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Role of Cerebro-Placental Ratio in Prediction of Perinatal Outcome in Preeclamptic Patients with Intrauterine Growth Restriction

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ABSTRACT

Background: The assessment of fetal hemodynamic status via Doppler flow is increasingly regarded as likely to aid in the detection of pregnancies at risk of developing adverse fetal outcomes. Doppler flow provides useful information beyond the ultrasound-based assessment of fetal growth alone.

Objective: This study aimed to evaluate the role of cerebro-placental ratio (CPR) in prediction of perinatal outcome in preeclamptic patients with intrauterine growth restriction (IUGR).

Patients and methods: This case-control study was conducted at Obstetrics and Gynecology Department, Zagazig University, on 50 pregnant women divided in to two groups: Group I (study group) that included 25 high risk pregnant women with IUGR. Group II (control group) included 25 high risk pregnant women without IUGR. The study was conducted during the period from December 2020 till July 2021.

Results: The current study showed that CPR had 90.9% sensitivity, 78.6% specificity and 84 % diagnostic accuracy to predict newborns with low Apgar score, with statistically significant positive correlation. CPR also had 100% sensitivity, 100% specificity and 100 % diagnostic accuracy to predict stillbirth, with highly statistically significant positive correlation. The CPR had 100% sensitivity, 83.3% specificity and 92 % diagnostic accuracy to predict newborns with NICU admission, with statistically significant positive correlation. Other complications as meconium aspiration and neonatal death had no statistically significant to be predicted by low CPR.

Conclusion: This study concluded that the Cerebro-Placental Ratio had high predictive value of perinatal out come in preeclamptic patients.

Keywords: Cerebro-placental ratio, Intrauterine growth restriction, Perinatal outcome.

INTRODUCTION

Intrauterine growth restriction (IUGR) is an indicator of the increased risk of perinatal and long-term mortality and morbidity when compared to those born with normal growth. There is a considerable difference in the incidence of IUGR across different populations [(1)]. Current challenges in the clinical management of IUGR include accurate diagnosis of the truly growth restricted fetus, selection of appropriate fetal surveillance, and optimizing the timing of delivery. Despite the potential for a complicated course, antenatal detection of IUGR and its antepartum surveillance can improve outcomes [(2)].

Pre-eclampsia (PE) is inconsistently associated with intrauterine growth restriction, but PE and gestational hypertension causes IUGR to occur in 30-40% of cases. Intrauterine growth restriction can be a serious problem in newborns because it is associated with increased morbidity and mortality and long-term neurological sequelae [(3)].

Current theories show that the primary cause of IUGR in preeclampsia is abnormal invasion of placental trophoblast. If this theory is correct, we can expect that women with severe PE to have the highest IUGR risk. Also, according to the same theory, we expected that women with mild PE would be less likely to have IUGR fetuses[(4)].

The use of cerebro-placental ratio (CPR) allows the assessment of blood flow disorders in the placenta, umbilical cord, and fetal-cerebral circulation. CPR reflects fetal adaptation to placental chronic hypoxia and appears to be more sensitive than the Doppler ultrasound of the umbilical and middle cerebral artery by detecting clinically unrecognized fetal compromise [(5)].

The current study aimed to evaluate the role of cerebro-placental ratio in prediction of perinatal outcome in preeclamptic patients with intrauterine growth restriction.

PATIENT AND METHODS

This case-control study was conducted at Obstetrics and Gynecology Department, Zagazig University, on 50 pregnant women during the period from December 2020 till July 2021.

Ethical approval:

Written informed consent was obtained from every participant and the study was approved by the Research Ethical Committee of Faculty of Medicine, Zagazig University International review board. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

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Inclusion criteria:

1. Age ranged from 20 to 35 years old.
2. Gestational age more than 32 weeks that was confirmed, either by menstrual dates or by first trimester ultrasonography.
3. Singleton intrauterine pregnancy.
4. Living fetus.
5. Pre-eclampsia diagnosed as new onset hypertension (Systolic blood pressure of 140 mm Hg or higher, or diastolic blood pressure of 90 mmHg or higher, on two occasions at least 6 hours apart while the patient is on bed rest unless antihypertensive therapy is initiated before this time) and Proteinuria (> 300 mg/24h).
6. For case group IUGR diagnosis by sonographic estimated fetal weight below 10th percentile for gestational age.

Exclusion criteria:

1. Refusal of the patient of sharing the study.
2. Women with multiple pregnancies.
3. History of chronic hypertension, diabetes mellitus or autoimmune diseases.
4. Intrauterine fetal death on admission.
5. Congenital abnormalities of the fetus.
6. The pregnant woman in labor.
7. Impending eclampsia.

Patients were divided into two groups: Group I: 25 patients with pre-eclampsia and IUGR, and Group II: 25 patients with pre-eclampsia and no IUGR.

All the patients were subjected to:

Clinical assessment:

- **Personal history:** Name, age, occupation, residence and special habits of medical importance.
- **Obstetric history:** Gravidity, parity, mode of previous delivery, gestational diabetes, weight gain in current pregnancy, first day of last menstrual period and menstrual regularity.
- **Past history:** History of any medical disorder or surgical history.
- **History of the present pregnancy:** Medical or surgical condition to define high risk pregnancy.

Examination:

- General examination: Vital signs and lower limb edema.
- Blood pressure was measured while patient is sitting and resting in the right arm on the desk, at rest and to be repeated after 6 hours.
- Body mass index = Weight (kg)/Height (m^2)

Laboratory assessment:

- Complete blood count, random blood sugar and urine analysis.

Ultrasonographic scanning: It was done trans-abdominally using MINDRAY DC-70 Exp B machine convex probe 3.5 MHZ to evaluate the presence of fetal heart activity and fetal biometry: biparietal diameter (BPD), abdominal circumference (AC), femur length (FL), gestational age (GA) and fetal weight (fetal weight was estimated).

Doppler studies: Umbilical artery (Um. A) and middle cerebral artery (MCA) were examined by color Doppler ultrasound and pulsed wave Doppler. Doppler indices were calculated by the built-in software programs in the machine.

Cerebroplacental ratio (middle cerebral artery to umbilical artery PI ratio) was estimated.

Neonatal assessment: Outcome variables included: Low APGAR score (1min, 5 min APGAR score less than 7).

Statistical Analysis: The collected data were entered to and analyzed by computer using Statistical Package of Social Sciences, version 25 (SPSS). Results were presented by tables and graphs. Quantitative data were represented as mean and standard deviation.
Qualitative data were represented as frequencies and proportions. Pearson Chi square test (χ^2) and fisher's exact were used to analyze qualitative independent data. P value of ≤ 0.05 was considered significant.

RESULTS

Table (1): Demographic data of the studied groups

Variable		Pre-eclampsia with IUGR (n=25)		Pre-eclampsia without IUGR (n=25)		t	P
Age: (years)	Mean ± SD Range	28.72 ± 4.12 22-35		27.44 ± 4.11 21-35		1.10	0.28 NS
BMI: (Kg/m^2)	Mean ± SD	27.22 ± 1		26.14 ± 2.49		1.44	0.16 NS
	Variable	**No**	**%**	**No**	**%**	**χ^2**	**P**
Parity:	PG P1 P2 P3	17 1 2 5	68 4 8 20	19 0 3 3	76 0 12 12	1.81	0.61 NS

SD: Standard deviation I t: Independent t test χ^2: Chi square test NS: Non-significant (P > 0.05)

Table (1) showed that there were no statistical significant differences between the studied groups in age, BMI or parity.

Table (2): Perinatal outcome among the studied groups

Variable		Pre-eclampsia with IUGR (n=25)		Pre-eclampsia without IUGR (n=25)		χ^2	P
		No	%	No	%		
Low Apgar Score	No	14	56	20	80	3.31	0.07
	Yes	11	44	5	20		NS
Stillbirth	No	24	96	25	100	1.02	0.31
	Yes	1	4	0	0		NS
NICU	No	12	48	19	76	**4.16**	**0.04***
	Yes	13	52	6	24		
Meconium aspiration	No	15	60	21	84	3.57	0.06
	Yes	10	40	4	16		NS
Neonatal Death	No	22	88	24	96	1.09	0.30
	Yes	3	12	1	4		NS

χ^2: Chi square test NS: Non-significant (P > 0.05) *: Significant (P < 0.05)

Table (2) showed that there were no statistical significant differences between the studied groups in frequency of low Apgar score, stillbirth, meconium aspiration or neonatal death but there was a statistical significant increase in frequency of NICU among group with IUGR compared to group without IUGR.

Table (3): Relation between CPR and perinatal outcome and mode of delivery among with IUGR group

Variable		No	CPR		t	P
			Mean	SD		
Mode	CS	19	0.97	0.25	0.38	0.71
	NVD	6	1.01	0.15		NS
Low Apgar Score	No	14	1.11	0.21	**4.18**	**<0.001**
	Yes	11	0.82	0.11		**
Stillbirth	No	24	1	0.21	**2.03**	**0.05***
	Yes	1	0.56	0		
NICU	No	12	1.13	0.25	**3.88**	**0.001***
	Yes	13	0.85	0.07		
Meconium aspiration	No	15	0.98	0.26	0.02	0.99
	Yes	10	0.98	0.18		NS
Neonatal Death	No	22	0.98	0.21	0.07	0.95
	Yes	3	0.97	0.37		NS

SD: Standard deviation t: Independent t test NS: Non-significant (P > 0.05) *: Significant (P < 0.05), **:Highly significant (P < 0.001)

There was a statistical significant decrease in CPR among cases who had low APGAR score, stillbirth & NICU compared to cases hadn't in group with IUGR as shown in table (3).

Table (4): Relation between CPR and perinatal outcome and mode of delivery among without IUGR group

Variable		No	CPR		t	P
			Mean	SD		
Mode:	CS	19	1.14	0.33	0.29	0.78
	NVD	6	1.18	0.23		NS
Low Apgar Score:	No	20	1.22	0.30	**2.47**	**0.02***
	Yes	5	0.87	0.12		
NICU	No	19	1.25	0.27	**3.75**	**0.001***
	Yes	6	0.82	0.08		
Meconium aspiration	No	21	1.18	0.32	1.37	0.18
	Yes	4	0.96	0.16		NS
Neonatal Death	No	24	1.17	0.30	1.54	0.14
	Yes	1	0.7	0		NS

SD: Standard deviation t: Independent t test NS: Non-significant (P > 0.05) *: Significant (P < 0.05)

Table (4) showed that there was a statistical significant decrease in CPR among cases had low APGAR score, stillbirth & NICU compared to cases hadn't in group with IUGR.

Table (5): Validity of CPR in prediction of perinatal outcome among IUGR group

Markers	Cutoff	AUC (95%Ci)	Sensitivity	Specificity	PPV	NPV	Accuracy	P
Low Apgar Score	<0.92	0.87 (0.73-1)	90.9%	78.6%	76.9%	91.7%	84%	**0.002***
Stillbirth	<0.64	1 (1-1)	100%	100%	100%	100%	100%	**<0.001 ****
NICU	<0.98	0.88 (0.7-1)	100%	83.3%	86.7%	100%	92%	**0.001***
Meconium aspiration	<0.98	0.48 (0.25-0.71)	70%	46.7%	46.7%	70%	56%	0.87 NS
Neonatal death	<0.81	0.63 (0.17-1)	66.7%	86.4%	40%	95%	84%	0.47NS

AUC: Area under curve CI: Confidence interval PPV: Positive predicted value NPV: Negative predicted value *: Significant (P < 0.05) NS: Non-significant (P > 0.05) **: Highly significant (P < 0.001)

Table (5) showe4d that CPR had significant validity in predication of stillbirth (AUC =1, Accuracy 100%), NICU (AUC = 0.88, accuracy 92%), low Apgar score (AUC=0.87, accuracy 84%).

DISCUSSION

Pre-eclampsia is a serious condition that may lead to serious complications for both mother and fetus. It is commonly associated with IUGR as pre-eclampsia affects the arteries carrying blood to the placenta leading to inadequate blood and oxygen and nutrients. This can lead to slow growth known as IUGR [(6)].

Many indices can be measured by Doppler velocimetry as UA PI, MCA PI and CPR. The use of CPR allows the assessment of blood flow disorders in the placenta, umbilical cord, and fetal-cerebral circulation. CPR reflects fetal adaptation to placental chronic hypoxia and appears to be more sensitive than the Doppler ultrasound of the umbilical and middle cerebral arteries by detecting clinically unrecognized fetal compromise [(7)].

This study was conducted to evaluate the Role of cerebro-placental ratio in prediction of perinatal outcome in pre-eclamptic patients with intrauterine growth restriction.

The demographic data in this study showed in IUGR group that the mean age was 28.72 years ranged from 22 to 35 years, the mean BMI was 27.22 ranged from 22.7 to 32, the mean gestational age was 35.41 weeks and most of them were primigravida (68%), 20% were para three, 8% were para two and only one case (4%) was para one. While in patients' group without IUGR the mean age was 27.44 years, the BMI was 26.14 and the mean gestational age was 37.56 weeks. There was a statistical significant decrease in GA among pre-eclampsia with IUGR compared to cases with pre-eclampsia without IUGR. Most of this group were primigravida 76% while para 2 along with para 3 were 12% for each and no patient was para 1 in this group.

Our demographic data agree with **El-Kady *et al.*** [(1)] who had mean age of 28.8 ± 3 years, the mean BMI was 27.2 ± 2.4 Kg/m^2, the mean gestational age was 35.7±1.5 weeks and regarding the parity 70% of the women were PG and 30% were multipara.

Regarding the Doppler findings among the studied groups, UA PI had statistical significant increase with IUGR group compared to non-IUGR group, as the mean UA PI was 0.84 & 0.68 respectively with P value 0.04. Our results are comparable with **Günay *et al.*** [(8)] who noted that women with adverse neonatal outcome had significantly higher UA PI when compared to those who had no adverse outcome, as the P value was 0.001. This does not agree with **Ghi *et al.*** [(5)] who documented that 55.6% of patients had abnormal UA PI associated with abnormal outcome, while the rest 44.4% had normal UAPI along with poor neonatal outcome and with no statistical significance.

The current study showed that among patients with IUGR, 11 (44%) had low APGAR, those patients had low CPR with mean of 0.82. While, 14 patients (56%) had normal APGAR score with mean CPR of 1.11. Also, stillbirth had 1 case (0.04%) with low CPR of 0.56 while live birth was 24 patients (99.96%) with mean CPR of 1. 13 patients (52%) were admitted to NICU with low mean CPR (0.85) and 12 patients (48%) did not admit to NICU with mean CPR of 1.13. All the previous complications had positive correlation with low CPR.

El-Kady *et al.* [(1)] results showed that among patients with IUGR, 14 (46.7%) had neonatal low APGAR, 12 of them had low CPR, 1 (3.3%) had neonatal stillbirth, 16 (53.3%) needed NICU admission, only one patient had normal CPR and the rest had low CPR. 13 (43.3%) had neonatal meconium aspiration, no one of them had normal CPR , 3 (10.0%) had neonatal death along with low CPR. These results showed strong correlation between low CPR and perinatal complications. Also, **Najam *et al.*** [(9)] who reported that the CPR was abnormal in 80% of IUGR

group while only abnormal in 38.24% of patients without IUGR.

The results among group without IUGR in relation with CPR showed significant positive correlation between low Apgar score and neonatal NICU along with low CPR. As no patient out of the 5 patients who had low Apgar score had CPR = 1.11 and the mean CPR of them were 0.87. Regarding the admission to NICU all of the 6 patients admitted to NICU had CPR = 1.11, while in the 19 patients who were not admitted to NICU, 13 of them had normal CPR and 6 patients had CPR < 1.11. The rest of complications had no significant correlation with low CPR. **El-Kady *et al.* [(1)]** documented that in patients without IUGR, 6 (20.0%) had neonate with low APGAR, 5 of them had low CPR. 7 (23.3%) had neonate need NICU admission only 2 of them had normal CPR while the rest had low CPR. Also, 5 (16.7%) had neonatal meconium aspiration, 4 of them had low CPR. In addition, 1 patient (3.3%) had neonatal death along with low CPR and no patient had neonatal still birth. They also documented that there were positive correlation between low CPR and low Apgar score, NICU admission and meconium aspiration as perinatal complications. While, they did not document any significant correlation between low CPR and neonatal death in non IUGR group. While, **Shahinaj *et al.* [(10)]** documented that the entire perinatal adverse outcome as low APGAR score, stillbirth, need for NICU admission and perinatal death were highly significantly correlated with low CPR among the non IUGR group. As the P-values of these entire outcome were = 0.001.

The current study showed that CPR had 90.9% sensitivity, 78.6% specificity, 84 % diagnostic accuracy, 76.9% positive predictive value and 91.7% negative predictive value to predict newborns with low Apgar score, with statistically significant positive correlation, as the p value was 0.002. CPR also had 100% sensitivity, 100% specificity, 100 % diagnostic accuracy, 100% positive predictive value and 100 % negative predictive value to predict stillbirth, with highly statistically significant positive correlation as p value was < 0.001.

The CPR had 100% sensitivity, 83.3% specificity, 92 % diagnostic accuracy, 86.7% positive predictive value and 100% negative predictive value to predict newborns with NICU admission, with statistically significant positive correlation, as the p value was 0.001. The other complications as meconium aspiration and neonatal death had no statistically significant to be predicted by low CPR.

This result agrees with **El-Kady *et al.* [(1)]** study, which had results showed low CPR in IUGR group had 89.5% sensitivity, 72.7% Specificity, 83.3% diagnostic accuracy, 60.0% positive predictive value and 80.0% negative predictive value to predict CS for fetal distress, while the low CPR in non-IUGR group had 72.7% sensitivity, 84.2% Specificity, 80.0% diagnostic accuracy, 72.7% positive predictive value and 84.2% negative predictive value to predict CS for fetal distress. So, low CPR had moderate diagnostic characteristics in predicting CS for fetal distress in study groups.

CONCLUSION

This study concluded that the Cerebro-Placental Ratio had high predictive value of perinatal out come in pre-eclamptic patients.

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