



## CEREBROPLACENTAL RATIO AS A PREDICTOR OF PERINATAL OUTCOME IN TERM PREGNANCY

Dr. Safora Shafaq<sup>1</sup>, Madhunala Sravanthi<sup>2\*</sup>, Thejavathy G.V.<sup>3</sup>

<sup>1,2\*,3</sup>Department of Obstetrics and Gynecology, Bhagwan Mahaveer Jain Hospital, Bengaluru, Karnataka, India

**\*Corresponding Author: Dr. Madhunala Sravanthi**

\*Department of Obstetrics and Gynecology, Bhagwan Mahaveer Jain Hospital, Bengaluru, Karnataka, India

### ABSTRACT

**Background:** The cerebroplacental ratio (CPR) the middle cerebral artery pulsatility index (MCA-PI) divided by the umbilical artery pulsatility index (UA-PI) reflects fetal blood-flow redistribution in response to placental insufficiency. Its value as a late-gestation screening tool for perinatal risk in unselected/heterogeneous high-risk cohorts warrants clarification.

**Objective:** To evaluate CPR ( $<1$  vs  $\geq 1$ ) as a predictor of adverse perinatal outcomes among late preterm and term pregnancies.

**Methods:** Prospective observational analytical study at a tertiary center (August 2018–July 2019). Singleton pregnancies  $\geq 34$  weeks underwent Doppler ultrasound within 7 days before delivery.  $\text{CPR} < 1$  was considered abnormal. Primary outcomes included operative delivery for fetal compromise (ODFC), birthweight  $< 10$ th percentile, Apgar  $< 7$  at 5 minutes, and NICU admission. Diagnostic metrics were calculated.

**Results:** Among 100 participants, 34 (34%) had  $\text{CPR} < 1$ . Compared with  $\text{CPR} \geq 1$ , abnormal CPR was associated with higher rates of: ODFC (64.7% vs 12.1%; sensitivity 73.3%, specificity 82.9%), birth weight  $< 10$ th percentile (94.1% vs 15.2%; sensitivity 76.2%, specificity 96.6%), Apgar  $< 7$  at 5 minutes (50.0% vs 4.5%; sensitivity 85.0%, specificity 78.8%), and NICU admission (79.4% vs 19.7%; sensitivity 67.5%, specificity 88.3%). Mean gestational age at delivery was earlier with  $\text{CPR} < 1$  ( $36.17 \pm 1.41$  vs  $37.94 \pm 1.45$  weeks,  $p < 0.001$ ) and mean birth weight was lower ( $2.05 \pm 0.40$  vs  $2.83 \pm 0.37$  kg,  $p < 0.001$ ).

**Conclusion:** In late preterm/term pregnancies,  $\text{CPR} < 1$  identifies fetuses at increased risk of intrapartum compromise and adverse neonatal outcomes. Incorporating CPR into third-trimester surveillance—especially when timing delivery—may improve risk stratification beyond isolated UA or MCA Dopplers.

**Keywords:** cerebroplacental ratio, MCA-PI, UA-PI, Doppler, fetal growth restriction, intrapartum fetal compromise, NICU admission, Apgar

### INTRODUCTION

Antepartum fetal surveillance has evolved to balance two competing risks: intervening too early in otherwise stable pregnancies and intervening too late in fetuses already decompensating from placental insufficiency<sup>1</sup>. Among the various tools available, Doppler velocimetry offers a physiological read-out of the maternal–placental–fetal circulation, enabling clinicians to infer fetal

adaptive responses before overt decompensation<sup>2,3</sup>. In chronic hypoxemia, the fetus redistributes cardiac output toward vital organs heart, brain and adrenals manifesting as cerebral vasodilation and reduced resistance in the middle cerebral artery (MCA), alongside rising resistance in the umbilical artery (UA) as placental pathology progresses<sup>4</sup>. The cerebroplacental ratio (CPR), defined as MCA pulsatility index divided by UA pulsatility index, condenses these reciprocal changes into a single, dimensionless index that reflects “brain-sparing” and placental load simultaneously<sup>5,6</sup>. A low CPR therefore signals blood-flow redistribution, suboptimal placental function and fetal circulatory compensation within an adverse intrauterine milieu<sup>5,6</sup>. Understanding placental physiology underscores why CPR is clinically informative. Normal gestation requires progressive spiral artery remodeling by extravillous trophoblasts to transform high-resistance maternal vessels into low-resistance channels; when this process is incomplete, uteroplacental perfusion becomes pulsatile and constrained, predisposing to late-onset placental insufficiency and intermittent fetal hypoxemia<sup>7-11</sup>. These pathophysiologic changes precede and predict abnormalities in fetoplacental Dopplers, intrapartum intolerance of labor and neonatal compromise.

Operationally, UA Doppler interrogated in a free cord loop and MCA measured in the proximal third on an axial transthalamic plane provide the components for CPR calculation; meticulous technique (appropriate insonation angle, minimal fetal breathing/movement artifact, and correct waveform sampling) is critical for reproducibility<sup>12-15</sup>. Clinical protocols commonly interpret CPR using absolute cut-offs (e.g., <1.0) or gestation-adjusted centiles/MoMs; both approaches have shown associations with fetal growth restriction (FGR), low Apgar, metabolic acidosis and neonatal unit admission near term<sup>13,14,16-18</sup>. Late-onset placental insufficiency is particularly challenging because UA resistance may remain within reference limits even when fetal cerebral redistribution is present. In such settings, a reduced CPR can unmask risk among fetuses that are appropriate for gestational age by biometry yet exhibit impaired growth velocity and diminished reserve during labor<sup>19-22</sup>. Consequently, CPR has been incorporated in many high-risk surveillance pathways to refine timing of delivery and to guide intrapartum monitoring intensity, alongside established parameters such as amniotic fluid assessment, biophysical profile and cardiotocography<sup>23-26</sup>. Nevertheless, CPR should be interpreted in context. Because it is a ratio, changes in either the numerator (MCA-PI) or denominator (UA-PI) can shift the value; gestational age, fetal behavioral state and estimated fetal weight centile influence distributions. Emerging reference ranges and centile-based approaches aim to standardize interpretation and to reduce false-positive classifications in low-risk cohorts<sup>27-29</sup>. Moreover, CPR is not intended to replace UA Doppler or clinical judgment but to complement them, particularly when surveillance and decisions about induction versus expectant management are being considered at  $\geq 34$  weeks<sup>30-33</sup>.

Against this backdrop, the present prospective observational study undertaken at a tertiary center evaluates whether a pragmatic CPR threshold obtained within one week of delivery in late preterm and term singleton pregnancies predicts clinically consequential outcomes—operative delivery for fetal compromise, low 5-minute Apgar and NICU admission thereby assessing the utility of CPR as an actionable adjunct in third-trimester surveillance<sup>19-22</sup>.

Standard late-gestation surveillance can miss placental insufficiency when UA Doppler and biometry appear normal. Because CPR captures both placental resistance and fetal brain-sparing, we evaluated a simple near-delivery CPR threshold to better predict intrapartum compromise and early neonatal morbidity in our tertiary setting.

## AIM OF STUDY

To study the Cerebroplacental ratio as a predictor of adverse perinatal outcome in late preterm and term patients.

## OBJECTIVES OF STUDY

To evaluate the role of middle cerebral to umbilical artery blood velocity waveforms and perinatal outcome in terms of fetal growth restriction, Operative delivery for fetal distress, meconium stained liquor, NICU admission, APGAR at 5min, mode of delivery, perinatal morbidity and mortality.

## MATERIAL AND METHODS

This prospective observational analytical study was conducted in the Department of Obstetrics and Gynecology, Bhagwan Mahaveer Jain Hospital, Bengaluru (August 2018–July 2019).

### Inclusion Criteria:

- Singleton pregnancy  $\geq 34$  weeks with delivery at our center and a Doppler assessment within 7 days before delivery.

### Exclusion Criteria

- Fetal anomalies
- intrauterine fetal demise
- multiple pregnancy
- refusal to participate.

Sample size was set at  $n=100$  based on precision targets for sensitivity / specificity with  $\alpha=0.05$  and 80% power.

**Doppler acquisition:** Examinations used a color Doppler ultrasound system with a 3.75-MHz transducer. UA-PI was measured in a free-loop cord segment; MCA-PI was obtained at the proximal third of the MCA in an axial transthalamic plane, maintaining minimal insonation angle. CPR was calculated as  $MCA-PI/UA-PI$ . A prespecified cut-off of 1.0 defined abnormal CPR.

### Outcomes:

Primary outcomes: (1) ODFC (emergency cesarean for non-reassuring fetal status), (2) birthweight <10th percentile, (3) Apgar <7 at 5 minutes, and (4) NICU admission for indications other than low birthweight alone.

Secondary outcomes: meconium-stained liquor (MSL), need for mechanical ventilation, and perinatal mortality. Additional variables: maternal risk factors (e.g., preeclampsia, growth restriction), onset of labor, gestational age at delivery, test-to-delivery interval, placental parameters.

**Statistical Analysis:** Categorical variables were compared using  $\chi^2$  or Fisher's exact tests; continuous variables via t-tests. Diagnostic performance of  $CPR < 1$  for predefined outcomes was summarized with sensitivity, specificity, PPV, NPV, and ROC curves with AUC.  $P < 0.05$  was considered statistically significant.

## RESULTS

**Table 1: Cohort characteristics**

| Characteristic                              | Value          |
|---------------------------------------------|----------------|
| Total participants, n                       | 100            |
| Maternal age, years (mean $\pm$ SD)         | 26.8 $\pm$ 4.3 |
| Gestational age at delivery 34–37 wk, n (%) | 34 (34.0%)     |
| Gestational age at delivery 37–40 wk, n (%) | 66 (66.0%)     |
| Primigravidae, n (%)                        | 52 (52.0%)     |
| CPR < 1, n (%)                              | 34 (34.0%)     |

Table 1 summarizes baseline characteristics of the study cohort (N=100). The mean maternal age was  $26.8 \pm 4.3$  years. Most deliveries occurred at 37–40 weeks (66%), with 34% delivering between 34–37 weeks. Just over half were primigravidae (52%). A CPR  $<1$  - the study's abnormal Doppler threshold was observed in 34% of participants, delineating the higher-risk subgroup evaluated in subsequent analyses.

| Table 2: Delivery characteristics by CPR group     |                  |                     |          |
|----------------------------------------------------|------------------|---------------------|----------|
| Delivery characteristic                            | CPR $<1$ (n=34)  | CPR $\geq 1$ (n=66) | P value  |
| Labor: Spontaneous, n                              | 12               | 31                  | —        |
| Labor: Induced, n (%)                              | 22 (64.7%)       | 12 (18.2%)          | $<0.001$ |
| Cesarean delivery, n (%)                           | 30 (88.2%)       | 24 (36.4%)          | $<0.001$ |
| Gestational age at delivery (weeks, mean $\pm$ SD) | $36.17 \pm 1.41$ | $37.94 \pm 1.45$    | $<0.001$ |

Table 2 compares delivery characteristics by CPR group. Among women with CPR  $<1$  (n=34), labor was induced in 64.7% (22/34) versus 18.2% (12/66) with CPR  $\geq 1$  ( $p<0.001$ ). Cesarean delivery occurred in 88.2% (30/34) vs 36.4% (24/66) ( $p<0.001$ ). Mean gestational age at delivery was earlier with CPR $<1$  ( $36.17\pm 1.41$  weeks) than with CPR $\geq 1$  ( $37.94\pm 1.45$  weeks) ( $p<0.001$ ). Numbers of spontaneous labor were 12 vs 31 (no formal p-value provided).

| Table 3. Neonatal outcomes by CPR group |                 |                     |          |
|-----------------------------------------|-----------------|---------------------|----------|
| Outcome                                 | CPR $<1$ (n=34) | CPR $\geq 1$ (n=66) | P value  |
| Birthweight (kg), mean $\pm$ SD         | $2.05 \pm 0.40$ | $2.83 \pm 0.37$     | $<0.001$ |
| Birthweight $<10$ th percentile, n (%)  | 32 (94.1%)      | 10 (15.2%)          | $<0.001$ |
| Apgar $<7$ at 5 minutes, n (%)          | 17 (50.0%)      | 3 (4.5%)            | $<0.001$ |
| NICU admission, n (%)                   | 27 (79.4%)      | 13 (19.7%)          | $<0.001$ |
| Meconium-stained liquor, n (%)          | 13 (38.2%)      | 4 (6.1%)            | $<0.001$ |

Table 3 compares key neonatal outcomes by CPR group. Infants in the CPR  $<1$  group had a markedly lower mean birthweight ( $2.05 \pm 0.40$  kg) than those with CPR  $\geq 1$  ( $2.83 \pm 0.37$  kg) ( $p<0.001$ ). Small-for-gestational-age ( $<10$ th centile) was far more frequent with CPR $<1$  (94.1% vs 15.2%,  $p<0.001$ ). Markers of intrapartum/neonatal compromise were also substantially higher with CPR $<1$ : Apgar  $<7$  at 5 minutes (50.0% vs 4.5%,  $p<0.001$ ), NICU admission (79.4% vs 19.7%,  $p<0.001$ ), and meconium-stained liquor (38.2% vs 6.1%,  $p<0.001$ ).

| Table 4. Diagnostic performance of CPR $<1$ and CPR $\geq 1$ |                                                |                 |                 |         |         |
|--------------------------------------------------------------|------------------------------------------------|-----------------|-----------------|---------|---------|
| Outcome                                                      |                                                | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
| CPR $<1$                                                     | Operative delivery for fetal compromise (ODFC) | 73.3            | 82.9            | 64.7    | 87.9    |
|                                                              | Birthweight $<10$ th percentile                | 76.2            | 96.6            | 94.1    | 84.8    |
|                                                              | Apgar $<7$ at 5 minutes                        | 85              | 78.8            | 50      | 95.5    |
|                                                              | NICU admission                                 | 67.5            | 88.3            | 79.4    | 80.3    |
| CPR $\geq 1$                                                 | Operative delivery for fetal compromise (ODFC) | 82.9            | 73.3            | 87.9    | 64.7    |
|                                                              | Birthweight $<10$ th percentile                | 96.6            | 76.2            | 84.8    | 94.1    |
|                                                              | Apgar $<7$ at 5 minutes                        | 78.8            | 85              | 95.5    | 50      |
|                                                              | NICU admission                                 | 88.3            | 67.5            | 80.3    | 79.4    |

Table 4 presents the diagnostic performance of the cerebroplacental ratio both as a positive test for adverse outcomes when CPR  $<1$  and as a reassuring test for the absence of adverse outcomes when CPR  $\geq 1$ , reporting sensitivity, specificity, PPV, and NPV for operative delivery for fetal compromise, small-for-gestational-age status, low 5-minute Apgar, and NICU admission.

## DISCUSSION

In this prospective cohort of 100 late-preterm and term pregnancies, a low cerebroplacental ratio (CPR<1) close to delivery identified a distinctly higher-risk subgroup and was associated with earlier birth, greater obstetric intervention, and worse neonatal condition. Exactly as observed in our results, women with CPR<1 delivered earlier ( $36.17 \pm 1.41$  vs  $37.94 \pm 1.45$  weeks,  $p<0.001$ ), underwent induction far more often (64.7% vs 18.2%,  $p<0.001$ ), and had a higher cesarean rate for intrapartum concerns (88.2% vs 36.4%,  $p<0.001$ ). Neonates in the CPR<1 group had a lower mean birth weight ( $2.05 \pm 0.40$  vs  $2.83 \pm 0.37$  kg,  $p<0.001$ ), were far more frequently small-for-gestational-age (<10th centile: 94.1% vs 15.2%,  $p<0.001$ ), and more commonly exhibited markers of intrapartum/neonatal compromise Apgar <7 at 5 minutes (50.0% vs 4.5%,  $p<0.001$ ), NICU admission (79.4% vs 19.7%,  $p<0.001$ ), and meconium-stained liquor (38.2% vs 6.1%,  $p<0.001$ ). The short test-to-delivery interval (mean  $4.02 \pm 1.949$  days; median 4) anchors these associations to the near-term window in which CPR is intended to inform management.

Baseline features in our cohort were typical of late-gestation populations (mean age  $26.8 \pm 4.3$  years; 52% primigravidae; 34% with CPR<1).

Our diagnostic accuracy findings reproduce those reported in key prior series. For SGA, CPR<1 yielded sensitivity 76.2%, specificity 96.6%, PPV 94.1%, and NPV 84.8%, closely matching the thesis-cited figures from Bahado-Singh RO et al., (1999)<sup>34</sup> (63.4%, 90%, 81%, 77%) and Shaheen S et al., (2014)<sup>35</sup> (76%, 80%, 76%, 86.8%). In the head-to-head comparison of overall diagnostic yield (Table 37), our PPV for SGA (94.1%) is comparable to Gramellini D et al., (1992)<sup>36</sup> (100%) and Deshmukh V et al., (2013)<sup>37</sup> (92.5%). For intrapartum compromise prompting operative delivery (ODFC), our sensitivity/specificity of 73.3%/82.9% align with ranges reported by Moreta D et al., (2019)<sup>38</sup> (55.6%, 87.9%), Sherrell H et al., (2018)<sup>39</sup> (100%, 86%), and Vollgraff Heidweiller-Schreurs CA et al., (2021)<sup>40</sup> (58%, 89%), supporting CPR's ability to anticipate emergency delivery beyond single-vessel Dopplers. For NICU admission, our PPV of 79.4% sat close to Gramellini D et al., (1992)<sup>36</sup> (77%) and above Deshmukh V et al., (2013)<sup>37</sup> (70%), confirming that low CPR flags infants likely to require intensive care.

The magnitude of neonatal size differences in our data mirrors earlier reports. Our mean birth weight gap ( $2.05 \pm 0.40$  vs  $2.83 \pm 0.37$  kg,  $p<0.001$ ) is directionally concordant with Macdonald TM et al., (2019)<sup>41</sup> (2680 g vs 3366 g,  $p<0.001$ ) and with the larger disparity described by Gramellini D et al., (1992)<sup>36</sup> (1.659 vs 3.031 kg,  $p<0.001$ ), while our NICU-stay signal (abnormal CPR mean  $4.15 \pm 2.68$  days) is consistent with NICU burden documented by Jain M et al., (2004)<sup>42</sup> (NICU stay >10 days more frequent with abnormal CPR,  $p<0.005$ ) and the stronger gradient reported by Flood K et al., (2014)<sup>43</sup> (NICU 64% vs 22%, mean stay 31 vs 14 days,  $p<0.0001$ ).

Immediate neonatal condition tracked CPR as well: we observed Apgar <7 at 5 minutes in 50.0% vs 4.5% ( $p<0.001$ ), paralleling Kibaru JG (2002)<sup>44</sup> (abnormal CPR predicting low 5-minute Apgar) and Gramellini D et al., (1992)<sup>36</sup> (16.6% vs 2.7%,  $p<0.001$ ), while differing from Maksheed M et al., (2000)<sup>45</sup>, who did not find a significant Apgar difference likely reflecting differences in case-mix and intrapartum practices. Grüttner B et al., (2019)<sup>46</sup> further corroborated lower Apgar scores at 1, 5, and 10 minutes with pathological CPR ( $p<0.001$ ).

Timing considerations in our study match prior recommendations. The significant association we found within a median 4-day window resonates with Alkolekar R et al., (2015)<sup>47</sup>, who demonstrated better prediction when the assessment-to-delivery interval is  $\leq 2$  weeks and superior performance at 36 weeks versus 32 weeks, and with Maksheed M et al., (2000)<sup>45</sup>, who also reported strongly positive timing associations. Our observed earlier delivery in abnormal CPR ( $36.17 \pm 1.41$  weeks) compares closely with means reported by Maksheed M et al., (2000)<sup>45</sup> ( $35.4 \pm 1.6$  weeks) and Grüttner B et al., (2019)<sup>46</sup> ( $36.53 \pm 2$  weeks) in pathological CPR groups, supporting the premise

that low CPR near term is linked to expedited birth through both clinical decision-making and genuine fetal intolerance.

Importantly, perinatal mortality did not differ by CPR status in our cohort ( $p = 0.629$ ), consistent with El Guindy AE et al., (2018)<sup>48</sup> (no significant correlation,  $p = 0.116$ ) but not with Regan J et al., (2015)<sup>49</sup> ( $8p < 0.001$  in high-risk pregnancies), a divergence likely due to baseline risk and power constraints; in our series, perinatal deaths were rare. Finally, our results reinforce the integrative value of CPR over isolated UA or MCA indices: despite mean UA-PI ( $1.027 \pm 0.194$ ) and MCA-PI ( $1.346 \pm 0.408$ ) in expected ranges,  $CPR < 1$  captured large risk gradients across SGA, Apgar, NICU, and ODFC echoing Prior et al. (88) and Arias F et al., (1994)<sup>50</sup>, and the foundational conclusions of Gramellini et al. (72) that the ratio offers better diagnostic accuracy than its components.

Overall, using the exact values from our results,  $CPR < 1$  emerged as a robust late-gestation marker that coincides with earlier delivery ( $36.17 \pm 1.41$  weeks), higher intervention (induction 64.7%; cesarean 88.2%), and materially worse neonatal endpoints (birth weight  $2.05 \pm 0.40$  kg; SGA 94.1%; Apgar  $< 7$  at 5 min 50.0%; NICU 79.4%; all  $p < 0.001$ ), with strong diagnostic performance for SGA (Se 76.2%, Sp 96.6%, PPV 94.1%, NPV 84.8%), balanced performance for ODFC (Se 73.3%, Sp 82.9%), and high NPV for low Apgar (95.5%).

Interpreted inversely,  $CPR \geq 1$  offered meaningful reassurance for Apgar  $\geq 7$  (PPV 95.5%) and absence of ODFC (PPV 87.9%). Taken together and consistent with at least two to three studies for each endpoint cited in the thesis (66, 70–89) these data support incorporating CPR into near-term surveillance to refine timing and intrapartum planning in late-onset placental insufficiency.

## CONCLUSION

In late-preterm and term pregnancies, an abnormal cerebroplacental ratio capturing longitudinal Doppler changes from umbilical artery to middle cerebral artery and integrating placental status with fetal adaptive response is associated with adverse neonatal outcomes and serves as a practical surveillance tool in high-risk conditions (e.g., preeclampsia, growth restriction) to guide optimal timing of delivery.

## REFERENCES

1. Arias F. Practical guide to high risk pregnancy and delivery. 2nd edition USA Mosby. 1998: 183-207.
2. Asma A. Khalil, Jose Morales-Rossello et al. The association between fetal Doppler and admission to neonatal unit at term. American Journal of Obstetrics & Gynecology 2014. [dx.doi.org/10.1016/j.ajog.2014.10.013](https://doi.org/10.1016/j.ajog.2014.10.013).
3. Berkley, E. Chauhan et al. Doppler assessment of the fetus with intrauterine growth restriction. American Journal of Obstetrics and Gynecology. 2012; 206, 300–308.
4. Ebbing C, Rasmussen S et al. Middle cerebral artery blood flow velocities and pulsatility index and the cerebroplacental pulsatility ratio: longitudinal reference ranges and terms for serial measurements. Ultrasound Obstet Gynecol. 2007; 30: 287-296.
5. Arbeille P, Perrotin F et al. Fetal Doppler hypoxic index for the prediction of abnormal fetal heart rate at delivery in chronic fetal distress. Eur J Obstet Gynecol Reprod Biol. 2005; 121:1717.
6. Farmakides G, Bracero L et al. Umbilical artery flow velocity waveforms and intrauterine growth retardation. Am J Obstet Gynecol. 1985; 151:502-5.
7. Cunningham, Leveno, Bloom, Spong, Dashe et al. Williams Obstetrics. 24th Edition. United States of America. McGraw - Hill Education. 2014. \
8. Rajan R. Basics of Doppler ultrasound applied to obstetrics. Ultrasound and colour Doppler in Obstetrics, Gynaecology and Infertility. 1st ed. India: Indian Academy of Human Reproduction 2004 Sep; 13(3):140.
9. Baker DW. Pulsed ultrasonic Doppler blood flow sensing IEEE Trans Sonic ultra-sonics. SU 1970; 17(3):170-85.

10. Fitzgerald DE, Drum JE. Non-invasive measurement of the human fetal circulation using ultrasound: A new method. *BM J*. 1977; 2:1450-1.
11. McCallum WD, Olson RF, Daigle RE et al. Real time analysis of Doppler signals obtained from the fetoplacental circulation. *Ultrasound Med*. 1977;3B:1361-4.
12. Kamini Rao, Supriya Sheshadri. Fetal Doppler. *Asian J Obstet Gynecol*. 2003 Aug; 7(7): 17-22.
13. Reid JM, Spencer MP. Ultrasonic Doppler technique for imaging blood vessels. *Science* 1972; 176:1235.
14. Namekawa K, Kasai C, Tsukamoto M, Koyano A. Imaging of blood flow using auto correlation. *Ultrasound Med Biol*. 1982; 8:138.
15. Cunningham FG, John CH, Kenneth JL, Bloom SL, Wenstrom KD, Gilstrap L III. Ultrasonography and Doppler. In: Williams Obstetric. 22nd ed. New York McGraw-Hill; 2005. p.400-4.
16. Cunningham FG, Gnat NF, Leneno KJ, Gils LC, John C, Katherine DH. Wenstrom Williams Obstetrics. 21st ed. New York: McGraw-Hill; 2010. p.567,651,743-64,1132-6.
17. Porcelot L. Applications cliniques de l'examen Doppler transcutané in: Peronneau P, ed. *Velocimetric ultrasonique Doppler*. Paris: INSERM; 1974. p.213-40.
18. Maulik D, Yarlaga P, Young Blood JP, Willoughby L. Components of variability of umbilical arterial Doppler velocimetry: a prospective analysis. *Am J Obstet Gynecol*. 1989; 160:1406
19. Arias F, Daftary SN, Bhide AG. Fetal growth restriction. In: Practical Guide to high-risk pregnancy and delivery. 3rd ed. Delhi: Elsevier; 2011. p.119-20,126-7.
20. Brar HS, Medearis AL, De Yore GR. A comparative study of fetal umbilical velocimetry with continuous and pulsed wave Doppler ultrasonography in high pregnancies its outcome. *Am J Obstet Gynecol*. 1989; 160:375.
21. Rochelson B, Schuman H, Farmakides G, Bracerol L, Ducey J, Fleischer A et al. Significance of absent end diastolic velocity in umbilical artery velocity waveforms *Am J Obstet Gynecol*. 1987; 156:1213-8.
22. Degani S, Paltieli Y, Gonem R, Sharf M. Fetal internal carotid artery pulsed Doppler flow velocity waveforms and maternal plasma glucose levels. *Obstet Gynecol*. 1991; 77:379.
23. Bocking AD, Gagnon R, White SE, Homan J, Milne KM, Richardson BS. Circulatory responses to prolonged hypoxemia in fetal sheep. *Am J Obstet Gynecol*. 1988; 159:1418.
24. Vyas S, Nicolaides KH, Bower S, Campbell S. Middle cerebral artery flow velocity waveforms in fetal hypoxemia. *Br J Obstet Gynaecol*. 1990; 97:797-803.
25. Ferrazzi E, Bozzo M, Rigano S, Bellotti M, Morabito A, Pardi G, et al. Temporal sequence of abnormal Doppler changes in the peripheral and central circulatory systems of the severely growth restricted fetus. *Ultrasound Obstet Gynecol* 2002; 19:140-6.
26. Brosens I, Robertson WB, Dixon HG. The role of spiral arteries in the pathogenesis of pre-eclampsia. *Obstet Gynecol Annu*. 1972; 1:177-91.
27. Hendrick SK, Seguin EM, Wang KY, Breshnell JM, Sorensen TK, Seingheid RN. Doppler umbilical artery waveforms indices normal values from fourteen to forty-two vessels. *Am J Obstet Gynecol*. 1989; 161:761.
28. Schulman H, Fleischer A, Farmakides G, Bracerol, Rochelson B, Carunfield. Development of uterine artery compliance in pregnancy as detected by Doppler ultrasound. *Am J Obstet Gynecol*. 1986; 155:1031.
29. Fleischer A, Schulman H, Farmakides G. uterine artery Doppler velocimetry in pregnant women with hypertension. *Am J Obstet Gynecol*. 1986; 154:806.
30. Abuhamad A (ed.). *ULTRASOUND in Obstetrics and Gynecology: A Practical Approach*. GLOWM. 2014: p.93-95.
31. Figueras rancesc, Eduard Gratacós. Update on the Diagnosis and Classification of Fetal Growth Restriction and Proposal of a Stage-Based Management Protocol. *Fetal Diagn Ther* 2014; 36:86–98.

32. Lausman A, Kingdom J; Maternal Fetal Medicine Committee. Intrauterine growth restriction: screening, diagnosis, and management. *J Obstet Gynaecol.* 2013; 35: 741–48.
33. Figueras F, Savchev S, Triunfo S, Crovetto F. An integrated model with classification criteria to predict small-for-gestational-age fetuses at risk of adverse perinatal outcome. *Ultrasound Obstet Gynecol.* 2015; 45: 279–285.
34. Bahado-Singh RO, Kovanci E, Jeffres A, Oz U, Deren O, Copel J, Mari G. The Doppler cerebroplacental ratio and perinatal outcome in intrauterine growth restriction. *Am J Obstet Gynecol.* 1999 Mar;180(3 Pt 1):750-6.
35. Shaheen S, Bano I, Ahmad I, Singh A. Doppler Cerebroplacental Ratio and Adverse Perinatal Outcome. *Journal of South Asian Federation of Obstetrics and Gynaecology*, January-April 2014;6(1):25-27.
36. Gramellini D, Folli MC, Raboni S, Vadora E, Merialdi A. Cerebral-umbilical Doppler ratio as a predictor of adverse perinatal outcome. *Obstet Gynecol.* 1992; 79:416-20.
37. Deshmukh V, Yelika KA, Deshmukh P. Cerebral-umbilical Doppler ratio as predictor of perinatal outcome in pregnancies with hypertension disorders. *Journal of Evolution of Medical and Dental Sciences.* 2013 Sep;2(38):7366-72.
38. Moreta D, Samuel Vo, Guy DE, Ronald Benzie. Re-evaluating the role of cerebroplacental ratio in predicting adverse perinatal outcome. *European journal of obstetrics and Gynecology and Reproductive biology.* 2019;242: 17-28.
39. Sherrell H, Clifton V, Kumar S. Predicting intrapartum fetal compromise at term using the cerebroplacental ratio and placental growth factor levels (PROMISE) study: randomised controlled trial protocol. *BMJ Open.* 2018 Aug 13;8(8):e022567. doi: 10.1136/bmjopen-2018-022567.
40. Vollgraff Heidweiller-Schreurs CA, van Osch IR, Heymans MW, Ganzevoort W, Schoonmade LJ, Bax CJ et al. Cerebroplacental ratio in predicting adverse perinatal outcome: a meta-analysis of individual participant data. *BJOG.* 2021 Jan;128(2):226-35.
41. MacDonald TM, Hui L, Robinson AJ, Dane KM, Middleton AL, Tong S, Walker Cerebral-placental-uterine ratio as novel predictor of late fetal growth restriction: prospective cohort study. *Ultrasound Obstet Gynecol.* 2019 Sep;54(3):367-375.
42. Jain M, Farooq T, Shukla RC. Doppler cerebroplacental ratio for the prediction of adverse perinatal outcome. *International Journal of Gynecology & Obstetrics.* 2004 Sep 1;86(3):384-5.
43. Flood K, Unterscheider J, Daly S, Geary MP, Kennelly MM, McAuliffe FM et al. The role of brain sparing in the prediction of adverse outcomes in intrauterine growth restriction: results of the multicenter PORTO Study. *American Journal of Obstetrics and Gynecology.* 2014;211(3):288-e1. <http://dx.doi.org/10.1016/j.ajog.2014.05.008>.
44. Kibaru JG, Outcome of pregnancies in patients with Hypertensive disease: MMED thesis – UON 1992, *East African Medical Journal* 2002.
45. Makhseed M, Jirous J, Ahmed MA, Viswanathan DL. Middle cerebral artery to umbilical artery resistance index ratio in the prediction of neonatal outcome. *Int J Gynaecol Obstet* 2000; 71:119-25.
46. Grüttner B, Ratiu J, Ratiu D, Gottschalk I, Morgenstern B, Abel JS et al. Correlation of Cerebroplacental Ratio (CPR) With Adverse Perinatal Outcome in Singleton Pregnancies. *In Vivo.* 2019 Sep-Oct;33(5):1703-06.
47. Akolekar R, Syngelaki A, Gallo DM, Poon LC, Nicolaides KH. Umbilical and fetal middle cerebral artery Doppler at 35-37 weeks' gestation in the prediction of adverse perinatal outcome. *Ultrasound Obstet Gynecol.* 2015 Jul;46(1):82-92.
48. El Guindy AE, Nawara M, ElSanter O. Cerebroplacental ratio and cerebrouterine ratio in predicting neonatal outcome in preeclamptic pregnant Women. *Int J Reprod Med Gynecol.* 2018 Jun 29;4(1):022-7.
49. Regan J, Masters H, Warshak CR. Association between an abnormal cerebroplacental ratio and the development of severe pre-eclampsia. *J Perinatol.* 2015 May;35(5):322-7.

50. Arias F. Accuracy of the middle-cerebral-to umbilical-artery resistance index ratio in the prediction of neonatal outcome in patients at high risk for fetal and neonatal complications. *Am J Obstet Gynecol* 1994; 171:1541-5.