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Original Research Article

# Cerebro placental ratio at 30–34 weeks' gestation in the prediction of perinatal outcome in low-risk and high-risk pregnancy

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ABSTRACT

**Background:** Doppler ultrasound velocimetry of umbilical and fetal vessels has become an established method of antenatal monitoring, allowing the non-invasive assessment of neonatal circulation. Cerebro placental ratio (CPR) is emerging as a significant predictor of adverse pregnancy outcome.
**Objectives:** To predict perinatal outcome in low and high-risk pregnancy in early and late-onset FGR using CPR.
**Materials and Methods:** The study group comprised 410 pregnant women at 30-34 weeks, evaluated with ultrasound Doppler study, and other routine investigations and CPR were calculated. Women were categorized into high-risk and low-risk pregnancies and followed up until delivery, and fetal outcome was noted.
**Results:** Period of prolongation of pregnancy was significantly lower with high-risk patients than low-risk patients (31.09 ± 13.9 vs 37.79 ± 15.1, p=0.0003). NICU admissions significantly increased with high-risk patients than low-risk patients (22.22% vs 9.4%, p=0.002). Low-risk patients underwent significantly more vaginal deliveries as compared to high-risk patients (74.22% vs 44.87%, $p < 0.0001$). Birth weight, period of prolongation of pregnancy, and gestation period were significantly lower in patients with abnormal CPR than normal CPR group (2.82 Kg vs 1.94 Kg, 37.56 weeks vs 14.64 weeks, 266.47 days vs 245.41 days, respectively).
**Conclusion:** Doppler velocimetry becomes an important tool for high-risk cases and late-onset mild FGR(after 32 weeks). CPR is helpful in high-risk pregnancies and also to predict peripartum fetal distress.



## 1. Introduction

Fetal circulation has been studied extensively in the last few decades. Knowledge of normal fetal blood flow in fetuses with adequate growth for gestational age is essential for early diagnosis of a pathological condition that could place fetal well-being at risk and prevent fetal morbidity and mortality. Adequate fetalblood flow circulation is mainly dependent on normal placental anatomy and development during pregnancy. An abnormal or malfunctioning placenta can directly affect fetal circulation. The umbilical artery (UA) is usually the first fetal blood vessel affected by placental insufficiency. The initial increase in placental blood flow, vascular impedance causes a retrograde rise in blood flow resistance in the UA.[1] When placental insufficiency further deteriorates, blood flow resistanc e in the descending aorta increases, resulting in more blood diverted through the aortic isthmus shunt to reach the fetal brain. This phenomenon is reflected by a decreased middle cerebral artery pulsatility index (MCA-PI), making it the second vascular marker in the cascade of placental insufficiency.[2,3] Correct diagnosis of early signs of placental insufficiency through fetal blood flow redistribution has been studied extensively in the literature.[4,5] Early detection

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of abnormal blood flow redistribution patterns is vital for efficient fetal Doppler monitoring. It is part of meticulous surveillance, with a potential benefit to reduce fetal morbidity and mortality.[6–8] Cerebroplacental ratio (CPR) has been studied and suggested as the most efficient vascular index to detect the above-mentioned fetal redistribution patterns.[9–12] It is the ratio of the middle cerebral artery pulsatility index (MCA-PI) to the umbilical artery PI (UA-PI) and is reflective of the severity of cerebral redistribution. CPR changes during gestation and is proportionate to relative fetal growth.[13]

This study was undertaken to evaluate the efficacy of CPR to assessperinatal outcome and consider it as a routine assessment tool in fetuses undergoing third-trimester ultrasound Doppler examination.

## 2. Aim and Objectives

1. To predict perinatal outcome in low risk and high-risk pregnancy in late-onset IUGR.
2. To evaluate CPR in early severe fetal growth restriction and late mild fetal growth restriction.

## 3. Material and Methods

### *3.1. Study design*

This was a prospective observational study conducted in the outpatients department of the Department of Obstetrics and Gynaecology of a teaching hospital in South India for one and a half year from November 2017 to May 2019. The study was approved by the hospital ethics committee.

### *3.2. Sample size*

A total of 410 women were included in the study, out of which ten women were lost to follow up; hence, 400 women were finally included in the study after taking informed consent.

### *3.3. Inclusion and exclusion criteria*

The antenatal mothers with i) gestational age of patient between 30 and 34 weeks, ii) singleton pregnancies and iii) willingness to participate were included in the study while antenatal mothers with a) multiple pregnancies and b) congenital abnormalities in the foetus were excluded from the study.

### *3.4. Methodology*

Following the selection of cases, a detailed history regarding age, BMI, obstetric score, period of gestation at the time of the study, risks associated, their Doppler studies, CPR, percentile, Amniotic fluid index, period of gestation at birth, period of prolongation of pregnancy, birth weight, ABG pH at birth, route of delivery, indication for LSCS, instrumental delivery, NICU admission, duration of stay, and use of ventilation were noted.

Women were categorized into high-risk pregnancy if they had gestational hypertension or gestational diabetes, otherwise low-risk pregnancy. They were followed up till delivery, and foetal outcome was noted. In addition, foetal arterial blood pH was recorded and correlated with the foetal outcome.

### *3.5. Doppler examination*

The Doppler waveform study was performed by GE LOGIQ PE6 scanner with a 3.5 MHz transducer. A routine Doppler velocimetry using B-mode was first conducted with the patient in a recumbent position. The UA and MCA flow velocity wave forms were obtained. The CPR was calculated by taking the ratio of pulsatility index of MCA to pulsatility index of UA.

The reference value for CPR was a single cut-off value of <1.08.

### *3.6. Statistical analysis*

Association of categorical variables was performed by Chi-square test. The difference in the mean values of the quantitative variables, such as CPR ratio between the low-risk versus high-risk) pregnant women were tested for statistical significance by student's t-test.

## 4. Results and Discussion

### *4.1. Age distribution*

The age distribution in the present study was in the range of 18 to 45 years. The mean age was 31.5 years. The mean age in the low-risk group (control group)was 25.6 ± 4.31 years, while in the high-risk group (study group) was 27.4 ± 4.1 years. A study done by Flatleyet al.[13] reported the mean age group of women included in the study observational to be 31.5± 5.8 years and that in the reference observational study was 30.3± 5.8 years. This was statistically significant. Another study done by Pe´rez-Cruz et al.[14] reported that age distribution was 32± 5 in the study group and 31±6 in the IUGR group, which was not statistically significant. The mean age in our study was lower as compared to the other two studies.

### *4.2. Distribution of BMI*

In the present study, the BMI of women ranged from 17.6 to 39.8 kg/m$^2$. The mean BMI was 28.7 kg/m$^2$. In a study done by Flatley et al.[13] the mean BMI of women in the control group was 23.9 kg/m$^2$ (20.8–28.9 kg/m$^2$), and the BMI of women in the reference group was 22.7 kg/m$^2$ (20.0–26.6 kg/m$^2$), and it was statistically significant. The higher BMI noted in our study could be due to the increased urbanization of our study population.

**Table 1:** The maternal characteristics of the women enrolled in the study

| | | | |
|---|---|---|---|
| | **Age** | **n** | **%** |
| Distribution of Age | ≤20 | 21 | 5.1% |
| | 20 – 24 | 151 | 37% |
| | 25 – 29 | 150 | 37% |
| | 30 – 34 | 73 | 17% |
| | 35 - 39 | 11 | 2% |
| | ≥ 40 | 4 | .9% |
| | | 410 | 100% |
| Distribution according to BMI in Kg/m$^2$ | BMI | N | % |
| | <18 | 1 | .2 |
| | 18 – 24.9 | 66 | 16.1 |
| | 25- 29.9 | 182 | 44 |
| | 30 – 35 | 140 | 34 |
| | >35 | 22 | 5 |
| | | 410 | 100 |
| Obstetric score | | N | % |
| | Primi | 176 | 42.82 |
| | Multi | 235 | 57.18 |
| | | 410 | 100 |
| Risks associated | | N | % |
| | Preeclampsia | 28 | 6.8% |
| | Gestational hypertension (PIH) | 24 | 5.9% |
| | Gestational diabetes mellitus (GDM) | 18 | 4.4% |
| | Chronic hypertension | 2 | 0.49% |
| | T2 DM | 6 | 1.5% |
| | | N =78 | |
| Classification of risk | | N | % |
| | Low risk | 322 | 80.59% |
| | High risk | 78 | 19.4% |
| | | 400 | 100% |
| Period of prolongation of pregnancy after 30 – 34 weeks period of gestation till delivery | | N | % |
| | 0 days | 5 | 1.25% |
| | <1 week | 2 | 0.5% |
| | 1 -2 weeks | 16 | 4% |
| | 2+1- 4 weeks | 114 | 28.5% |
| | 4 +1– 6 weeks | 251 | 62.75% |
| | 6+1 – 8 weeks | 12 | 3% |
| | | 400 | 100% |

### *4.3. Distribution of parity*

In the present study, 57% of cases were multiparous, and 43% were nulliparous. There is an almost equal distribution among the primigravida and multigravida. In a study done by Flatley et al.[13] 41.6% of women were nulliparous. In another study done by Pe´rez-Cruz et al. 57% of women were nulliparous in the control group, and 67% were nulliparous in the high-risk group. The high risk/ FGR group had more nulliparous women than the low-risk/ control group.

### *4.4. Risks associated*

In the present study, the commonest risk factors were hypertension (12.6%) and diabetes (6.9%). In a study conducted by Flatley et al.,[13] 11.5% of women had hypertension in the study group, and 35.8% of women had diabetes. The incidence of hypertension is similar in both studies. But there was a considerable difference in the incidence of diabetes.

### *4.5. Period of prolongation of pregnancy*

In the present study, the maximum prolongation of pregnancy was achieved in 62.75%( 251) of cases for a period of 4 weeks +1 day to 6 weeks. In 1.25% (5) of cases, pregnancy could not be prolonged, women delivered on the same day of the Doppler study. The cases in which pregnancy was extended beyond four weeks were closely followed up with NST, AFI, diastolic flow, Ductusvenosus, Doppler, and we were able to prolong the pregnancy and had a better foetal outcome with a reduced duration of NICU stay.

### *4.6. Birth weight*

In the present study, the mean birth weight of babies among the normal Doppler group was 2.82 Kg. However, Pe´rez-Cruz et al.[14] reported the mean birth weight to be 3.35 Kg in the reference group.

In the present study, the mean birth weight of babies among the FGR babies was 1.94 Kg. However, Pe´rez-Cruz et al.[14] reported the mean birth weight to be 2.14 Kg in the study group.

In the present study, the difference between the mean birth weight of FGR babies and normal babies was statistically significant.

### *4.7. Arterial blood gas pH at birth*

In the present study, the ABG pH of babies with normal Doppler was in the range of 7.3 to 7.5, while the babies with abnormal Doppler had a pH of less than 7.3. In comparison, the study by Perez Cruz et al.[14] reported the pH range to be 7.23 ± 0.08 for babies with normal Doppler and 7.24 ± 0.08 for babies with abnormal Doppler.

**Table 2:** The neonatal characteristics of the delivered babies

| | **Birth weight** | **N** | **%** |
|---|---|---|---|
| Birth weight | <1.5 kg | 12 | 3% |
| | 1.5 – 2 kg | 21 | 5.25% |
| | 2.1 – 2.5kg | 46 | 11.5% |
| | 2.6 – 3 kg | 195 | 48.75% |
| | >3 kg | 126 | 31.5% |
| | | 400 | 100% |
| | | N | % |
| ABG pH at birth | Normal | 366 | 91.5% |
| | Abnormal | 34 | 8.5% |
| | | 400 | 100% |
| | | N | % |
| Period of gestation at birth | 30 – 31+6 weeks | 12 | 3% |
| | 32 – 33+6weeks | 21 | 5.25% |
| | 34 – 35+6weeks | 46 | 11.5% |
| | 36 – 37+6 weeks | 180 | 45% |
| | ≥38 weeks | 141 | 35.25% |
| | | 400 | 100% |
| | | N | % |
| Amniotic Fluid Index at 30-34 weeks | <5 | 19 | 4.63% |
| | 5 – 25 | 388 | 94.63% |
| | >25 | 3 | 0.73% |
| | | 410 | 100% |
| | | N | % |
| Route of delivery | Vaginal | 267 | 66.75% |
| | Elective LSCS | 26 | 6.5% |
| | Emergency LSCS | 107 | 26.75% |
| | | 400 | 100% |
| | | N | % |
| Instrumental delivery | Forceps | 0 | 0% |
| | Vacuum | 39 | 97.5% |
| | Forceps + vacuum | 1 | 2.5% |
| | | 40 | 100% |
| | | N | % |
| Indication for emergency LSCS | Indication | N | % |
| | Fetal distress | 48 | 44.85% |
| | NPOL | 26 | 24.29% |
| | Patients choice | 25 | 23.36 |
| | Scar dehiscence | 3 | 2.8% |
| | Breech presentation | 4 | 3.73% |
| | Cord prolapse | 1 | 0.93% |
| | | 107 | 100% |

In the present study, in babies with normal Doppler, 6.2% (20 babies among 322 babies) had abnormal ABG pH, which may be due to the perinatal insult. Of these, 16 babies were shifted to NICU, and only one baby was on ventilation (CPAP). The mean duration of NICU stay was 5.89 days.

In the babies with abnormal Doppler (FGR), 33.3% (6 babies among 18 babies) had abnormal ABG pH, which is in line with the result reported by Pe´rez-Cruz et al.[14] Babies having abnormal Doppler were shifted to NICU, of which six babies were on ventilation (three babies were on SIMV mode, and three babies were on CPAP), with a mean duration of NICUstay of 20 days.

### *4.8. Period of gestation at birth*

In the present study, the period of gestation (POG) at birth is as shown in Table 2 . The mean POG at birth was 38 weeks (266 days) for babies who had normal Doppler, and it was 35 weeks (245 days) for babies with FGR. These results coincide with those reported by Pe´rez-Cruz et al.

### *4.9. Route of delivery*

In the present study, 66.75% (267) of women had a vaginal delivery, of which six women had abnormal Doppler reading; 26.5% (107) of women underwent Emergency LSCS of which 12 women had an abnormal Doppler reading, and 6.5% (26) underwent Elective LSCS. Among the six women who had abnormal CPR but had a vaginal delivery, the onset of FGR was more than 32 weeks (late-onset FGR). Of the 107 women who underwent emergency LSCS, 44.85% (48) underwent LSCS for foetal distress, of which 45(93.5%) had normal Doppler, and three women (6.25%) had abnormal Doppler. The babies of these three women were shifted to NICU for observation but not on ventilation. All babies were eventually discharged without any immediate morbidity.

In a study by Perez-Cruz et al.,[14] 79.3% (238) had a vaginal delivery. 20.6% (62) underwent Emergency LSCS. Elective LSCS was not mentioned in this study. Of the 62 women who underwent emergency LSCS, 47 had abnormal Doppler, while 15 women had normal Doppler.

In a study by Ganju et al.,[15] in 117 study women, abnormal CPR (<1.08) was found in 65 cases with a statistically significant correlation for prediction of cesarean section delivery ($p<0.001$).

A systematic review of 13 prospective and eight retrospective studies by Dunn et al. concluded that Fetal CPR was predictive of caesarean section for intrapartumfetal compromise, small for gestational age and fetal growth restriction and neonatal intensive care unit admission.

However, in our study, abnormal CPR value was not a contraindication for vaginal delivery.

### 4.10. NICU admissions

In the present study, the number of NICU admissions was 47. Most of them were premature babies who required surfactant administration.

In the present study, in the babies with normal Doppler, the mean duration of NICU stay was eight days, while in babies with abnormal Doppler, the NICU stay was 103 days. Of the 18 babies who had abnormal CPR, 13 babies were admitted to the NICU (72%). Ganju et al.[15] also noted a strong association of CPR < 1.08 with admission to the NICU (86%). In a study by Perez-Cruz et al.,[14] none of the babies with normal Doppler required NICU admission, while the mean duration in the NICU for babies whose mothers had abnormal Doppler was 14 days, which was very much less as compared to our study.

The association of risk factors with the outcome in late-onset FGR is given in Table 3 .

The association of high risk and low-risk pregnancies with various variables is given in Table 4.

In our study, high-risk pregnancywas defined as having at least one of the following conditions: preeclampsia or gestational hypertension or gestational diabetes mellitus.

As shown in Table 4, significantly more women in the low-risk group had vaginal deliveries than women in the high-risk group (74.22% vs 44.87%, p <0.001).

NICU admissions significantly increased with high-risk patients than low-risk patients (22.22% vs 9.4%, p=0.002).

Women with abnormal Doppler are almost double (7.6%) in high-risk cases compared to women belonging to low-risk groups (3.41%).

The period of prolongation of pregnancy was significantly lower in the high-risk group as compared to the low-risk group (31.09 ± 13.9 vs 37.79 ± 15.1, p=0.003).

The CPR in early severe fetalgrowth restriction (FGR)and late mild fetal growth restriction(FGR) is shown in Table 5 .

The boxplot of birth weight of neonates, mean period of prolongation of pregnancy and mean period of gestation inbabies who had normal vs abnormal CPR values is shown in Figures 1, 2 and 3 , respectively.

Women with normal CPR values had neonates whose birth weight was higher than women with abnormal CPR (2.82 Kg vs 1.94 Kg). Similar to our study, a study by Ganju et al.[15] reported that abnormal CPR (<1.08) had a statistically significant correlation for the prediction of low birth weight (p<0.001).

A higher period of prolongation of pregnancy was achieved in women who had normal CPR compared to women who had abnormal CPR. (37.56 weeks vs 14.64 weeks).

The mean period of gestation was significantly higher for babies with normal CPR values than those who had abnormal CPR values (266.47 days vs 245.41 days).

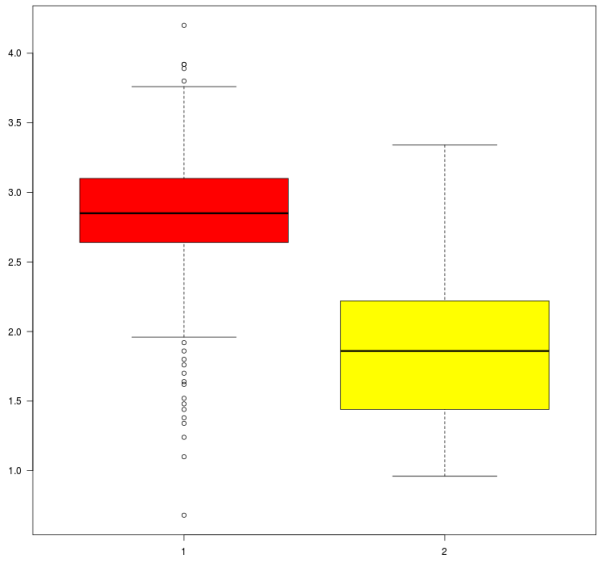


**Fig. 1:** The boxplot of birth weight of neonates who had normal vs abnormal CPR

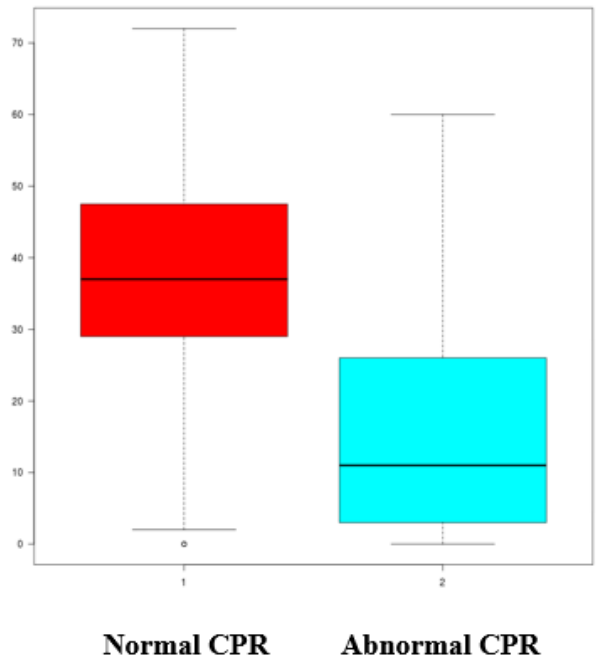


**Fig. 2:** The boxplot of the period of prolongation of pregnancy for babies who had normal vs abnormal CPR values

**Table 3:** Association of outcome in late-onset FGR with risk factors

| Risks associated | POG at birth (mean) | Vaginal | LSCS | CPR Normal/ Abnormal | ABG pH Normal/ Abnormal | Birth weight <2.5KG/>2.5Kg | NICU stay (duration in days) (mean) | Ventilation (yes/no) |
|---|---|---|---|---|---|---|---|---|
| Preeclampsia [n=3] | 36 | 2 | 1 | 2/1 | 1/2 | 3/0 | 3,13,4(6.6) | 0/3 |
| Gestational hypertension (PIH)(n=5) | 36 | 3 | 2 | 5/0 | 3/2 | 3/2 | 7,12(9.5) | 0/5 |
| GDM + Preeclampsia/ PIH (n=13) | 37+3 | 11 | 2 | 11/2 | 10/3 | 3/10 | 6,35,0.5,5 (11.6) | 2/11 |

**Table 4:** The association of high risk and low-risk pregnancies with various variables

| Variables | High risk N, % (78, 19.5%) | Low risk N, % (322, 80.5%) | Total N, % (400, 100%) | Chi-Square | p-value |
|---|---|---|---|---|---|
| Route of delivery | | | | | |
| Emergency CS | 30 (38.46) 13 | 71 (22.04) 12 (3.72) | 101 (25.25) 25 | 38.71 | <.0001 significant |
| Elective CS | (16.66) 35 (44.87) | 239 (74.22) | (6.25) 274 (68.5) | | |
| Vaginal | | | | | |
| NICU admissions | | | | | |
| Yes | 31 (22.22) | 16 (9.4) | 47 (11.72) | | |
| Mean stay,days | 8.42 | 5.89 | | 9.35 | 0.002 significant |
| Ventilation(y/n) | 6/72 | 1/321 | | | |
| No | 47 (77.77) | 306 (90.57) | 353 (88.28) | | |
| CPR | | | | | |
| Normal | 72 (92.30) | 310 (96.5) | 382 (95.5) | 3.5 | 0.061 Not significant |
| Abnormal | 6 (7.6) | 12 (3.41) | 18 (4.5) | | |
| | Mean ± std | Mean ± std | Mean ± std | T value | p-value |
| POG at Birth, days | 262.36 ± 16.7 | 266.3 ± 18.1 | 265.58 ± 17.16 | -1.78 | 0.075 Not significant |
| Birth weight | 2.73± 0.39 | 2.79± 0.41 | 2.79 ± 0.48 | -0.98 | 0.33 Not significant |
| Period of prolongation, weeks | 31.09 ± 13.9 | 37.79 ± 15.1 | 36.5 ± 14.5 | -3.62 | 0.0003 significant |

**Table 5:** CPR in early severe fetal growth restriction (FGR)and late mild fetal growth restriction (FGR)

| | Early-onset FGR (<32 weeks) with abnormal Doppler = CPR abnormal (mean) | Late-onset FGR (>32 weeks) with abnormal Doppler (mean) |
|---|---|---|
| Total cases = 18 | 2 | 16 |
| CPR (Percentile)(mean) | 1 | 2.2 |
| Duration of prolongation of pregnancy (mean) | 2 days | 2weeks+3days (mean) |
| Vaginal | 0 | 6 |
| LSCS | 2 | 10 |
| ABG pH (Normal/Abnormal) | 0/2 | 4/12 |
| NICU Stay =Yes | 2 | 11 |
| Duration: mean days | 20 | 8.5 |

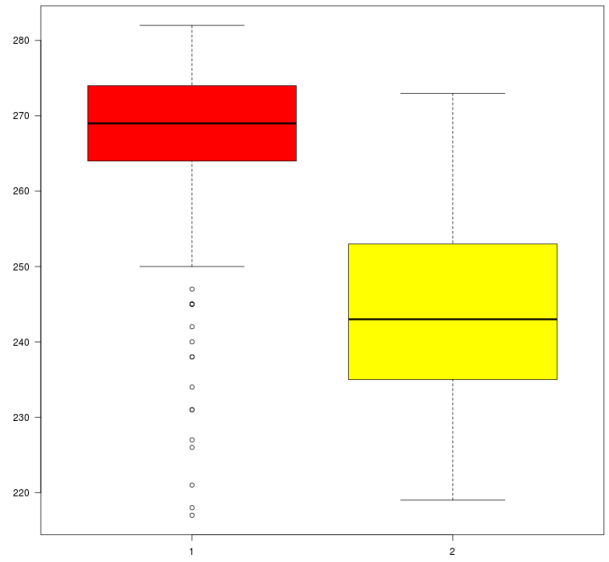


**Fig. 3:** The boxplot of the period of gestation before birth for neonates whose mothers had normal vs abnormal CPR values

The above three results indicate that period of gestation, birth weight, and prolongation period are significantly lower with patients with abnormal CPR compared to patients with normal CPR.

## 5. Conclusion

Doppler ultrasound velocimetry of umbilical and foetal vessels has become an established method of antenatal monitoring, thereby allowing the non-invasive assessment of neonatal circulation and its perinatal outcome.In low-risk cases, following up patients with Doppler has less significance than high-risk cases. However, Doppler velocimetry should be done in high-risk cases at 30 – 34 weeks to detect FGR since the morbidity and mortality associated with late-onset FGR are high compared to early-onset FGR.

Doppler velocimetry helps significantly for the detection and follow up in late-onset FGR and will also help decide the time of delivery or prolongation of pregnancy.

Babies with abnormal CPR can be followed up or monitored with daily AFI and NST. Still, Doppler velocimetry becomes an important tool for the decision of timing of delivery after lung maturity.

It is also a significant parameter to differentiate early-onset severe FGR and late-onset mild FGR, which is difficult to diagnose without Doppler velocimetry, although comparatively easier to manage. Late-onset FGR babies do not adapt well to the sudden onset of hypoxia, unlike the early onset fetuses who adapt well to the hypoxia.

There is no contraindication for vaginal delivery in low-risk cases with abnormal Doppler, provided we monitor them with other parameters like NST, AFI, and flow in DuctusVenosus. Hence, Doppler velocimetry becomes an essential tool for high-risk cases and late-onset (after 32 weeks) mild FGR.

Yet, more extensive studies are needed to state the need for routine Doppler at 30 weeks or more to detect and manage FGR in both high risk and low-risk cases. In addition, long term morbidity needs to be studied in both early-onset and late-onset FGR in our population.

## 6. Source of Funding

None.

## 7. Conflict of Interest

The authors declare no conflict of interest.

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