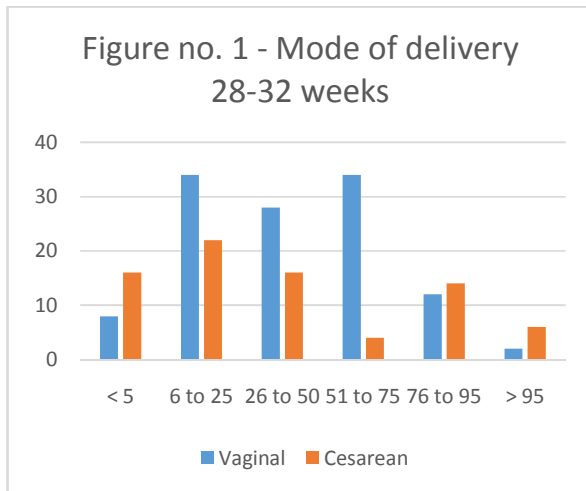
Appropriate for gestational age (AGA) was defined as birth weight or estimated fetal weight between 10th and 90th centiles.

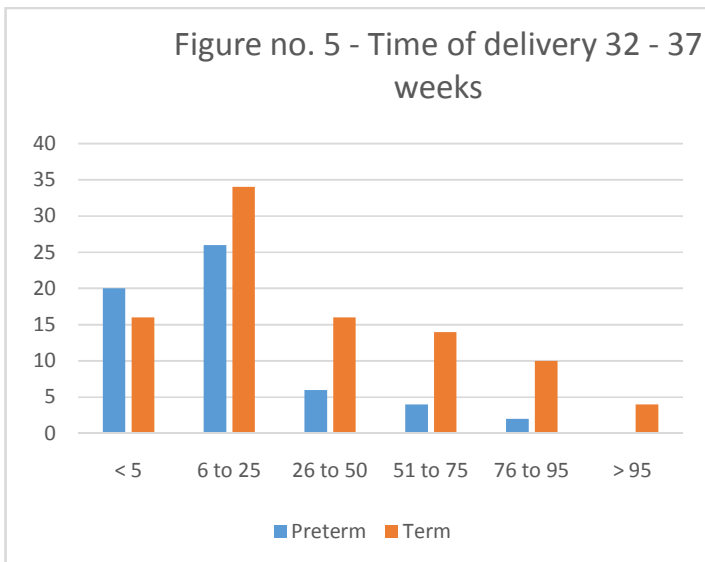
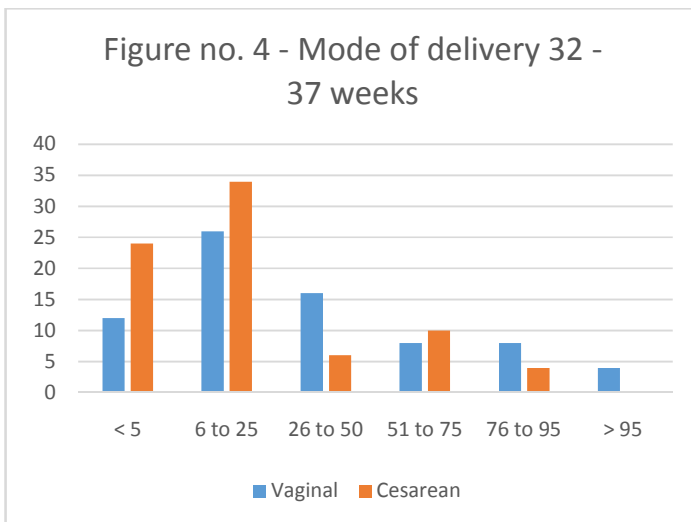
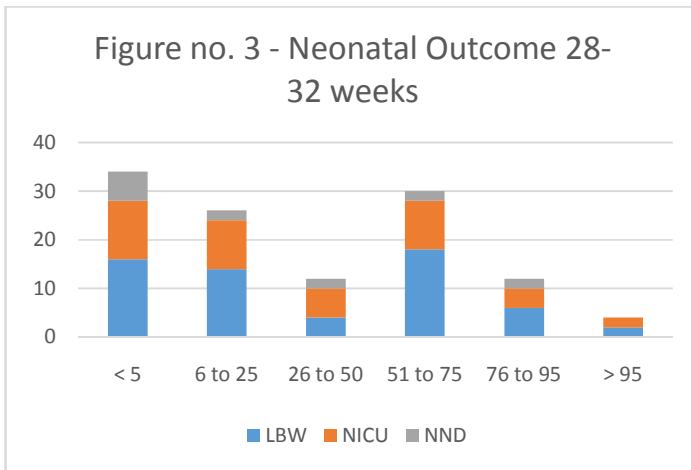
An abnormal CPR was associated with an overall increase for birth by emergency caesarean section (CS).

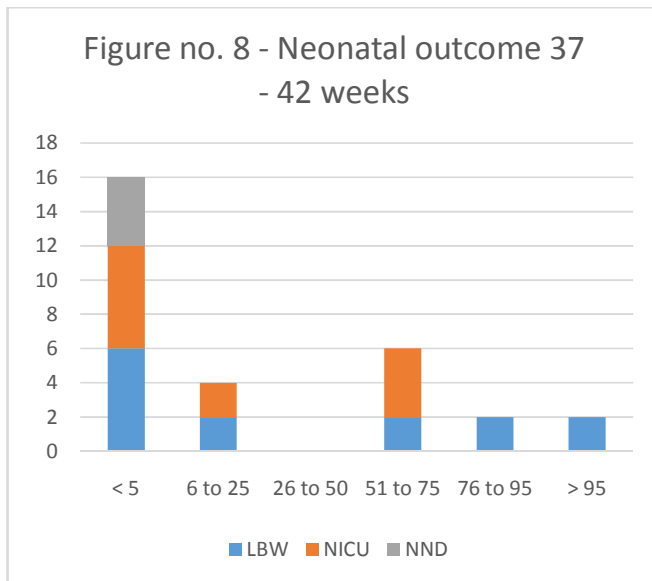
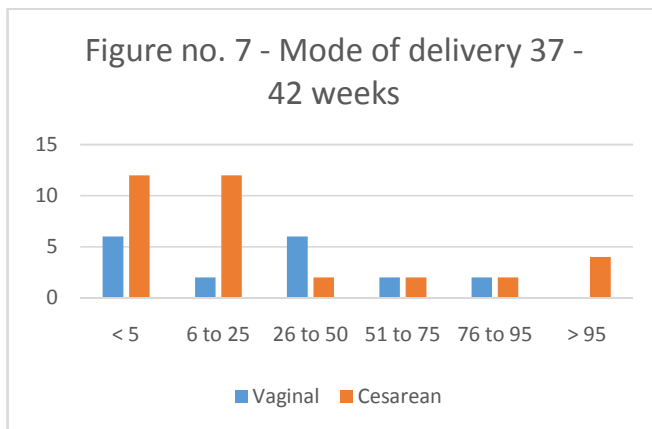
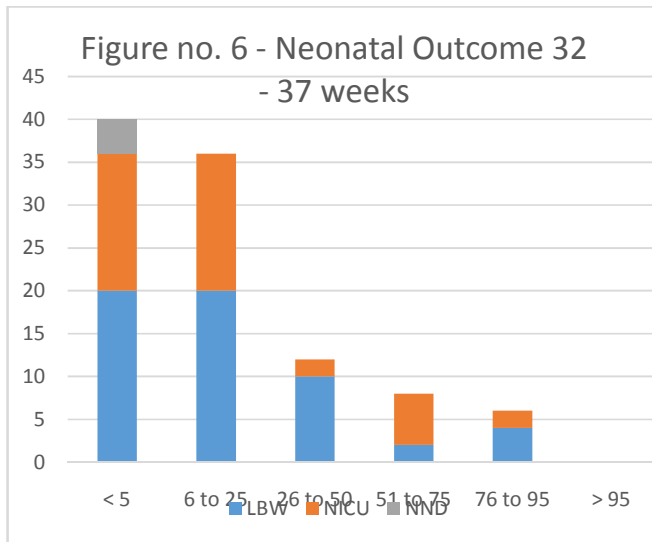
Overall caesarean rate is increased for delivering babies between 28 - 32 weeks gestation irrespective of CPR values possibly due to policy of caesarean section in preterm deliveries. (Figure no.1)

Whereas abnormal CPR values at 28 - 32 weeks, 32 - 37 weeks & 37 - 42 weeks (Figure no. 2 - 8) has shown clear cut increase in caesarean section rate, NICU admission and duration of stay in NICU, Intrauterine deaths, low birth weight. We have categorically identified that CPR values < 5<sup>th</sup> centile and > 95<sup>th</sup> centile increases perinatal morbidity & mortality. We have seen that there is substantial increase in intrauterine and neonatal deaths at < 5<sup>th</sup> centile. Khalilet al., 2015 (10), also described the association of low CPR with both instrumental delivery and caesarean section, with the CPR being an independent predictor any operative delivery for intrapartum fetal compromise, irrespective of fetal size. Conversely, a normal CPR was more likely to be associated with spontaneous vaginal delivery.

Lam et al., 2005 (11) did not demonstrate any correlation between a low CPR and MSL (meconium stained liquor), whereas three other studies (12,13) reported a higher prevalence of MSL amongst the low CPR cohort. Even amongst AGA cohorts, those with lower birthweights had a significantly lower CPR.







## **DISCUSSION**

The CPR offers the advantage of detecting redistribution of blood flow due to two potential mechanisms.

1. 'Forced centralization' that may be observed with elevated resistance placental blood flow
2. Decreasing ' cerebral blood flow resistance due to 'brain sparing' can both affect the CPR.

When compared to the individual vascular beds, the ratio shows greater variation and appears to offer earlier detection of fetal adaptation to placental insufficiency than either the umbilical or middle artery. This concept has been explored to predict fetal and/or neonatal compromise using the CPR.(10) Some SGA fetuses with abnormal Doppler results were delivered by elective Cesarean section and therefore the performance of low CPR in the prediction of Cesarean section for fetal distress in labor would have been underestimated so we have masked the outcome in the interest of the baby. Similarly, some stillbirths and cases of asphyxia at birth, reflected in a low Apgar score and low cord blood pH, could have been avoided. However, the impact of these cases on the overall performance of low CPR on prediction of adverse outcome would have been small.

This was similar to study by Akolekar et al.(14)

CPR between 28 - 31 weeks 6 days doesn't correlate well with perinatal outcome, though it indicates for close monitoring & how baby is responding to anoxia by cerebral redistribution. CPR between 32 - 36 weeks 6 days correlates with fetal hypoxia. In compromised or hypoxic condition, there is progressive rise in umbilical artery PI & decrease in MCA PI. CPR < 1 indicates poor outcome.

## **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 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.

## **LIMITATIONS –**

1. Biases of selective assessment of a population referred for scan assessment a term so there will be a slightly higher than the expected proportion of at risk fetuses.
2. The results of the ultrasound and Doppler assessment were not blinded, giving rise to the possibility of subsequent clinical intervention and a 'treatment effect' in view of fetal safety.
3. The threshold for the diagnosis of fetal compromise is also likely to have been influenced by changing personnel and attitudes toward intrapartum management.

## **STRENGTH OF STUDY -**

1. Single operative scans to minimize interobserver variation.
2. Assessment of outcome data as delivered in the single institute with common local protocol of fetal compromise.

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