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Cerebroplacental Doppler Ratio and Cerebrouterine Doppler Ratio in Predicting Neonatal Outcome in Preeclamptic Pregnant Women

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Umbilical artery and middle cerebral artery Doppler ultrasound clearly depict the information about placental resistance and the changes in the fetal hemodynamics in response to it. The aim of this work was to assess the role of cerebroplacental ratio and cerebrouterine ratio in prediction of neonatal outcome in preeclamptic women.
Methods: This prospective observational study was carried out on 110 pre eclamptic women. Patients were divided into two groups: Preeclampsia with severe features (n=58) and preeclampsia (n=52). All patients were subjected to laboratory testing (complete blood count (CBC), coagulation profile, liver and kidney function tests, 24 hours urine sample collection) and ultrasonographic scanning trans - abdominal sonographic examinations.
Results: The cut off value of CP ratio was 1.09 with sensitivity 84%, specificity 89%, PPV (positive predictive value) 94%, NPV (negative predictive value) 73% and accuracy 85% while the study cut off value of CU ratio was 1.3 with sensitivity 97%, specificity 93%, PPV 95%, NPV 95% and accuracy 95%. UTA, UMBA, MCA, CP and CU were significantly higher in Preeclampsia with severe features than Preeclampsia (P value <0.05).

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Conclusions: Most of unfavourable neonatal outcome associated with abnormal cerebroplacental and cerebrouterine ratio so cerebroplacental and cerebrouterine ratio were complementary to each other in predicting the adverse neonatal outcomes.

Keywords: Cerebroplacental doppler; cerebrouterine doppler; neonatal outcome; preeclamptic, pregnant.

1. INTRODUCTION

Preeclampsia, one of the leading causes of maternal and fetal morbidity and mortality, affecting 2-5% of pregnancies, is a specific syndrome characterized by reduced organ perfusion secondary to vasospasm and endothelial pathophysiology [1]. A diagnosis of preeclampsia is made based on the presence of systolic blood pressure greater than 140 mm Hg or diastolic blood pressure greater than 90 mm Hg on two occasions at least 4 hours apart and presence of proteinuria or severe features [2].

Preeclampsia contributes greatly to IUGR (Intra Uterine Growth Restriction), preterm labor through affecting development of uteroplacental and fetoplacental circulation necessary for a normal pregnancy outcome [3].

Doppler velocimetry provides valuable information about hemodynamic status of the fetus and is an efficient diagnostic test of fetal jeopardy that helps in management of high-risk pregnancy [4]. Umbilical artery and middle cerebral artery Doppler ultrasound clearly depict the information about placental resistance and the changes in the fetal hemodynamics in response to it. Umbilical artery Doppler reflects the maldevelopment of the placental tertiary stem villi which increases the placental resistance [1]. Doppler evaluation of blood flow through cerebral vessels allows detection of altered cerebral circulation, much before significant fetal heart rate changes due to hypoxemia. Middle cerebral artery is the most accessible vessel and has been reported to demonstrate reduction in the Pulsatility index at onset of hypoxemia [5].

The cerebroplacental ratio (CPR) is a measure that quantifies the brain-sparing effect and provides information on how fetal cardiac output is distributed. It is calculated by dividing the middle cerebral artery (MCA) Doppler flow by the umbilical artery (UA) Doppler flow. Either the pulsatility index (PI), resistance index (RI) or the systolic/diastolic ratio (S/D) can be used for the calculation. More recently the PI has been the computation of choice [6].

One of the hypotheses discussed in the etiology of preeclampsia is incomplete trophoblastic invasion to the uterine artery in normal endovascular implantation process whereby these cells replace the endothelial and muscular lining of blood vessels and cause increase in vascular diameter. This situation causes a decrease in placental perfusion and eventually leads to an increase in uterine artery resistance [7]. However, early diagnosis and proper administration of preeclampsia can lead to improved maternal and neonatal outcomes. Regarding the prevalence of preeclampsia, the importance of its proper administration to promote health indicators is clear. With the help of Doppler ultrasound, today, uterine arteries can be examined and, by analysing existing indicators, can largely evaluate the high risk pregnancies [8]. The aim of this work was to assess the role of cerebroplacental ratio and cerebrouterine ratio in prediction of neonatal outcome in preeclamptic women.

2. PATIENTS AND METHODS

This prospective observational study was carried out on 110 pre eclamptic women aged from 18 to 45 years old, ≥32 weeks of gestation, singleton viable pregnancy, BMI (≥18-≤30) kg/m2 and primigravida or multigravida.

Agreement for this study was obtained from the hospital's ethical committee. An informed consent was obtained from pregnant women. There were adequate provisions to maintain privacy of participants and confidentiality of the data.

Exclusion criteria were women with chronic diseases like chronic hypertension, diabetes mellitus, renal diseases, liver diseases and vascular diseases, patients with fetal congenital anomalies, Intra Uterine Growth Restriction (IUGR) and Rh incompatibility, smokers, drug intake e.g., vasodilators, antiplatelet drugs, anticoagulant drugs, multiple gestations.

Patients were divided into two groups: Preeclampsia with severe features (n=58) and preeclampsia (n=52).

All patients were subjected to: history (personal history, obstetric history, past history, history of present pregnancy), general examination, abdominal examination, laboratory testing (complete blood count (CBC), coagulation profile, liver and kidney function tests, 24 hours urine sample collection for proteinuria mainly) and ultrasonographic scanning.

ultrasonographic scanning: trans - abdominal sonographic examinations were performed with convex probe using Mindray DC-70 Exp and Mindray DC-30 to evaluate (fetal biometry, fetal weight).

Umbilical artery Doppler technique: with a pulsed wave Doppler system, an ultrasound scan was first carried out, a free-floating portion of the cord is identified, and the Doppler sample volume was placed over an artery and the vein, parallel to blood flow, using color-flow mapping with low-pass filter was set at 50Hz, the angle of insonation should be minimized and kept between 150 - 60°[9].

Middle cerebral artery technique: The transducer was then moved towards the base of the skull at the level of the lesser wing of the sphenoid bone. Using color flow imaging, the middle cerebral artery can be seen as a major lateral branch of the circle of Willis. The pulsed Doppler sample gate was then placed on the middle portion of this vessel. Using color-flow mapping with low-pass filter was set at 50Hz, the angle of insonation should be minimized and kept < 150 [9].

Uterine artery technique: doppler velocity of uterine artery was recorded at the point at which they crossed over the external iliac artery cranial to crossing of iliac artery. Mean of the PI of both uterine arteries was taken, values of PI > 95th percentile is abnormal [9].

2.1 Statistical Analysis

IBM's SPSS statistics (Statistical Package for the Social Sciences) for windows (version 25, 2017) was used for statistical analysis of the collected data. Shapiro-Wilk test was used to check the normality of the data distribution. All tests were conducted with 95% confidence interval. P (probability) value < 0.05 was considered statistically significant. Charts were generated using SPSS' chart builder and Microsoft Excel for windows 2019. Descriptive.

Quantitative variables were expressed as mean and standard deviation, median, inter-quartile range, minimum and maximum as appropriate while categorical variables were expressed as frequency and percentage. ROC curve Receiver operating characteristic (ROC curve) analysis was used to find out the overall predictivity of parameter in and to find out the best cut-off value with detection of sensitivity and specificity at this cut-off value.

3. RESULTS

Table 1 shows maternal demographics, parity and gestational age and hypertension grade among the studied cases.

Table 1. Maternal demographics, parity and gestational age at presentation in the studied sample and hypertension grade among the studied cases

Age	27.22 ± 5.97
BMI (Kg/m2)	26.16 ± 1.74
Gestational age (weeks)	34.18 ± 1.736
Gravidity	2.59 ± 1.599
Parity	1.24 ± 1.394
Systolic	154.32 ± 7.50
Diastolic	98.64 ± 7.66
Preeclampsia with severe features	58(52.7%)
Preeclampsia	52 (47.3%)

Data is expressed as mean ±SD or frequency (%), BMI: Body mass index

Table 2 shows parity and degree of preeclampsia in the studied sample.

Table 2. Parity and degree of preeclampsia in the studied sample

Parity	Primigravida	Multigravida	No. (%)
preeclampsia	20	32	52 (47.3%)
Preeclampsia with Severe features	44	14	58 (52.7%)
Total	64 (58.18%)	46 (41.82%)	110(100%)

Table 3 shows umbilical artery and MCA and Doppler abnormality among studied cases

Table 3. Doppler assessment of uterine artery, umbilical artery and MCA and Doppler abnormality among studied cases

			Range	Mean ± S. D
UTA	RI	Normal	0.43 – 0.66	0.56 ± 0.05
		Abnormal	0.7 – 0.89	0.78 ± 0.05
	PI	Normal	0.69 – 0.94	0.83 ± 0.06
		Abnormal	1.13 – 2.89	1.58 ± 0.42
UMBA	RI	Normal	0.52 – 0.74	0.66 ± 0.05
		Abnormal	0.7 – 0.76	0.73 ± 0.01
	PI	Normal	0.84 – 1.25	1.02 ± 0.11
		Abnormal	1.06 – 1.82	1.26 ± 0.17
MCA	RI	Normal	0.74 – 0.92	0.80 ± 0.04
		Abnormal	0.63 – 0.76	0.73 ± 0.02
	PI	Normal	1.11 – 2.89	1.56 ± 0.56
		Abnormal	0.99 – 1.54	1.27 ± 0.09
CP		Normal	1.03 – 2.78	1.31 ± 0.35
		Abnormal	0.68 – 1.11	0.98 ± 0.13
CU		Normal	1.21 – 3.26	1.74 ± 0.53
		Abnormal	0.43 – 1.4	0.86 ± 0.22
Doppler abnormality				
UTA		46(41.8%)		
UMBA		58(52.7%)		
MCA		78(70.9%)		
CP		36(32.7%)		
CU		48(43.6%)		

MCP: middle cerebral artery, UTA: uterine artery, PI: pulsatility index, RI: resistance index, UMBA: umbilical, middle cerebral artery, MCA: middle cerebral artery, CP: cerebroplacental ratio, CU: Cerebrouterine ratio

UTA, UMBA, MCA, CP and CU were significantly higher in Preeclampsia with severe than Preeclampsia (P value <0.05). There was insignificant difference between cerebroplacental, cerebrouterine ratio, and demographic characteristics Table 4.

Poor outcomes (except death) were significantly more frequent among cases with abnormal CP and CU Table 5.

The cut off value of CP ratio was 1.09 with sensitivity 84%, specificity 89%, PPV (positive predictive value) 94%, NPV (negative predictive value) 73% and accuracy 85% while the study cut off value of CU ratio was 1.3 with sensitivity 97%, specificity 93%, PPV 95%, NPV 95% and accuracy 95% Fig. 1.

CP ratio had higher sensitivity 96%, PPV 70%, NPV 67%and accuracy 70% in prediction of SGA while it had low specificity 17%, APGAR 1 < 7 its sensitivity was 74%, specificity 76%, PPV 87%, NPV 58% and accuracy 75%, APGAR 5 < 7 its sensitivity was 76%, specificity 56%, PPV 78%, NPV 53% and accuracy 69%, NICU its sensitivity was 59%, specificity 69%, PPV 80%, NPV 45% and accuracy 63% while in neonatal death its sensitivity was 95%, specificity 14%, PPV 69%, NPV 56% and accuracy 68%. SGA (small gestational age) CU ratio had higher sensitivity 97%, PPV 59%, NPV 78%, accuracy 61% and specificity 15%, APGAR 1 < 7 its sensitivity was 68%, specificity 44%, PPV 61%, NPV 51% and accuracy 57%, APGAR 5 < 7 its sensitivity was 85%, specificity 52%, PPV 70%, NPV 74% and accuracy 71%, NICU its sensitivity was 69%, specificity 75%, PPV 78%, NPV 65% and accuracy 72% while in neonatal death its sensitivity was 97%, specificity 15%, PPV 59%, NPV 78% and accuracy 61% Fig. 2.

4. DISCUSSION

Preeclampsia is best described as a pregnancy-specific syndrome that can affect virtually every organ [10]. The cerebroplacental ratio (CPR), the ratio of the pulsatility index (PI) of the MCA (middle cerebral artery) to that of the UA (umbilical artery), can detect fetal hypoxemia occurring via two different mechanisms: reduced resistance in the MCA (brain sparing effect) and increasing placental resistance [11].

A novel combination of Doppler parameters, the CU, was the best Doppler predictor of delivery of

a SGA or growth-restricted infant in late pregnancy. In late pregnancy, CU performed better than did either of its constituent parameters in the prediction of birth weight < 10th, < 5th and < 3rd centiles. Furthermore, CU demonstrated a strong biological gradient across all pregnancies with birth weight < 50th centile, with an exponential increase in the rate of low CU in pregnancies with birth weight < 10th centile [12].

Table 4. Comparison between hypertension grades regarding abnormal indices, Comparison between cerebroplacental, cerebrouterine ratio and demographic characteristics

Abnormal indices		Preeclampsia with severe features (n=58)	Preeclampsia (n=52)	P value
		No. (%)	No.%	
UTA		33(56.9%)	13(25%)	0.001*
UMBA		40(69%)	18(34.6%)	0.001*
MCA		46(79.3%)	32(61.5%)	0.040*
CP		34(58.6%)	2(3.8%)	0.001*
CU		35(60.3%)	13(25%)	0.001*
		Normal CP (n=74)	Abnormal CP (n=36)	P value
Age		26.50 ± 5.82	28.69 ± 6.08	0.070
BMI (Kg/m2)		26.17 ± 1.75	26.13 ± 1.74	0.919
Systolic		153.45 ± 6.62	156.11 ± 8.87	0.080
Diastolic		98.85 ± 7.38	98.19 ± 8.29	0.675
Parity	Primi	43 (58.1%)	21 (58.3%)	0.982
	Multi	31 (41.9%)	15 (41.7%)	
		Normal CU (n=62)	Abnormal CU (n=48)	P value
Age		27.55 ± 6.09	26.79 ± 5.84	0.512
BMI (Kg/m2)		26.22 ± 1.54	26.07 ± 1.99	0.637
Systolic		154.76 ± 7.70	153.75 ± 7.26	0.487
Diastolic		97.58 ± 7.72	100.00 ± 7.44	0.101
Parity	Primi	35 (56.5%)	29 (60.4%)	0.676
	Multi	27 (43.5%)	19 (39.6%)	

MCP: middle cerebral artery, UTA: uterine artery, UMBA: umbilical, middle cerebral artery, MCA: middle cerebral artery, CP: cerebroplacental ratio, CU: Cerebrouterine ratio, Primi: Primigravida, Multi: Multigravida

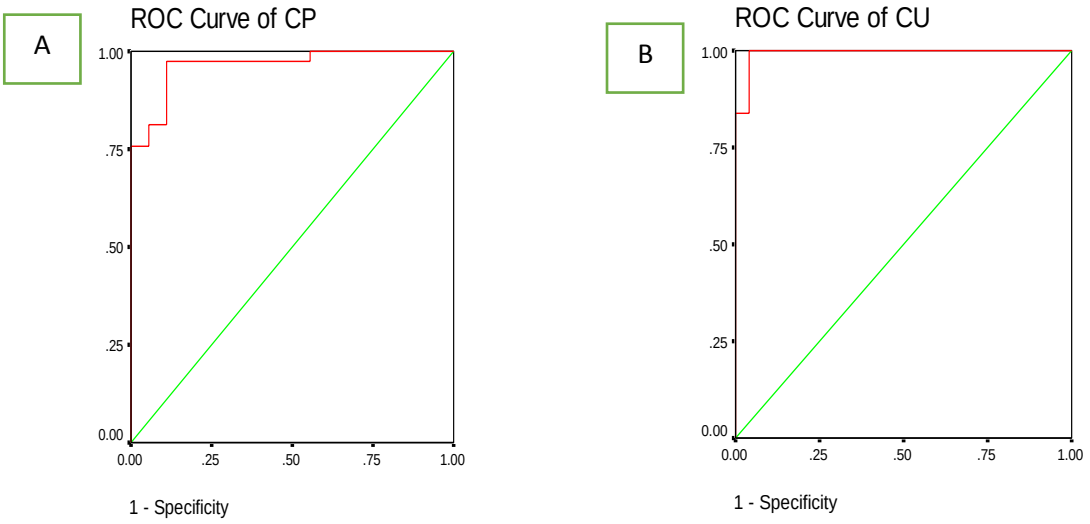

Fig. 1. (A) ROC Curve of cerebroplacental ratio and (B) cerebrouterine ratio

Table 5. Neonatal outcomes among the studied cases and Comparison between cerebroplacental ratio, cerebrouterine ratio regarding outcomes

Outcomes				
MOD	NVD	26(23.6%)		
	CS	84(76.4%)		
Small GA		9(8.2%)		
APGAR 1 < 7		47(42.7%)		
APGAR 5 < 7		34(30.9%)		
NICU		55(50%)		
Death		9(8.2%)		
	Normal CP (n=74)	**Abnormal CP (n=36)**	**P value**	**RR (95%CI)**
Small GA	3(4.1%)	6(16.7%)	0.024*	0.211 (0.050 – 0.901)
APGAR 1 < 7	19(25.7%)	28(77.8%)	0.001*	0.099 (0.038 – 0.253)
APGAR 5 < 7	18(24.3%)	16(44.4%)	0.032*	0.402 (0.173 – 0.935)
NICU	30(40.5%)	25(69.4%)	0.004*	0.300 (0.129 – 0.700)
Death	4(5.4%)	5(13.9%)	0.128	0.354 (0.089 – 1.410)
CS	54(73%)	30(83.3%)	0.230	1.852 (0.671 – 5.113)
	Normal CU (n=62)	**Abnormal CU (n=48)**	**P value**	**RR (95%CI)**
Small GA	2(3.2%)	7(14.6%)	0.031*	0.195 (0.039 – 0.987)
APGAR 1 < 7	20(32.3%)	27(56.3%)	0.012*	0.370 (0.170 – 0.808)
APGAR 5 < 7	9(14.5%)	25(52.1%)	0.001*	0.156 (0.063 – 0.386)
NICU	19(30.6%)	36(75%)	0.001*	0.147 (0.063 – 0.344)
Death	2(3.2%)	7(14.6%)	0.031*	0.195 (0.039 – 0.987)
CS	45(72.6%)	39(81.3%)	0.289	1.637 (0.656 – 4.086)

Data are represented by frequency (%), MOD: mode of delivery, NVD: normal vaginal delivery, CS: cesarean section, GA: gestational age, CP: cerebroplacental ratio, CU: Cerebrouterine ratio, NICU: neonatal intensive care unit, RR: Relative risk

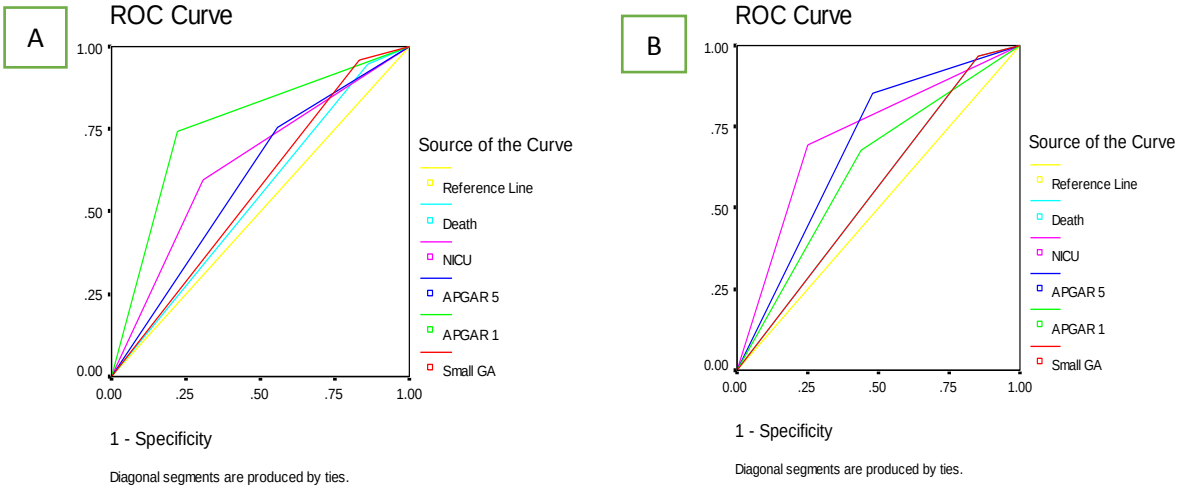

Fig. 2. (A) ROC Curve of cerebroplacental ratio and neonatal outcome and (B) cerebrouterine ratio and neonatal outcome

The prevalence of preeclampsia was more in primigravida in our study as is also seen in general. Nulliparous women are at increased risk, which is related to maternal first exposure to chorionic villi.

Maeda et al. [13] conducted a single-center, retrospective chart review study of 85 pregnant women and used multiple logistic regression analysis to assess the association between parity and preeclampsia in women with SLE. Their

results showed that Multiparity was significantly associated with a low risk of preeclampsia (adjusted odds ratio: 0.08; 95% confidence interval: 0.01–0.95).

Das et al. [14] made a retrospective study included 4820 pregnant women which aimed to determine the incidence of preeclampsia and distribution of risk factors of preeclampsia at Paropakar Maternity and Women's Hospital, Kathmandu, Nepal. The incidence rate of preeclampsia in the study population was 1.8% (n = 85). Higher incidence of preeclampsia was observed in primiparous women 64.7 % (n = 55) more than multipara35.3 % (n = 30).

The current study showed that among patients with preeclampsia with severe features (n = 58), 33(56.9%) of cases had abnormal uterine artery Doppler, 40(69%) of cases had abnormal umbilical artery Doppler, 46(79.3%) of cases had abnormal middle cerebral artery Doppler. This show that abnormal uterine (P value = 0.001), umbilical (P value = 0.001) and middle cerebral artery (P value = 0.040) ratio were significantly more frequent in patients with preeclampsia with severe features.

In agreement with our result, Adekanmi et al. [15] conducted a prospective study was done among 98 high‑risk singleton pregnant women, five were lost to follow‑up, whereas 93 delivered at their institution. There was a statistically significant difference in the mean uterine artery PSV (peak systolic velocity) of pregnant women who had mild PE (preeclampsia) and that of women who developed severe PE (P = 0.024). The mean uterine S/D ratio of pregnant women with mild PE was statistically significantly lower than mean uterine S/D (the ratio of peak systolic to end-diastolic velocity) ratio of pregnant women who had severe PE.

Deshmukh et al. [16] divided their study into two groups-Group A "n=110" with MCA/UA PI>1.08 and Group B "n=40" with MCA/UA PI<1.08. In group B "abnormal CPR" 92.5% of cases were severe preeclampsia and 7.5% of cases were mild preeclampsia (P value <0.0001). Mean UA PI in study population was statistically significant higher in those with severe preeclampsia (p value<0.0001). On other hand mean MCA PI had no statistically significant difference (P value =0.4354) in mild and severe preeclampsia and this disagrees with our result.

The current study showed that abnormal CP (P value = 0.001) ratio and CU (P value = 0.001) ratio were significantly more frequent in patients with preeclampsia with severe features.

Eser et al. [17] carried out their study on 64 preeclamptic and 131 normal pregnancies at or beyond 26 weeks of gestation and found that in 11(42.3%) of the preeclamptic pregnancies, the MCA/uterine artery PI was below the fifth percentile, related with fetal circulation redistribution. Four of these 11 cases had severe preeclampsia (36.3%) and seven had mild preeclampsia (63.6%), this disagrees with our study, while Simanaviciute and Gudmundsson [18] was conducted a cross sectional study on 231 normal pregnancies at or beyond 26 weeks of gestation to construct the reference range and a further 115 pregnancies with preeclampsia (50 mild and 65 severe) were assessed prospectively and the results were related to perinatal outcome. A low MCA/uterine artery PI ratio was seen in 30% of the mild (n = 15) and 46% of the severe (n = 30) preeclamptic cases and this is agreeing with our results.

The current study show that CP ratio had higher sensitivity in prediction of SGA while it had low specificity, NICU its sensitivity was 59%, specificity 69%, PPV 80%, NPV 45% and accuracy 63% while in neonatal death its sensitivity was 95%, specificity, while in SGA CU ratio had higher sensitivity, NICU its sensitivity was 69%, specificity 75%, PPV 78%, NPV 65% and accuracy 72% while in neonatal death its sensitivity was 97%, specificity 15%, PPV 59%, NPV 78% and accuracy 61%.

Adiga et al. [19] results showed that CU ratio had 54.5% sensitivity, 67.7% specificity, 47.4% PPV, 73.7% NPV and 63.2% accuracy in prediction of SGA, in poor Apgar score, CU ratio had 62.5% sensitivity, 64.6% specificity, 26.2% PPV, 89.5% NPV and 64.2% accuracy, while CP ratio had 33.3% sensitivity, 83.9% specificity, 52.4% PPV, 70.3%NPV and 66.3%accuracy in prediction of SGA, in poor Apgar score, CU ratio had 56.3% sensitivity, 84.8%specificity, 42.9% PPV, 90.5% NPV and 80.0% accuracy.

In Eser et al. [17] study, CU ratio sensitivity in prediction of NICU admission was 59.2%, specificity 73.8%, PPV 58.7% and NPV 73.4%.CP ratio sensitivity was 46.1%, specificity 87.8%, PPV 70.3% and NPV 71.9%. In Apgar 5 min < 7 prediction CU ratio had 27.2% sensitivity, 57.9% specificity, 3.8% PPV, and 89.8% NPV and CP ratio had 42.8% sensitivity, 74.3% specificity, 9.7% PPV, and 94.1% NPV. In SGA

prediction CU ratio had 47.8% sensitivity, 63.9% specificity, 38% PPV, and 72.9% NPV and CP ratio had 31.1% sensitivity, 75.4% specificity, 36.2% PPV, and 70.4% NPV.

5. CONCLUSIONS

Most of Cases with preeclampsia with severe features associated with abnormal uterine, umbilical and middle cerebral artery Doppler. Most of unfavourable neonatal outcome associated with abnormal cerebroplacental and cerebrouterine ratio so cerebroplacental and cerebrouterine ratio were complementary to each other in predicting the adverse neonatal outcomes. Cut off value of the study cerebroplacental ratio was 1.09 and cerebrouterine ratio was 1.3.

6. LIMITATIONS

One of the limitations of this study is that it was a single – center study and may not be representative of the general population. Second, small sample size selected which may make results of the study less generally applicable in a country as populous as Egypt.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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