

A Comparative Study of Perinatal Outcome in Women with Pre-Eclampsia Using Cerebroplacental Ratio of Fetal Middle Cerebral Artery and Umbilical Artery on Doppler Ultrasound

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Abstract: We conducted an observational prospective study from May 2018 to October 2019 in which Doppler Ultrasonography was done in 100 Antenatal women with pre-eclampsia, beyond 34 weeks of gestation. Based on cerebroplacental ratio patients were divided into two groups: 1. cerebroplacental ratio ≥ 1 , 2. cerebroplacental ratio < 1 . There were 65 cases with a CPR > 1 and 35 with CPR < 1 . More women with CPR < 1 required caesarean section (85.7%), developed IUGR (85.7%), required early termination with average gestational age at termination being 36.1 weeks, had low birth weight babies, mean birth weight being 2208g, thus higher number of babies required NICU care (71.4%). In women with CPR > 1 , caesarean section rate was 46.2%, average age for termination of pregnancy was 37.4 weeks, mean birth weight 2426 g with 30.5% fetuses developing IUGR and 30.5 % neonates requiring NICU care. Our study showed that women with CPR < 1 had higher chances of development of IUGR and undergoing caesarean section. They required preterm termination of pregnancy and had low birth weight babies who needed NICU care. There were no still births or neonatal deaths indicating that timely intervention in delivering a woman with pre-eclampsia with changes on Doppler ultrasound can prevent adverse neonatal outcomes.

Keywords: Pre-eclampsia, Doppler Ultrasonography, Cerebroplacental Ratio, Neonatal Outcome

1. Introduction

Pre-eclampsia is a multisystem disorder specific to pregnancy and puerperium, which manifests by onset of hypertension and proteinuria after 20 weeks of gestation and resolves by 12 weeks postpartum. (1) It is associated with increased perinatal morbidity and mortality due to compromised uteroplacental and fetoplacental perfusion. (2)

Doppler ultrasound allows safe, non-invasive, rapid investigation of the uteroplacental and fetoplacental circulation using three arterial indices devised to assess quality of flow in vessels, namely Resistive Index (RI), Pulsatility Index (PI) and Systolic/Diastolic ratio (S/D ratio). (3) (4)

Doppler studies of fetal circulation in growth restricted and hypoxic fetuses of pre-eclamptic mothers demonstrate increased resistance to flow in the umbilical arteries and redistribution of fetal cardiac output to favour the cranial circulation and myocardium at the expense of splanchnic circulation. This brain sparing effect is seen when circulatory adaptation occurs with chronic hypoxia in form of cerebral vasodilatation to preserve blood flow to the brain. This is demonstrated by a lower value of MCA RI relative to gestational age and UA RI. Its disappearance is a critical event and precedes fetal death (6). Also, studies have shown

the CPR to be predictive of adverse perinatal outcome. Doppler studies of multiple fetoplacental vessels can be used to monitor compromised fetus predicting adverse perinatal outcome and assisting in optimal time of delivery. (7) (8) (9) (10)

2. Literature Survey

Hypertensive disorders represent the most common medical complications of pregnancy affecting 7-15% of all gestations and account for approximately a quarter of all antenatal admissions (11).

Hypertensive disorders also carry a risk for the baby. Hypertension and/or proteinuria are leading identifiable risk factors in pregnancy associated with stillbirth. In the most recent UK perinatal mortality report, 1 in 20 (5%) stillbirths in infants without congenital abnormality occurred in women with pre-eclampsia. Pre-eclampsia is strongly associated with fetal growth restriction, low birth weight, spontaneous or iatrogenic preterm delivery, respiratory distress syndrome and admission to neonatal intensive care (12).

Pre-eclampsia contributes significantly to overall preterm birth rate, both spontaneous and iatrogenic. About 1 in 250 primigravidae (0.4%) will give birth prior to 34 weeks as a

consequence of pre-eclampsia and 8-10% of all preterm births result from hypertensive disorders. Half of women with severe preeclampsia give birth preterm. Growth restriction arising from placental disease is common, with 20-25% of preterm births and 14-19% of term births in women with preeclampsia being less than 10th centile of birth weight for gestation (13).

In women with pre-eclampsia, trophoblastic invasion during placental development is incomplete and shallow, deeper myometrial arterioles do not lose their endothelial lining and musculo-elastic tissue and their mean diameter is half that of vessels in normal placenta resulting in reduced uteroplacental blood flow.

Compromised uteroplacental and fetoplacental perfusion is almost certainly a major culprit in the greater perinatal mortality and morbidity rates seen in preeclampsia. Measurement of uterine artery, umbilical artery and fetal middle cerebral artery blood flow velocity by Doppler ultrasound has been used to estimate resistance to uteroplacental and fetoplacental circulation.

Resistive Index (RI) is an indicator of resistance of an organ to perfusion. It is the most commonly used index as it is easier to calculate and is reflective of vascular resistance (5)

- Resistive Index (RI) = $\frac{\text{Peak Systolic Velocity (PSV)} - \text{End Diastolic Velocity (EDV)}}{\text{Peak Systolic Velocity (PSV)}}$

The cerebroplacental resistive index ratio is the ratio of the Middle cerebral artery resistive index (MCA R. I) to the Umbilical artery resistive index (UA R. I.). It is calculated as shown in the formula below:

- Cerebroplacental ratio (CPR) = $\frac{\text{Resistive index of middle cerebral artery (MCA RI)}}{\text{Resistive index of Umbilical artery (UA R. I)}}$

A ratio >1.0 indicates preferential flow to vital structures like brain, heart and adrenal glands and is therefore considered normal while that <1.0 is indicative of high resistance in utero-placental circulation via Umbilical Artery (UA) Doppler waveform and inadequate supply to fetal brain via Middle Cerebral Artery (MCA) Doppler waveform known as centralization and is considered to be predictive of adverse perinatal outcome. The brain sparing effect is seen when circulatory adaptation occurs with chronic hypoxia in form of cerebral vasodilatation to preserve blood flow to the brain. This is demonstrated by a lower value of MCA RI relative to gestational age and UA RI. Its disappearance is a critical event and precedes fetal death (14)

A prospective cohort study conducted by PL Parshuram et al at Kenyatta National Hospital, Nairobi in 2013 studied the cerebroplacental ratio as a prognostic factor of fetal outcome in patients with Hypertensive states of pregnancy in third trimester. It was concluded that cerebroplacental ratio was predictive of adverse perinatal outcomes in patients with hypertensive disorders. Low birth weight was 4.7 times more likely in CPR <1 and that lower segment cesarean section should be a recommended mode of delivery for hypertensive mothers. (15)

3. Problem Definition

Abnormal placentation plays one of the key roles in development of pre-eclampsia and altered uteroplacental circulation which leads to increased perinatal morbidity and mortality.

Measurement of uterine artery, intervillous and placental blood flow would be informative to assess the uteroplacental perfusion. Attempts to assess these in humans have been hampered by several obstacles that include inaccessibility of the placenta, the complexity of its venous effluents and the need for radioisotopes or invasive techniques.

Doppler Ultrasound provides a safe, non-invasive, rapid method for measurement of uterine artery, umbilical artery and fetal middle cerebral artery blood flow velocity to estimate resistance to uteroplacental and fetoplacental circulation. Thus it can be used to predict neonatal morbidity and plan for timely intervention.

4. Materials and Methodology

We conducted an observational prospective study from May 2018 to October 2019 in which 100 Antenatal women in the age group of 18 to 35 years, fulfilling the inclusion criteria of a singleton pregnancy with pre-eclampsia, with gestational age beyond 34 weeks, visiting antenatal OPD or admitted, were subjected to history followed by clinical examination, BP monitoring, basic antenatal investigations, ultrasonography and Doppler ultrasonography.

Ultrasonography was done using 3.5Mhz convex assay and linear assay by "Toshiba-SSA-660A XARIO-USG" USG machine. The ultrasonography was done by Senior Medical Officer of the Radiology department and on a single machine to avoid errors.

Blood flow indices namely, the S/D ratio, Pulsatility Index and Resistance Index were studied in the uterine artery, umbilical artery and fetal middle cerebral artery by Doppler ultrasonography. Cerebroplacental ratio of the resistance indices of the fetal middle cerebral artery and mid-cord of umbilical artery was calculated. Doppler ultrasound was repeated weekly after 34 weeks of gestation and the last ultrasound before termination of pregnancy was taken into account for the study.

Patients were divided into two groups based on the value of their cerebroplacental ratio. One group with cerebroplacental ratio ≥ 1 , considered normal, and the other with cerebroplacental ratio <1 suggestive of altered fetomaternal circulation.

Outcome was assessed in terms of:

- Need for preterm or immediate termination of pregnancy.
- Mode of delivery-vaginal or lower segment caesarean section. Indications of LSCS taken into consideration were either elective LSCS for Doppler changes or emergency LSCS for fetal compromise such as, fetal distress or meconium stained liquor. Cases in which LSCS was done for any other reasons not pertaining to

fetal compromise such as failure of induction were excluded from the study.

- Development of IUGR.
- Intra-Uterine fetal demise.
- Need for resuscitation after birth.
- Need of NICU admission.
- Neonatal death.

This study was approved by the Institutional Ethics Committee.

5. Results

There were 65 cases out of 100 with a CPR >1 and 35 with CPR<1. Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical Variables were determined. Association between Variables was analyzed by using Chi-Square test for categorical Variables. Level of significance was set at 0.05.

• Association between Mode of Delivery and Cerebroplacental Ratio (Table 1)

In our study a higher rate of caesarean section was noted in women with CPR <1.30 out of the 35 patients (85.7%) with CPR <1 were delivered by caesarean section to avoid adverse effect on neonate as most of these fetuses had IUGR or developed fetal distress or passed meconium during labour. Only 5 patients (14.3) were delivered by vaginal delivery. In comparison 35 out of 65 patients (53.8%) with CPR >1 delivered vaginally without any adverse neonatal outcome and only 30 out of 65 (46.2%) had to undergo caesarean section.

Table 1: Association between Mode of Delivery and Cerebroplacental Ratio (N=100)

Mode of Delivery	Cerebroplacental Ratio (CPR)	
	<1 (n=35) n (%)	>1 (n=65) n (%)
NVD	5 (14.3)	35 (53.8)
LSCS	30 (85.7)	30 (46.2)
Chi-Square Test, P Value <0.001, Significant		

• Association between Gestational Age at delivery and Cerebroplacental Ratio (Table 2)

In our study, the mean gestational age at delivery was 36.1 weeks in patients with CPR <1 whereas it was 37.4 weeks in patients with CPR >1. The Doppler changes warranted early termination of pregnancy to avoid adverse neonatal outcomes.

Table 2: Association between Gestational Age and Cerebroplacental Ratio (N=100)

Gestational Age (in weeks)	Cerebroplacental Ratio (CPR)	
	<1 (n=35) n (%)	>1 (n=65) n (%)
<37	30 (85.7)	20 (30.8)
>37	5 (14.3)	45 (69.2)
Mean (SD)	36.1 (1.66)	37.4 (1.30)
Chi-Square Test, P Value <0.001, Significant		

• Association between Birth Weight and Cerebroplacental Ratio (Table 3)

In our study the mean birth weight in patients with CPR <1 was 2208 g. Out of 35 patients with CPR <1, 10 (28.6%) had very low birth weight less than 2000 g, 15 (42.9%) had a low birth weight of 2000 g to 2499 g and only 10 (28.6%) had a normal birth weight more than 2500 g. This was seen due to development of IUGR and need for early termination of pregnancy due to changes on Doppler ultrasound. Patients with a normal CPR >1 had a mean birth weight of 2426 g with 35 (53.8%) out of 65 babies having a normal birth weight of more than 2500 g.

Table 3: Association between Birth Weight and Cerebroplacental Ratio (N=100)

Birth Weight (in grams)	Cerebroplacental Ratio (CPR)	
	<1 (n=35) n (%)	>1 (n=65) n (%)
<2000	10 (28.6)	15 (23.1)
2000-2499	15 (42.9)	15 (23.1)
≥ 2500	10 (28.6)	35 (53.8)
Mean (SD)	2208.6 (429.2)	2426.9 (430.5)
Chi-Square Test, P Value = 0.039, Significant		

• Association between Cerebroplacental Ratio and Neonatal Outcome (Table 4)

In our present study, 30 (85.7%) out of 35 patients with CPR <1 developed IUGR and 25 (71.4%) required NICU admission as compared to only 20 (30.5%) out of 65 patients with CPR >1 developed IUGR and 20 (30.5%) required NICU admission. In our study there were no still births or neonatal deaths noted.

Table 4: Association between Cerebroplacental Ratio and Neonatal Outcome (N=100)

Neonatal Outcome	Cerebroplacental Ratio (CPR)		P Value
	<1 (n=35) n (%)	>1 (n=65) n (%)	
IUGR	30 (85.7)	20 (30.8)	<0.001*
Need for ICU Admission	25 (71.4)	20 (30.8)	<0.001*
Chi-Square Test, P Value *Significant			

6. Discussion

In our study we could see that more women with CPR <1 required caesarean section (85.7%), developed IUGR (85.7%), required early termination with average gestational age at termination being 36.1 weeks, had low birth weight babies with mean birth weight of 2208g and thus a higher number of babies required NICU care (71.4%). In the group with CPR>1 the caesarean section rate was only 46.2%, average age for termination of pregnancy was 37.4 weeks with a mean birth weight of 2426 g with only 30.5% fetuses developing IUGR and 30.5 % neonates requiring NICU care.

• Mode of Delivery

In a study conducted by P L Parshuram (15) in 2013, 78% patients out of a total of 160 with CPR <1 were delivered by caesarean section and only 22% had normal vaginal delivery.

Robert et al (16) had 100 % caesarean section rate in patients with CPR <1 in a study conducted with 106 pre-eclamptic women in 2016.

Yalti et al (17) , Maria et al (18) and Shahinaj et al (19) each reported a caesarean section rate of 75%, 44.44% and 76.8% in patients with CPR <1 and only 35.3%, 15.5% and 62.5% respectively in CPR >1 which is corresponding with our study

• Mean Gestational Age at Delivery

Robert et al (16) , Maria et al (18) and Shahinaj et al (19) also found that early termination was required in patients with CPR <1 and the mean gestational age was reported as 32.78 weeks, 36.3 weeks and 34.8 weeks respectively. Whereas patients with CPR >1 safely carried the pregnancy to term with mean gestational ages being 37.07 weeks, 38 weeks and 38.4 weeks respectively.

• Mean birth weight at delivery

Smitha et al (20) reported that only 12 (20.68%) patients out of 58 with CPR <1 had a birth weight more than 2500 g whereas the rest 48 (79.31%) had a low birth weight below 2500 g. Comparatively in the patients with CPR >1 only 18 (42.85%) out of 42 patients had a low birth weight, rest 24 (57.14%) had a normal birth weight.

Patil et al (21) reported that 43 (68.25%) patients out of 63 with CPR <1 had a low birth weight whereas only 20 (31.74%) had a normal birth weight more than 2500g.

Other studies conducted by Robert et al (16) , Yalti et al (17), Maria et al (18) and Shahinaj et al (19) also reported a low mean birth weight in patients with CPR <1 of 1658 g, 2892 g, 2405 g and 2174 g respectively. In comparison the mean birth weight reported in patients with CPR >1 were 2832 g, 3292 g, 3100 g and 3215 g respectively.

• Neonatal Outcome

In a study conducted by Patil et al (21) 44 (69.84%) out of 63 patients with CPR <1 required NICU admission. In a study conducted by Ebrashy et al (22) out of the 38 patients who developed IUGR, 32 had a CPR <1.

Other studies conducted by Maria et al (18) , Shahinaj et al (19) and Robert et al (16) showed that a higher percentage of patients developed IUGR when the CPR was <1 than when CPR was >1. Maria et al (18) and Shahinaj et al (19) reported that 18.46% and 64.33 % of babies required NICU admission when CPR was <1, whereas only 7.69% and 47.41% babies needed NICU when CPR was >1.

In our study there were no still births or neonatal deaths but Patil et al (21) reported 10 (15.87%) still births out of 63 patients with CPR <1 whereas no still births were reported in patients with CPR >1.

7. Conclusion

Our study was conducted to determine the role of Cerebroplacental ratio in predicting neonatal outcome in women with pre-eclampsia. It showed that women with CPR <1 had a higher chance of development of IUGR due to high

resistance to blood flow in the umbilical artery leading to poor blood and inadvertently poor nutrition supply to the growing fetus. Compensatory low resistance in the fetal middle cerebral artery spares the brain of the reduced blood flow but when the CPR falls below 1 even this advantage is lost and chances of adverse outcome of the neonate increases. We observed that women with CPR <1 had a higher rate of undergoing caesarean section for fetal distress or meconium stained liquor as the compromised blood flow to the fetus caused fetal hypoxia. They also needed preterm termination of pregnancy with the average gestational age at delivery being 36.1 weeks. As a combined effect of preterm termination of pregnancy and higher chances of developing IUGR, neonates born to mother with a CPR <1 had a low birth weight, average being 2208 g and an increased need for NICU admission. We had no still births or neonatal deaths indicating that timely intervention in delivering a woman with pre-eclampsia with changes on Doppler ultrasound can prevent adverse neonatal outcomes. Thus we came to a conclusion that cerebroplacental ratio in women with pre-eclampsia can help us to detect IUGR and determine the time and mode of delivery so as to avoid adverse neonatal outcomes.

8. Clinical Significance

Doppler ultrasound is an inexpensive, non-invasive investigation which can be easily done in all women with pre-eclampsia to detect any significant uteroplacental and fetoplacental insufficiency based on which timely intervention can be done to prevent adverse neonatal outcomes.

9. Future Scope

The incidence of Pre-eclampsia in pregnant women in India was studied to be 10.3% in 2019 (23). With increasing age of pregnancy, obesity, pre-existing type 2 diabetes and chronic hypertension this incidence is likely to increase. Thus monitoring the uteroplacental and fetoplacental circulation in these women with the help of Doppler Ultrasound will be an essential tool in predicting neonatal morbidity and deciding the appropriate time for intervention to prevent neonatal mortality.

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