Original Article

Evaluation Of Middle Cerebral/Umbilical Artery Resistance And Pulsatility Indices Ratio As Predictors Ffor Fetal Well-Being And Neonatal Outcome In Preeclampsia With Or Without Intrauterine Growth Restriction

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Abstract

Background Pre-eclampsia is linked to abnormal uteroplacental circulation, which could have a negative perinatal result by affecting foetal growth and oxygenation. Doppler ultrasound is a good tool for examining the aberrant vascular resistance to blood flow in the uteroplacental and fetoplacental circulation. **Objective** Detection of the middle cerebral to umbilical arteries with accuracy Prediction of foetal health and newborn outcome using the Doppler indices ratio in pregnancies complicated by pre-eclampsia with or without signs of intrauterine growth restriction. **Methods** This study included 90 pregnant patients attending to Kasr El-Ainy Hospital high risk pregnancy unit from 2014 to 2016. Patients were divided into two groups, *first group included* 30 cases with normal uncomplicated pregnancies. The *second group included* 60 cases with pregnancies complicated by pre-eclampsia Patients of the preeclamptic group were subdivided further into two subgroups first is mild pre-eclampsia and second is sever pre-eclampsia and all subgroups were assessed for the presence of IUGR. **Results** IUGR and adverse neonatal outcome were significantly associated with the severity of preeclampsia. The ability of CPR and R.I ratio to predict IUGR in mild group was evaluated; the sensitivity, specificity, positive predictive value, negative predictive value and accuracy for the CPR were 100%, 96%, 83.3%, 96% and 96.7% respectively. The corresponding figures for the RI ratio were 80%, 92%, 66.7%, 95.8% and 90%, respectively. Furthermore, in the sever group, the ability of CPR and R.I ratio to predict IUGR was evaluated ;the sensitivity, specificity, positive predictive value, negative predictive value and accuracy for the CPR were 94.4%, 100%, 94.4%, 92.3% and 96.7%. For detection of adverse neonatal outcome in the mild group, both CPR and R.I ratio showed similar values of sensitivity, specificity, positive predictive value, negative predictive value and accuracy of CPR and R.I ratio in detection of adverse neonatal outcome were 100%, 85.7% , 33.3%, 85, 7% and 86.7% respectively. Where as in the sever group the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of CPR and R.I ratio in detection of adverse outcome were 91.7%, 66.7%, 64.7%, 92.3%, 76.7% and 91.7%, 61.1%, 61.1%, 91.7% and 73.3% respectively. **Conclusion** When it comes to IUGR and poor neonatal outcomes in the foetuses of preeclamptic and gestational hypertensive women, CPR is a very good predictor. When it comes to detecting IUGR and a poor newborn outcome in pre-eclampsia, CPR is more accurate than R.I ratio.

Keywords: Middle Cerebral Artery; Umbilical Artery; Resistance Index; Pulsatility Index, Fetal Well-Being; Neonatal Outcome; Preeclampsia; Intrauterine Growth Restricti

INTRODUCTION

Up to 10% of all pregnancies worldwide are complicated by hypertensive disorders of pregnancy, including pre-eclampsia, which is one of the leading causes of maternal and perinatal morbidity and mortality [(1)].
Pre-eclampsia is linked to abnormal uteroplacental circulation, which could have a negative perinatal result by affecting foetal growth and oxygenation. Doppler ultrasound is a good tool for examining the aberrant vascular resistance to blood flow in the uteroplacental and fetoplacental circulation. A routine, non-invasive method for hemodynamically monitoring the health of the foetus is the use of colour Doppler investigations. These vascular Doppler analyses are mostly used in high-risk obstetric patients while making decisions. Although pre-eclampsia screening with uterine artery Doppler is the main application, its examination was included to learn more about materno-placental circulation and to investigate the relationship with unfavourable perinatal outcomes [(2)].

The foetus uses a compensatory mechanism to adjust the cardiac output and the blood supply to the brain in order to maintain continuous oxygen delivery to this important organ in response to foetal hypoxia [(3)].
Intrauterine growth restriction is thought to affect foetuses whose estimated foetal weight is less than the 10th percentile (foetus weighs less than 90% of all other foetuses of the same gestational age) and who do not develop to their full growth potential as seen by their growth curves (IUGR). According to estimates, foetal growth restriction affected between 3 and 10 percent of all newborns in preeclampsia situations [(4)].

Based on similar placental abnormalities known as improper implantation and characterised by trophoblast inability to develop, invade, and remodel the spiral arteries, some instances of IUGR have been etiologically related to pre-eclampsia. These parallels support the theory that although having different clinical presentations, pre-eclampsia and IUGR related to placental insufficiency have a shared aetiology [(5)].

An important part of screening for poor placentation and its consequences, including as pre-eclampsia and intrauterine growth restriction, is the use of Doppler measurement of placental circulation [(6)].
foetal growth limitation management. Middle cerebral artery and umbilical artery together Doppler displays the equilibrium between foetal hypoxia and declining placental perfusion [(7)].

In pre-eclamptic patients, the umbilical artery Doppler indices offer better values for predicting IUGR or a poor perinatal outcome. Since the MCA pulsatility index (PI) often paradoxically displays normal values in certain severe cases, it does not accurately reflect the severity of pathology in the early gestational weeks. As a result, the cerebralumbilical ratio should offer more diagnostic precision than either vascular Doppler indices used independently [(8)].

Doppler testing every two weeks will be sufficient in instances of pregnancy at risk for hypertensive diseases with or without IUGR to monitor the development of placental function and foetal oxygenation. On the other hand, it is advised to repeat the Doppler measurements more frequently at the cerebral and umbilical in the event of substantial IUGR with abnormal Doppler indices in order to measure the foetal flow redistribution, which is closely related to variations in foetal PO2 [(9)].

Methods

90 pregnant patients who visited the high-risk pregnancy unit at Kasr El-Ainy Hospital between 2014 and 2016 were included in this study. Two groups of patients were formed, the first of which contained 30 instances with typical, straightforward pregnancies. Pregnancies complicated by pre-eclampsia were present in 60 cases in the second group. Pre-eclamptic patients were then separated into two subgroups: mild pre-eclampsia and severe pre-eclampsia. Each subgroup was tested for the presence of IUGR.

Inclusion criteria
Women in Group 1 (the control group) ranged in age from 20 to 40 and had single, viable pregnancies with gestational ages between 34 and 40 weeks. No obstetrical or medical issues with pregnancy existed in any of the patients, which were all normotensive.

Our patients were selected from instances scheduled for elective caesarean sections for a variety of reasons in the absence of pregnancy-related medical illnesses. These cases typically involved repeated caesarean sections, primary infertility, or breech mal-presentations.

Women in Group 2 (the pre-eclamptic group) ranged in age from 20 to 40, had single, viable pregnancies, ranged in gestational age from 34 to 40 weeks, and had no other obstetric or medical pregnancy issues save pre-eclampsia.

Blood pressure 140/90 on two different occasions, no history of hypertension prior to pregnancy, persistent proteinuria 1+ dipstick, or patients exhibiting any linked criteria confirming diagnosis and denoting severity were the characteristics of the cases.
To classify all of the patients in this group as mild or severe, each was examined for the existence of any severity criteria. A fresh development of a visual or cerebral problem, pulmonary oedema, thrombocytopenia (CBC indicates platelets count less than 100,000/microlitre), excessively high liver enzymes, and renal insufficiency (serum creatinine greater than 1.1 mg/dL) were the required conditions. All of these individuals were selected from instances that were admitted for scheduled elective caesarean sections in order to terminate pregnancies due to preeclampsia. Group 2a was created from the patients in this group and contained 30 cases of mild pre-eclampsia with blood pressure readings between 140 and 160, persistent proteinuria more than 1, and no severity criterion. Group 2b consisted of 30 cases of severe pre-eclampsia with blood pressure less than 160/100 and at least one of the following conditions: new onset of a visual or cerebral disturbance, pulmonary oedema, thrombocytopenia (CBC shows platelets count less than 100,000/microliter), impaired liver enzymes, renal insufficiency (serum creatinine greater than 1.1 mg/dL), and massive proteinuria greater than 5g.

Exclusion criteria
All cases with any maternal complications other than pre-eclampsia and pregnancies complicated by intrauterine fetal death (IUFD) or congenital anomalies were excluded.

Methodology in details
This study was done on 90 pregnant patients. This study included 30 cases that have normal pregnancies used as control group and 60 cases s with pre-eclampsia, subdivided into two groups of mild and severe preeclampsia each subgroup of them included 30 patients. Patients included in the study were subjected to the following:

1. The pregnant women who participated in the study provided verbal consent.
2. A thorough history-taking procedure that includes determining the patient's age, gestational age (confirmed on the first day of her LMP or during a first-trimester ultrasound), gravidity, and parity.
3. Through clinical examination, which comprised a comprehensive obstetric examination, a general examination, and vital signs.
4. Lab testing such as a full blood count, liver and kidney function checks, and a thorough urine analysis.
5. Fetal biometry and weight estimation, evaluation of the foetal biophysical profile, and amniotic fluid index were all part of the ultrasound and Doppler investigation. Gestational age was also determined.

The estimated foetal weight (EFW) less than the 10th percentile for gestational age was checked for in all patients.
The middle cerebral artery resistance and pulsatility indices as well as umbilical artery resistance and pulsatility indices were performed on all patients.

Technique of ultrasonography
To prevent supine hypotension, the examination was conducted with the patient lying on their left side with a slight left lateral tilt.
The umbilical and middle cerebral arteries were studied using ultrasonography and Doppler flow velocity waveforms (FVW) using a voluson 730 pro V from GE Healthcare in the United States.

Doppler Study
Using a colour Doppler device and curved trans-abdominal probe, Doppler velocimetry of the UA and MCA was carried out. The Doppler ultrasonography beam and the direction of blood flow in each vessel were angled in an effort to get as near to a 0 degree angle as possible. Despite the UA's coiling, it is still possible to position the sample gate so that it is parallel to the direction that blood is flowing through the cord. The internal carotid artery's division into the anterior cerebral artery and the MCA will be visible close to the location of the MCA. Measurements will be made during times of foetal inactivity and apnea. The umbilical artery Doppler indices from at least 3 consecutive waveforms will be obtained and averaged to determine the resistance index (RI) & pulsitivity index (PI) where:

RI = Maximal systolic velocity - Least diastolic velocity / Maximal systolic velocity
PI = Maximal systolic velocity - Least diastolic velocity / Average
The Middle cerebral artery Doppler indices from at least 3 consecutive waveforms were obtained and averaged to determine the resistance index (RI) &. Pulsitivity index (PI). The R.I Ratio, defined as the MCA-RI divided by the UA-RI, was considered abnormal if <1.0.
The cerbroplacental ratio (CPR), defined as the MCA-pI divided by the UA-pI, was considered abnormal if <1.08.

Neonates evaluation
The neonates were subjected to APGAR scoring at 1 and 5 minutes.
Apgar stands for'' **A**ppearance, **P**ulse, **G**rimace, **A**ctivity, and **R**espiration''
In the test five things are used to check a neonatal health. Each is scored on a scale of 0 to 2, with 2 being the best score:

	0 (points)	1	2
Appearance (skin color)	Blue or pale all over	Blue extremities	Pink all over
Pulse (heart rate)	None	< 100	>100
Grimace (reflexes)	No response	Weak grimace when stimulated	Cries or pulls away when stimulated
Activity (muscle tone)	None	Some flexion of arms	Arms flexed, legs resist extension
Respiration (breathing rate and effort)	None	Weak, irregular or grasping	Strong cry

Ponderal index: Roher's ponderal index in newborns (birth weight * 100/height3) has been used as indicator of relative fatness at birth ponderal index is arrived by the following formula:
Ponderal index = Birth weight (in gm) / Length (in cm) x 100

Adverse neonatal outcome is considered by the following criteria:
1. APGAR score is less than 7 at 5 minutes.
2. Neonatal admission to neonatal intensive care unit.
3. Neonatal death.

Statistical Analysis

Utilizing version 23.0 of the statistical software for the social sciences, recorded data were analysed (SPSS Inc., Chicago, Illinois, USA). When the distribution of the quantitative data was parametric (normal), the data were provided as mean, standard deviation, and ranges; however, when the distribution was non-normal, the data were presented as median and interquartile range (IQR). Qualitative variables were also shown as percentages and numbers. Using the Kolmogorov-Smirnov test, data were examined for normality. The subsequent tests were conducted: When comparing more than two means, use a one-way analysis of variance (ANOVA). Tukey's test was employed as a post hoc analysis for multiple comparisons between several variables. For multiple-group comparisons in non-parametric data, use the Kruskall Wallis test. Whitney Mann For two-group comparisons in non-parametric data, use the U test. The proportions between qualitative measures were compared using the Chi-square (x2) test of significance. If one or both sets of variables were skewed, the degree of relationship between them was evaluated using Spearman's rank correlation coefficient (rs). To determine the parameter's overall predictiveness and to determine the appropriate cut-off value with detection of sensitivity and specificity at this cut-off value, receiver operating characteristic (ROC curve) analysis was employed. Sensitivity = (true +ve)/ [(true +ve) + (false –ve)], Specificity = (true –ve) / [(true –ve) + (false +ve)], PPV = (true +ve) / [(true +ve) + (false +ve)], NPV = (true –ve)/ [(true –ve) + (false –ve)] & Accuracy = (TP+TN)/[TP+FP+TN+FN]; The allowable margin of error was set at 5%, while the confidence interval was set at 95%. The p-value was therefore deemed significant because it fell within the following ranges: P-value 0.05 was significant, P-value 0.001 was highly significant, and P-value >0.05 was considered inconsequential.

Results

Table (1) Comparison between groups according to demographic data, Blood Pressure & ultrasonic parameters

	Control group (n=30)	**Mild preeclampsia (n=30)**	**Sever preeclampsia (n=30)**	**Test value**	**p-value**	**Multiple comparison**		
						P1	**P2**	**P3**
Demographic data								
Age (years)	29.67±4.82	30.27±5.17	30.13±4.98	0.119	0.888	0.644	0.714	0.919
Parity	2.0 (0.0-3.0)	2.0 (0.0-4.0)	2.0 (1.0-3.0)	1.162	0.612	0.895	0.661	0.493
GA by date (week)	38.70±0.70	37.87±0.90	37.10±0.96	25.939	<0.001**	0.001*	0.001*	0.002*
Blood pressure								
SBP (mm Hg)	113.17±11.48	146.33±5.56	178.67±12.38	305.523	<0.001**	0.001*	0.001*	0.001*
DBP (mm/Hg)	68.33±7.58	94.17±3.96	109.83±5.17	395.805	<0.001**	0.001*	0.001*	0.001*
Ultrasonic parameters								
GA U/S	37.90±0.61	37.10±1.18	35.07±1.57	45.289	<0.001**	0.002*	0.001*	0.001*
EFW	3263.57±292.15	2876.60±342.37	2364.20±399.94	50.528	<0.001**	0.001*	0.001*	0.001*
AFI	10.53±2.36	8.43±2.18	5.70±1.84	38.510	<0.001**	0.001*	0.001*	0.001*
BPP	7.87±0.51	6.73±1.34	5.67±1.49	25.480	<0.001**	0.001*	0.001*	0.001*

Data are expressed as Mean±SD, #median (minimum-maximum) or number (%)
Using: One way Analysis of Variance test was performed for Mean±SD & Multiple comparison between groups through Post Hoc test: Tukey's test
Kruskal–Wallis was performed for Median (Min-Max) & Multiple comparison between groups through Mann-Whitney test
x2: Chi-square test for Number and (%);p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.001 is highly significant
P1: Significant level between control versus mild preeclampsia
P2: Significant level between control versus severe preeclampsia
P3: Significant level between mild preeclampsia versus mild preeclampsia
GA: Gestational age; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; G.A U/S: Gestational age by ultrasound; EFW: Estimated fetal weight; AFI: Aminiotic fluid index; BPP: biophysical profile

This table shows that there were no significant changes between control and mild groups regarding their age or parity but there were significant higher values concerning gestational age, and both systolic and diastolic blood pressure for pre-eclamptic group as compared to control group. This table shows also that there were no significant difference between control and sever pre-eclamptic groups regarding age or parity but both gestational age, systolic and diastolic blood pressure values were significantly higher in severe pre-eclamptic group when compared to control group. This table shows that there were no significant changes between mild and severe groups regarding age or parity but values of gestational age, systolic and diastolic blood pressure were significantly higher in severe pre-eclamptic group compared to mild pre-eclamptic group. Ultrasonic evaluation of fetal biometry and parameters of fetal wellbeing between these 2 groups showed high significant values of all parameters including GA, EFW, AFI as well as BPP in control group compared to mild pre-eclamptic group. Ultrasonic evaluation of fetal parameters between these 2 groups showed lowered significant values of all parameters including GA, EFW, AFI as well as BPP in severe pre-eclamptic group as compared to control group. Ultrasonic evaluation of fetal parameters between these 2 groups showed lower significant values of all parameters including GA, EFW, AFI as well as BPP in severe pre-eclamptic group compared to mild preeclamptic group. This table shows that there is high significant incidence of remarkable albuminuria ≥2 in all cases of severe preeclamptic group where non of cases of mild preeclampsia showed such remarkable degree of albuminuria, with p-value (p<0.001).

Table (2) Comparison between groups according to intrauterine growth restriction (IUGR)

	Control group (n=30)	Mild pre-eclampsia (n=30)	Severe pre-eclampsia (n=30)	x^2	p-value	Multiple comparison		
						P1	P2	P3
Intrauterine growth restriction (IUGR)	1 (3.3%)	5 (16.7%)	18 (60.0%)	26.932	<0.001**	0.085	0.001*	0.001*

Data are expressed as number (%)
x^2: Chi-square test for Number and (%)
p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.001 is highly significant
P1: Significant level between control versus mild preeclampsia
P2: Significant level between control versus severe preeclampsia
P3: Significant level between mild preeclampsia versus mild preeclampsia
IUGR: Intrauterine growth restriction

In this table IUGR diagnosed one out of 30 (3.3%) in control group and 5 out of 30 (16.7%) in mild group. Statistical analysis shows that there was no significant difference regarding incidence IUGR between both groups. This table shows that there is a significant higher incidence of cases IUGR in severe pre-eclamptic group (60%) compared to an incidence of only 3.3% in control group. This table denotes that there is a significant higher incidence of cases IUGR in severe pre-eclamptic group (60%) compared to an incidence of only 16.7% in mild pre-eclamptic group.

Table (3) Comparison between groups according to neonatal outcome and Doppler indices

	Control group (n=30)	Mild pre-eclampsia (n=30)	Severe pre-eclampsia (n=30)	Test value	p-value	Multiple comparison		
						P1	P2	P3
Neonatal outcome								
APGAR score in 1-min.	9.0 (7.0-10.0)	8.0 (4.0-9.0)	6.0 (2.0-8.0)	9.682	<0.001**	0.001*	0.001*	0.001*
APGAR score in 5-min.	10.0 (9.0-10.0)	10.0 (6.0-10.0)	8.0 (4.0-10.0)	8.261	<0.001**	0.044*	0.001*	0.001*
Birth weight	3195.0±324.93	2756.67±382.31	2201.67±477.15	46.521	<0.001**	0.001*	0.001*	0.001*
Ponderal index	2.73±0.13	2.40±0.21	2.26±0.14	65.025	<0.001**	0.001*	0.001*	0.005*
NICU admission	0 (0%)	2 (6.7%)	12 (40.0%)	20.977	<0.001**	0.150	0.001*	0.002*
Neonatal death	0 (0.0%)	0 (0.0%)	3 (10.0%)	6.207	0.045*	----	0.076	0.076
Doppler indices								
UA- R.I	0.6±0.05	0.68±0.09	0.83±0.11	54.053	<0.001**	0.001*	0.001*	0.001*
UA- P.I	1.05±0.09	1.33±0.3	1.77±0.41	44.538	<0.001**	0.001*	0.001*	0.001*
MCA-R.I	0.79±0.06	0.75±0.09	0.7±0.11	7.689	<0.001**	0.078	0.001*	0.056
MCA -P.I	1.6±0.19	1.58±0.14	1.49±0.32	1.954	0.148	0.698	0.123	0.169
CPR	1.54±0.31	1.27±0.36	0.91±0.3	28.480	<0.001**	0.002*	0.001*	0.001*
RI ratio	1.31±0.24	1.13±0.24	0.88±0.22	25.654	<0.001**	0.006*	0.001*	0.001*

Data are expressed as Mean±SD, #median (minimum-maximum) or number (%)
Using: One way Analysis of Variance test was performed for Mean±SD & Multiple comparison between groups through Post Hoc test: Tukey's test
Kruskal–Wallis was performed for Median (Min-Max) & Multiple comparison between groups through Mann-Whitney test
x^2: Chi-square test for Number and (%);p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.001 is highly significant
P1: Significant level between control versus mild preeclampsia

P2: Significant level between control versus severe preeclampsia
P3: Significant level between mild preeclampsia versus mild preeclampsia
NICU: Neonatal Intensive Care Unit
UA- R.I: Umbilical artery resistance index; UA- P.I: Umbilical artery pulsatility index; MCA-R.I: Middle cerebral artery resistance index; MCA-P.I: Middle cerebral artery pulsatility index; CPR: Cerebro-placental ratio (cerebro-umbilical pulsatility index ratio); R.I ratio (cerebroumbilical resistance index ratio)

Neonatal outcome

Regarding neonatal outcome, this table shows that APGAR score for 1-minute was significant higher in the control group compared to mild preeclamptic group, and there was no changes regarding APGAR score for 5 minutes between 2 groups. There is significant lower values for both birth weight and ponderal index in mild pre-eclamptic group compared to control group. No significant change between rate of NICU admission between both groups. This table shows that there were high significant lower values for both APGAR score in 1-min and for 5-min in the severe pre-eclamptic group compared to control group. Severe group showed also Lower significant values for Birth weight, ponderal index and higher rate of NICU admission. However, no significant changes rate of neonatal death was found between both groups. This table shows that there were significant lower values for both APGAR score in 1-min and 5-min in the severe pre-eclamptic group compared to mild pre-eclamptic group. Also significant lower values were found for Birth weight, ponderal index with significant higher rate of NICU admission. However no significant changes rate of neonatal death was found between both group. This table compares total adverse neonatal outcome in the 3 studied groups. Adverse outcome was defined to be associated with the presence of one or more of the following factors; low 5-minute Apgar score <7, need for NICU admission or neonatal death. According to this table all cases of control group showed no evidence of any adverse outcome. This is compared to an incidence of low 5-minute Apgar score of 6.7% in mild group and 36.7% in sever group. Regarding cases needing NICU admission an incidence of 6.7% was found in mild group compared to 40% in sever group. Early Neonatal death was not noted in any of cases of control or mild groups compared to incidence of 10% reported in severe pre-eclamptic group.

Doppler indices for CPR and R.I

This table compare Doppler indices of both cerebro-umbilical pulsatility index ratio (CPR) and cerebro-umbilical resistance index ratio (R.I) in the 3 studied groups, CPR considered abnormal if it is (<1.08) and R.I ratio considered abnormal if it is (<1). Abnormal CPR showed an incidence of 6.7% in control group, and 20% in mild group and incidence of 56.7% in severe group, while abnormal R.I ratio showed incidence of 3.3% in control group, and 20% in mild group and incidence of 60% in severe group.

Doppler indices

This table shows that a significant higher values regarding UA- R.I and UA- P.I in mild group as compared to controls. As regards middle cerebral artery there were no significant difference for values of MCA-R.I and MCA -P.I between both groups. Comparing CRP and RI ratio of both groups showed a lower significant both values for mild group compared to controls. This table shows that there is significant higher values regarding UA-R.I and UA-P.I in severe group as compared to controls. On the other hand, regarding middle cerebral artery severe pre-eclamptic group showed significant lower values for MCA-R.I but not in MCA-P.I Comparing CRP and RI ratio of both groups however showed a lower significant values for severe group compared to controls of both indices. This table shows that for umbilical artery, UA- R.I and UA- P.I values were significantly higher in severe group compared to the mild preeclamptic group. For middle cerebral artery there was no significant difference in the values of both pulsatility or resistance indices in both groups. Comparing CRP and RI ratio of both groups however showed a lowered significant values in both indices for severe Pre-eclamptic group compared to mild group.

Table (4) Incidence of IUGR and adverse neonatal outcome in relation to both CPR and RI ratio in mild preeclampsia group and severe preeclampsia group

		Intrauterine growth restriction (IUGR)			
		Mild preeclampsia group		**Severe preeclampsia group**	
		No (n=25)	**Yes (n=5)**	**No (n=12)**	**Yes (n=18)**
CPR	Normal (≥1.08)	24 (96.0%) TN	0 (0.0%) FN	12 (100.0%) TN	1 (5.6%) FN
	Abnormal (<1.08)	1 (4.0%) FP	5 (100.0%) TP	0 (0.0%) FP	17 (94.4%) TP
RI ratio	Normal (≥1.08)	23 (92.0%) TN	1 (20.0%) FN	9 (75.0%) TN	3 (16.7%) FN
	Abnormal (<1.08)	2 (8.0%) FP	4 (80.0%) TP	3 (25.0%) FP	15 (83.3%) TP
		Neonatal outcome			
		Mild preeclampsia group		**Sever preeclampsia group**	
		Abnormal (n=2)	**Normal (n=28)**	**Abnormal (n=12)**	**Normal (n=18)**
CPR	Normal (≥1.08)	0 (0.0%) FN	24 (85.7%) TN	1 (8.3%) FN	12 (66.7%) TN
	Abnormal (<1.08)	2 (100.0%) TP	4 (14.3%) FP	11 (91.7%) TP	6 (33.3%) FP
RI ratio	Normal (≥1)	0 (0.0%) FN	24 (85.7%) TN	1 (8.3%) FN	11 (61.1%) TN
	Abnormal (<1)	2 (100.0%) TP	4 (14.3%) FP	11 (91.7%) TP	7 (38.9%) FP

Data are expressed as number (%);
IUGR: Intrauterine growth restriction
CPR: Cerebro-placental ratio (cerebro-umbilical pulsatility index ratio)
R.I ratio: (cerebro-umbilical resistance index ratio)
Data are expressed as number (%)
TN =true negative; FN =false negative; TP =true positive; FP =false positive

This table shows the results of CPR and R.I ratio in relation to IUGR in mild pre-eclamptic group. An abnormal CPR parameter was shown to be positive in all cases of IUGR whereas R.I ratio parameter was abnormal in 80% of cases of IUGR. This table shows the results of CPR and R.I ratio in relation to IUGR in severe pre-eclamptic group. An abnormal CPR parameter was shown to be positive in 94.4% of cases of IUGR whereas R.I ratio parameter was abnormal in only 83.3% of cases of IUGR. This table shows the results of CPR and R.I ratio in relation to adverse neonatal outcome in mild pre-eclamptic group. Abnormal values of both CPR and R.I ratio were found in 100% of cases of adverse neonatal outcome. This table shows the results of CPR and R.I ratio in relation to adverse neonatal outcome in sever pre-eclamptic group. An abnormal values of both CPR and R.I ratio were found in the same percentage of 91.7% for all cases of adverse neonatal outcome.

Table (5) Efficacy of CPR and RI ratio in predicting IUGR and adverse neonatal outcome in mild preeclampsia group and severe preeclampsia group

	Sensitivity	**Specificity**	**PPV**	**NPV**	**Accuracy**
IUGR					
Mild Preeclampsia Group					
CPR	100.0%	96.0%	83.3%	96.0%	96.7%
RI ratio	80.0%	92.0%	66.7%	95.8%	90.0%
Sever preeclampsia group					
CPR	94.4%	100.0%	94.4%	92.3%	96.7%
RI ratio	83.3%	75.0%	83.3%	75.0%	80.0%
Adverse neonatal outcome					
Mild preeclampsia group					
CPR	100.0%	85.7%	33.3%	85.7%	86.7%

RI ratio	100.0%	85.7%	33.3%	85.7%	86.7%
Sever preeclampsia group					
CPR	91.7%	66.7%	64.7%	92.3%	76.7%
RI ratio	91.7%	61.1%	61.1%	91.7%	73.3%

PPV=positive predictive value
NPV=negative predictive value
CPR: cerebro-placental ratio (cerebro-umbilical pulsatility index ratio)
R.I ratio (cerebro-umbilical resistance index ratio)

Mild preeclamptic group: There was no much significant difference between both ratios as regards the accuracy of prediction of IUGR for cases of mild preeclampsia, which was slightly better for CPR (96.7%) versus 90.0% for RI. The ability of CPR and R.I ratio to predict IUGR was calculated regarding Sensitivity, Specificity, PPV, NPV and diagnostic accuracy. Using results of CPR parameters, values were shown to be 100.0%, 96.0%, 83.3%, 96.0% and 96.7%, respectively. The corresponding figures for the R.I ratio were 80.0%, 92.0%, 66.7%, 95.8% and 90.0%, respectively.

Sever preeclampsia group: For cases of severe pre-eclampsia, there is much significant difference between both ratios as regards their Accuracy of prediction of IUGR, which is higher for CPR ratio (96.7%) than for that for RI (80.0%). The ability of CPR and R.I ratio to predict IUGR was calculated regarding Sensitivity, Specificity, PPV, NPV and diagnostic accuracy. Using results of CPR parameters, values were shown to be 94.4%, 100.0%, 94.4%, 92.3% and 96.7%, respectively. The corresponding figures for the R.I ratio were 83.3%, 75.0%, 83.3%, 75.0% and 80.0%, respectively.

Mild preeclampsia group: There was no much significant difference between both ratios as regards the Accuracy of prediction of adverse neonatal outcome for cases of mild Pre-eclampsia. Both showed a similar value 86.7%. The ability of CPR and R.I ratio to predict adverse neonatal outcome was calculated regarding Sensitivity, Specificity, PPV, NPV and diagnostic accuracy. Values were shown to be 100.0%, 85.7%, 33.3%, 85.7% and 86.7%, respectively for both CPR and R.I ratio.

Sever preeclampsia group: For cases of severe pre-eclampsia, there is no significant difference between both ratios as regards their Accuracy of prediction of adverse neonatal outcome, which is slightly higher for CPR ratio (76.7%) than for that for RI (73.3%). The ability of CPR and R.I ratio to predict adverse neonatal outcome was calculated regarding Sensitivity, Specificity, PPV, NPV and diagnostic accuracy. Using results of CPR parameters, values were shown to be 91.7%, 66.7%, 64.7%, 92.3% and 76.7%, respectively. The corresponding figures for the R.I ratio were 91.7%, 61.1%, 61.1%, 91.7% and 73.3%, respectively

Table (6) Correlation between neonatal outcome and different Doppler indices in both mild and severe preeclampsia groups

	Mild pre-eclampsia		**Severe pre-eclampsia**	
	r-value	**p-value**	**r-value**	**p-value**
UA-R.I	0.564	0.001*	0.765	0.001*
UA-P.I	0.514	0.004*	0.818	0.001*
MCA-R.I	-0.433	0.017*	-0.729	0.001*
MCA-P.I	-0.286	0.126	-0.633	0.001*
CPR	-0.439	0.016*	-0.818	0.001*
RI ratio	-0.432	0.023*	-0.747	0.001*

Using: Spearman's Rank correlation coefficient
p-value >0.05 is insignificant; *p-value <0.05 is significant; **p-value <0.001 is highly significant
UA- R.I: umbilical artery resistance index
UA- P.I: Umbilical artery pulsatility index

MCA-R.I: Middle cerebral artery resistance index
MCA-P.I: Middle cerebral artery pulsatility index
CPR: Cerebro-placental ratio (cerebro-umbilical pulsatility index ratio)
R.I ratio (cerebro-umbilical resistance index ratio)

According to this table, for the mild preeclamptic group, adverse neonatal outcome was significantly correlated to for abnormal values of UA-RI, UA-PI and MCA-R.I. and abnormal values of both CPR and R.I ratio but showed no significant correlation with MCA-P.I values. However for severe pre-eclamptic group, adverse neonatal outcome was significantly correlated to all abnormal values of all Doppler indices as well as to both ratios of CPR and R.I.

Discussion

In the current study, the incidence of IUGR was 3.3%, 16.7%, and 60%, respectively, in the control, moderate, and severe groups. Our current study's findings are close to those of a 1994 study by Arbeille and colleagues, which revealed that 19% of preeclamptic patients had IUGR, which is comparable to the outcome of our mild group (10).

A 2013 study by Singh and coworkers for pregnancies affected by pre-eclampsia indicated that the incidence of IUGR in pre-eclamptic women was 60%, which is comparable with the outcome of our severe group and supports the findings of our investigation (11).

The findings of the current study are close to those of a study conducted in 2015 by Adiga, who discovered that all infants of pre-eclamptic patients had an incidence of IUGR of 34.7%. (12).
Our findings conflict with those of a 2010 study by Shahinaj and colleagues, which revealed a lower incidence of IUGR in preeclamptic patients of just 8.94%. (13).

In our current study, the incidence of a bad neonatal outcome was 6.7% for the mild group and 40% for the severe group, while in all cases of the control group, there was no indication of a bad end.
6.7% of cases in the mild group had abnormal perinatal outcomes. 6.7% of cases had poor Apgar scores, it was discovered. When NICU admission was necessary, the similar incidence was recorded. Neonatal fatalities were not reported in any cases.

In the severe group, 40% of cases had a poor neonatal outcome. A prevalence of poor Apgar scores was discovered in 36.7% of infants. Babies who needed NICU admission for a variety of conditions, such as birth asphyxia, low birth weight, prematurity, etc., were reported to require hospitalisation at a rate of (40%) while newborn deaths were observed to occur at a rate of (10%).
In a 2013 study on unfavourable newborn outcomes in pregnancies affected by pre-eclampsia, Singh and coworkers showed that the incidence of low Apgar score cases was 40% and the incidence of cases that required NICU hospitalisation was 32%. Our current study is comparable to that study (11).
Additionally, a study conducted in 2014 by Smitha K. and colleagues indicated that (46%) of instances resulted in an unfavourable pregnancy outcome. Their study found that (45.65%) of cases required NICU hospitalisation, (34.7%) of cases had low Apgar scores, and (6.52%) of cases experienced newborn death (14).

Our findings do not support the findings of the 2016 study by Rani and colleagues, who discovered a decreased frequency of unfavourable newborn outcomes in preeclamptic pregnancies. The incidence of cases requiring NICU admission was reported to be 15.2%, and the overall incidence of newborn deaths was reported to be 1.3%. (15).

Doppler measurements of the umbilical and middle cerebral arteries were employed in our investigation to identify foetuses with elevated placental and/or decreased cerebral resistance. We concentrated on the CPR (cerebroplacental ratio), also known as the MCA/UA PI and R.I ratios. CPR has a single cutoff value of 1.08, below which it is regarded abnormal, and R.I. ratio has a single cutoff value of 1, below which it is deemed abnormal.

Our findings demonstrated that sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 100%, 96%, 83.3%, 96%, and 96.7% correspondingly for the identification of IUGR in

the mild group using the CPR. In contrast, utilising the R.I. ratio revealed accuracy of 90%, sensitivity of 80%, specificity of 92%, 66.7%, and positive predictive value of 95.8%, respectively.
In the severe group, the CPR and R.I ratio's sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in detecting IUGR were, respectively, 94.4%, 100%, 94.4%, 92.3%, 96.7%, and 83.3%, 75%, 83.3%, and 80%.

The cerebroplacental ratio is very sensitive and specific in predicting IUGR in pregnancies affected by pregnancy-induced hypertension, according to a 1994 study by Arbeille and coworkers. It revealed that CPR might predict IUGR with a sensitivity of 82.2%, specificity of 98.6%, positive predictive value of 93.8%, and negative predictive value of 97.3%. (10).

Additionally, a 1999 study conducted by Ozeren and colleagues revealed that CPR had diagnostic accuracy of 87%, PPV of 84%, NPP of 86%, and sensitivity of 84% in predicting IUGR (16).
Additionally, a 2010 study by Shahinaj and collaborators revealed that CPR is an excellent indicator of IUGR in the foetuses of women with preeclampsia and gestational hypertension (13).

In their 2013 study of pregnancies complicated by pre-eclampsia, Singh and colleagues observed the following overall outcomes for all the cases. 96.6%, 90%, 93.5%, 94.7%, and 94%, respectively, were the sensitivity, specificity, positive predictive value, and accuracy of CPR in detecting IUGR. The comparable numbers for the R.I ratio, however, were 96.6%, 90%, 93.5%, 90.4%, and 94%, respectively (11).

Our findings conflict with those of Simanaviciute D and colleagues from a cross-sectional analysis of 231 healthy pregnancies and 115 pregnancies with preeclampsia done in 2006. In order to predict the perinatal outcome, they compared CPR with the MCA/uterine artery PI ratio. They discovered sensitivity and specificity of CPR in predicting IUGR to be 47.6% and 88.6%, respectively. This research was done on a bigger patient population of 346 cases (17).

According to Smitha K. and colleagues' 2014 research, CPR exhibited lower sensitivity (66.66%), specificity (71.87%), PPV (57.14%), NPP (79.31%), and accuracy (70%) values for predicting IUGR (14).
The test had a strong specificity of (83.9%) and NPV of (70.3%), but poor sensitivity of (33.3%), low PPV of (52.4%), and the accuracy was (66.3%), according to a 2015 study by Adiga and coworkers (12).
A lower birth weight for the foetus was found to be substantially linked with the severity of preeclampsia in our study. Our findings for foetal birth weight are consistent with those of Xiong and colleagues, who found a substantial correlation between prenatal hypertension and preeclampsia and low birth weight and small-for-gestational age newborns. Preeclamptic moms who gave delivery before 37 weeks had statistically significantly lower birth weights (Xiong et al., 2002). (18).

According to the findings of our investigation, both CPR and R.I ratio demonstrated comparable levels of sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in detection of bad neonatal outcome in the mild group. These values produced results of 100 percent, 85.7%, 33.3%, 85.7%, and 86.7%, respectively.

The CPR and R.I ratio's sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in detecting unfavourable outcomes were, in comparison to the severe group, 91.7%, 66.7%, 64.7%, 92.3%, 76.7%, and 91.7%, 61.1%, 61.1%, 91.7%, and 73.3%, respectively.
In accordance with our findings, a 1999 study by Ozeren and coworkers found that CPR had a diagnostic accuracy of 85%, sensitivity of 81%, specificity of 89%, PPV of 84%, and NPP of 86% for the prediction of a poor newborn fate (16).

According to Shahinaj and coworkers' 2010 research on 738 singleton pregnancies in women with preeclampsia and gestational hypertension, the sensitivity, specificity, positive predictive value, and negative predictive value of CPR for adverse neonatal outcomes were 98%, 66%, 30.8%, and 99.7%, respectively (13).

The use of CPR for forecasting a poor newborn outcome demonstrated specificity of 87.5%, PPV of 61.9%, NPV of 75.7%, and diagnostic accuracy of 72.6%, according to a 2015 study by Adiga and coworkers. But it revealed a reduced sensitivity value of 41.9%. (12).

Eser and coworkers, who conducted a cross-sectional doppler investigation on 195 patients, 64 of whom were preeclamptic, did not reach the same conclusions as we did. They noted a substantial variation in CPR between preeclamptic and regular pregnancies. According to their findings, CPR has a 46.2% sensitivity for predicting poor perinatal outcomes (19).

Our current research does not agree with Smitha and colleagues' findings, which revealed greater specificity and positive predictive values (PPV) of CPR for predicting unfavourable newborn outcomes of 82.65% and 86.42%, respectively. The study's results, however, were equivalent to ours in terms of sensitivity (94.42%) and NPP (96.41%). (2014) (Smitha K et al) (14).

Our findings differ from those of the 2016 study conducted by Rani and colleagues. Using the sensitivity, specificity, positive predictive value, and negative predictive value, they investigated the capacity of CPR and RI ratio to predict the unfavourable neonatal outcome. CPR values ranged from 8% to 98% to 81.8% to 48.3%. For the RI ratio, the equivalent numbers were 9.3%, 97%, 78.5%, and 48.5%. However, the gestational age in our study was 34–40 weeks, whereas this study included 223 pregnant women with a gestational age of 30-36 weeks (15).

Negative newborn outcomes were strongly connected with abnormal UA-RI, UA-PI, MCA-RI, abnormal CPR, and abnormal R.I ratio values for the mild group in our study, however there was no significant correlation with MCA-PI value.

According to our findings for the severely affected group, poor newborn outcomes were substantially connected with aberrant values of all Doppler indices as well as with both CPR and R.I. ratios.
Our current analysis is in agreement with numerous investigations, including Bilardo and coworkers (2004) and Arauz and coworkers (2008). In patients with preeclampsia, their research found a strong association between UA Doppler indices and a poor perinatal outcome. They came to the conclusion that an aberrant Doppler UA waveform is a reliable indicator of prenatal mortality and is linked to a poor perinatal outcome (20, 21).

The same conclusion was reached by Arauz and coworkers in 2008, who noted that preeclamptic patients with abnormal doppler indices for the MCA and umbilical artery compared to those with normal velocimetry (p0.05), especially those with severe preeclampsia, had significantly higher neonatal morbidity (21).
Pregnancy-related hypertensive disorders are linked to a higher incidence of IUGR and a poor newborn outcome, both of which are correlated with the severity of the ailment.
When assessing such pregnancies, Doppler velocimetry of umbilical and cerebral blood flow is a helpful technique.

Both CPR and R.I ratio were found to have great outcomes in identifying IUGR; however, when utilised in cases of severe preeclampsia, CPR showed a substantially higher degree of accuracy.
According to our findings, the CPR is extremely sensitive to preeclampsia (94.4%) in severe instances and 100% in moderate cases. However, the specificity of such a technique in ruling out IUGR was shown to be (96%) in moderate preeclampsia instances and (100%) in severe cases, making it a very sensitive tool for IUGR identification in mild cases and extremely specific in severe situations.
While the R.I. ratio has a strong sensitivity of (80%) in moderate instances and of (83.3%) in severe cases of preeclampsia, it is less sensitive. However, the specificity of such a tool in excluding IUGR was found to be (92%) in mild cases and (75%) in severe cases of preeclampsia, indicating that it has a high degree of specificity, particularly in lesser forms of preeclampsia rather than severe degree of preeclampsia for detection of IUGR.

However, it has been demonstrated that the predictive values for diagnosing a poor neonatal fate in preeclampsia patients for both CPR and R.I ratio differ.
Our findings suggested that the CPR is extremely sensitive in mild cases of preeclampsia (100%) and somewhat sensitive in severe cases (91.7%) for the diagnosis of unfavourable newborn outcomes.
However, the specificity of such a test in excluding an adverse newborn outcome was shown to be (85.7%) in moderate preeclampsia cases and (66.7%) in severe cases, making it a highly sensitive tool for detecting an adverse neonatal result but with a low level of specificity.

In moderate cases of preeclampsia, the R.I. ratio was found to be very sensitive (100%) and to be highly insensitive (91.7%) in severe cases. However, this test's specificity in excluding unfavourable newborn outcomes was shown to be (85.7%) in moderate cases and (61.1%) in severe cases of preeclampsia, making it a highly sensitive tool for detecting adverse neonatal outcomes but with a low level of specificity.

Conclusion

However, it has been demonstrated that CPR is the best parameter test currently available for assessing foetal outcome in terms of birthweight or for foretelling the probability of a poor neonatal prognosis following delivery. We advocate for its inclusion in every diagnostic assessment of preeclamptic patients. More extensive research is required to introduce new Doppler measurements to various foetal vasculature and measure various indices that may be useful in predicting the unfavourable neonatal outcome and IUGR in preeclamptic pregnant women.

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