Role of cerebro-placental ratio in prediction of perinatal outcome in high-risk pregnancies with intrauterine growth restriction

Original Article

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ABSTRACT

Introduction: Doppler ultrasound velocimetry of uteroplacental umbilical and fetal vessels has become established method of antenatal monitoring. Cerebroplacental ratio has been studied to predict neonatal outcomes.

Aim of the work: Our aim was to assess role of cerebro-placental ratio in prediction of perinatal outcome in high-risk pregnancies with intrauterine growth restriction.

Patients and Methods: In this study was held in Ain Shams university maternity hospital which included 60 high risk pregnant women divided in to two groups: Group I: study group: 30 high risk pregnant women with IUGR, Group II- control group: 30 high risk pregnant women without IUGR.

Results: The current study showed that among patients with IUGR and low CPR, 17 (56.7%) had CS for fetal distress, 12 (40.0%) had neonate with low APGAR, 13 (43.3%) had neonatal meconium aspiration, 6 (20.0%) had neonatal Hypoxic ischemic Encephalopathy, 15 (50.0%) had neonate need NICU admission, 3 (10.0%) had neonatal death, 1 (3.3%) had neonatal still birth. The current study showed that among patients without IUGR and low CPR, 8 (26.7%) had CS for fetal distress, 5 (16.7%) had neonate with low APGAR, 4 (13.3%) had neonatal meconium aspiration, 1 (3.3%) had neonatal Hypoxic ischemic Encephalopathy, 5 (16.7%) had neonate need NICU admission, 1 (3.3%) had neonatal death, 0 (0.0%) had neonatal still birth.

Conclusion: Cerebro -placental ratio has high predictive value of perinatal outcome in high risk pregnancy with intrauterine growth restriction.

Key Words: Cerebro-placental ratio, high-risk pregnancies, intrauterine growth restriction, perinatal outcome.

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INTRODUCTION

Intrauterine growth restriction (IUGR) is defined as sonographic estimated fetal weight below 10th percentile for gestational age[21]. According to the American College of Obstetricians and Gynecologists, IUGR is one the most common and complex problems in modern obstetrics[2].

This characterization is understandable considering the various published definitions, poor detection rate, limited preventive or treatment options, multiple associated morbidities, and increased likelihood of perinatal mortality associated with IUGR. Suboptimal growth at birth is linked with impaired intellectual performance and diseases such as hypertension and obesity in adulthood[6] . 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[12].

It is important to synthesize and assess the strength of evidence of the current literature regarding the use of Doppler velocimetry of the umbilical artery and middle cerebral artery for non-anomalous fetuses with suspected IUGR, and to provide recommendations regarding antepartum management of these pregnancies, in particular for singleton gestations[3]. It has been acknowledged that defining small for gestational age (birthweight below 10th percentile for gestational age) by general population charts vs customized charts is an important issue, but this is not the focus of this clinical opinion[10].

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. In babies born with a birth weight less than 2500 gms, its prevalence is almost 33%. The incidence of IUGR shows a dependence on economic growth too, with a relatively lower incidence in developed countries (4-8%) as compared to that in

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developing countries (6%-30%)[5].

The average incidence of IUGR is nearly 8% in the general population. In nearly 35%-40% of the cases, IUGR is the consequence of an abnormal condition. Factors like placental insufficiency, maternal hypertension, cardiovascular disease, diabetes, infections, low socioeconomic status, previous history and preeclampsia are some of the known risk factors for IUGR[1].

The maintenance of good utero-placental circulation is necessary to continue a normal pregnancy. The progression of pregnancy is marked by a number of changes and adaptations in the maternal, placental and fetal vasculatures[23]. An inability to adapt to these changes results in the development of abnormal vascular resistance patterns, which might consecutively lead to the compromise of fetal well-being and ultimately IUGR[19]. Early identification and prediction of IUGR, to a great extent, rests in an ability to evaluate the maternal, placental and fetal vascular patterns effectively and efficiently.

A number of indices based on color Doppler flowmetry have been proposed to evaluate the risk of intrauterine growth restriction in an ongoing pregnancy, some of these include the pulsatility and resistive indices (PI and RI) of the umbilical artery (UA) and that of the middle cerebral artery (MCA) in predicting adverse perinatal outcome[11].

In the present study, an attempt will be made to evaluate the efficacy of these Doppler indices in our settings in third trimester pregnancies.

AIM OF THE STUDY

The aim of the study is to assess role of cerebro-placental ratio in prediction of perinatal outcome in high-risk pregnancies with intrauterine growth restriction.

PATIENTS AND METHODS

This case control study that was held in Ain Shams university maternity hospital, during the period between March 2019 to October 2019. The aim was to evaluate the role of cerebro-placental ratio in predictability of perinatal outcome in high-risk category of pregnancies having intrauterine growth restriction. This research recruited 60 high risk pregnant women categorized in to two research groups: Group I: study group: 30 high risk pregnant women with IUGR, Group II: control group: 30 high risk pregnant women without IUGR. With inclusion criteria of study group are: maternal age more than 20 years old, singleton Pregnant women, third trimester gestational age, high risk pregnancy as pregnancy-induced hypertension (PIH), sure of last menstrual period (LMP) date, IUGR diagnosis by sonographic estimated fetal weight below 10th percentile for gestational age. And inclusion criteria of control group are: maternal age more than 20 years old, singleton pregnant women, third trimester gestational age, high risk pregnancy as pregnancy-induced hypertension (PIH), sure of last menstrual period (LMP) date, no IUGR diagnosis by sonographic estimated fetal weight for gestational age. While exclusion criteria for both group are :gestational diabetes mellitus, congenital malformation in the present fetus, multiple fetal pregnancy, wrong LMP date. All participants in the study will receive both oral and written informed consent after explaining the details of the study for them, as agreed upon by the ethical committee. Gestational age determination was based on the best estimate from the last menstrual history and by ultrasonography (USG) or routine fetal biometry in the first trimester or early second trimester.All participants then will have ultrasound Doppler study of the following arteries: Umbilical artery, Middle cerebral artery (MCA), were examined by Color Doppler ultrasound and Pulsed wave Doppler, All Doppler examinations were performed using Medison R5 Ultrasound machine equipped with a 3.5 MHz Convex probe. Doppler indices were calculated by the built-in software programs in the machine.

Statistical methods

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 18.0, IBM Corp., Chicago, USA, 2009. The level of significance was taken at P value < 0.050 is significant, otherwise is non-significant.

RESULTS

Table 1 shows that no significant differences between the studied groups regarding demographic characteristics.

Table 2 shows that poor outcomes were more frequent among IUGR group; the differences were statistically signfciant except Hypoxic ischemic encephalopathy, death and still birth.

Table 3 shows that there was significant moderate agreement between low CPR and CS for fetal distress.

Table 4 shows that there was significant moderate agreement between low CPR and low APGAR.

Table 5 shows that there was significant moderate agreement between low CPR and meconium aspiration.

Table 6 shows that there was non-significant low agreement between low CPR and hypoxic ischemic encephalopathy. Table 7 shows that there was significant moderate agreement between low CPR and NICU admission.

Table 8 shows that There was non-significant low agreement between low CPR and neonatal death in study groups.

Table 1: Comparison between the studied groups regarding demographic characteristics

Variables		IUGR (N=30)	Non-IUGR (N=30)	P
Age (years)	Mean±SD	28.8±3.0	29.2±2.8	0.629^
	Range	24.0-34.0	24.0-34.0	
BMI (kg/m2)	Mean±SD	27.2±2.4	26.3±2.2	0.629^
	Range	22.7-32.0	22.6-31.2	
Parity	Primi	21 (70.0%)	23 (76.7%)	0.559#
	Multi	9 (30.0%)	7 (23.3%)	
GA (weeks)	Mean±SD	35.7±1.5	35.9±1.0	0.611^
	Range	34.0-38.0	34.0-38.0	

Q2

^Independent t-test. #Chi square test

Table 2: Comparison between the studied groups regarding perinatal outcomes

Outcomes	IUGR (N=30)	Non-IUGR (N=30)	P	OR (95% CI)
CS for fetal distress	19 (63.3%)	11 (36.7%)	#0.039*	2.98 (1.04-8.53)
Low APGAR	14 (46.7%)	6 (20.0%)	#0.028*	3.50 (1.11-11.02)
Meconium aspiration	13 (43.3%)	5 (16.7%)	#0.024*	3.82 (1.15-12.71)
Hypoxic ischemic encephalopathy	6 (20.0%)	1 (3.3%)	§0.103	7.25 (0.82-64.46)
NICU	16 (53.3%)	7 (23.3%)	#0.017*	3.76 (1.24-11.38)
Death	3 (10.0%)	1 (3.3%)	§0.612	3.22 (0.32-32.89)
Still birth	1 (3.3%)	0 (0.0%)	§1.000	--

#Chi square test. §Fisher's Exact test. *Significant

Table 3: Agreement between low CPR and CS for fetal distress

	IUGR (N=30)			
CPR	CS for fetal distress		Total	
	Present	Absent		
Low	17 (56.7%) TP	3 (10.0%) FP	20 (66.7.0%)	
Normal	2 (6.7%) FN	8 (26.7%) TN	10 (33.3%)	
Total	19 (63.3%)	11 (36.7%)	30 (100.0%)	
Kappa (95% CI)	0.634 (0.344-0.924)		P	<0.001*
	Non-IUGR (N=30)			
Low	8 (26.7%) TP	3 (10.0%) FP	11 (36.7%)	
Normal	3 (10.0%) FN	16 (53.3%) TN	19 (63.3%)	
Total	11 (36.7%)	19 (63.3%)	30 (100.0%)	
Kappa (95% CI)	0.569 (0.264-0.875)		P	<0.001*

Percentages are from the total (30), TP: True positive, TN: True negative, FP: False positive, FN: False negative

Table 4: Agreement between low CPR and low APGAR

CPR	Low APGAR		Total	
	Present	Absent		
IUGR (N=30)				
Low	12 (40.0%) TP	8 (26.7%) FP	20 (66.7.0%)	
Normal	2 (6.7%) FN	8 (26.7%) TN	10 (33.3%)	
Total	14 (46.7%)	16 (53.3%)	30 (100.0%)	
Kappa (95% CI)	0.384 (0.042-0.653)		*P*	<0.001*
Non-IUGR (N=30)				
Low	5 (16.7%) TP	6 (20%) FP	11 (36.7%)	
Normal	1 (3.3%) FN	18 (60.0%) TN	19 (63.3%)	
Total	6 (20.0%)	24 (80.0%)	30 (100.0%)	
Kappa (95% CI)	0.444 (0.120-0.769)		*P*	<0.001*

Percentages are from the total (30), TP: True positive, TN: True negative, FP: False positive, FN: False negative

Table 5: Agreement between low CPR and meconium aspiration

CPR	Meconium aspiration		Total	
	Present	Absent		
IUGR (N=30)				
Low	13 (43.3%) TP	7 (23.3%) FP	20 (66.7.0%)	
Normal	0 (0.0%) FN	10 (33.3%) TN	10 (33.3%)	
Total	13 (43.3%)	17 (56.7%)	30 (100.0%)	
Kappa (95% CI)	0.553 (0.294-0.812)		*P*	<0.001*
Non-IUGR (N=30)				
Low	4 (13.3%) TP	7 (23.3%) FP	11 (36.7%)	
Normal	1 (3.3%) FN	18 (60.0%) TN	19 (63.3%)	
Total	5 (16.7%)	25 (83.3%)	30 (100.0%)	
Kappa (95% CI)	0.351 (0.025-0.678)		*P*	<0.001*

Percentages are from the total (30), TP: True positive, TN: True negative, FP: False positive, FN: False negative

Table 6: Agreement between low CPR and hypoxic ischemic encephalopathy

CPR	Encephalopathy		Total	
	Present	Absent		
IUGR (N=30)				
Low	6 (20.0%) TP	14 (46.7%) FP	20 (66.7.0%)	
Normal	0 (0.0%) FN	10 (33.3%) TN	10 (33.3%)	
Total	6 (20.0%)	24 (80.0%)	30 (100.0%)	
Kappa (95% CI)	0.222 (0.035-0.409)		*P*	0.053
Non-IUGR (N=30)				
Low	1 (3.3%) TP	10 (33.3%) FP	11 (36.7%)	
Normal	0 (0.0%) FN	19 (63.4%) TN	19 (63.3%)	
Total	1 (3.3%)	29 (96.7%)	30 (100.0%)	
Kappa (95% CI)	0.351 (0.025-0.678)		*P*	0.181

Percentages are from the total (30), TP: True positive, TN: True negative, FP: False positive, FN: False negative

Table 7: Agreement between low CPR and NICU admission

CPR	NICU admission Present	NICU admission Absent	Total	
IUGR (N=30)				
Low	15 (50.0%) TP	5 (16.7%) FP	20 (66.7.0%)	
Normal	1 (3.3%) FN	9 (30.0%) TN	10 (33.3%)	
Total	16 (53.3%)	14 (46.7%)	30 (100.0%)	
Kappa (95% CI)	0.591 (0.310-0.827)		*P*	<0.001*
Non-IUGR (N=30)				
Low	5 (16.7%) TP	6 (20.0%) FP	11 (36.7%)	
Normal	2 (6.6%) FN	17 (56.7%) TN	19 (63.3%)	
Total	7 (23.3%)	23 (76.7%)	30 (100.0%)	
Kappa (95% CI)	0.444 (0.120-0.769)		*P*	<0.001*

Percentages are from the total (30), TP: True positive, TN: True negative, FP: False positive, FN: False negative

Table 8: Agreement between low CPR and neonatal death

CPR	Neonatal death Present	Neonatal death Absent	Total	
IUGR (N=30)				
Low	3 (10.0%) TP	17 (56.7%) FP	20 (66.7.0%)	
Normal	0 (0.0%) FN	10 (33.3%) TN	10 (33.3%)	
Total	3 (10.0%)	27 (90.0%)	30 (100.0%)	
Kappa (95% CI)	0.105 (0.000-0.230)		*P*	0.197
Non-IUGR (N=30)				
Low	1 (3.3%) TP	10 (33.3%) FP	11 (36.7%)	
Normal	0 (0.0%) FN	19 (63.3%) TN	19 (63.3%)	
Total	1 (3.3%)	29 (96.7%)	30 (100.0%)	
Kappa (95% CI)	0.112 (0.000-0.319)		*P*	0.181

Percentages are from the total (30), TP: True positive, TN: True negative, FP: False positive, FN: False negative

DISCUSSION

Predictability of gestation having the of adverse perinatal outcome development is a cornerstone obstetric challenges in every day practice. sonography could aid in detectability of those clinically challenging gestations e.g by growth restriction identification. On the other hand, fetal growth pattern solely couldn't detect all foetuses at risk and could easily miss those category that grow within normal ranges but are not approaching their maximum growth potential[4].

Doppler flow indices of placental and fetal vessels when properly integrated and calculated could enhance the detectability of the detailed fetal hemodynamic status and placental perfusion pathologies that could affect the clinical prognosis of perinatal outcomes[14].

The current research is a case control study that was held in Ain Shams university maternity hospital, during the period between March 2019 to October 2019. The aim was to evaluate the role of cerebro-placental ratio in predictability of perinatal outcome in high-risk category of pregnancies having intrauterine growth restriction.

This research recruited 60 high risk pregnant women categorized in to two research groups:

Group I: study group: 30 high risk pregnant women with IUGR.

Group II: control group: 30 high risk pregnant women without IUGR.

As regards the demographic research data of study subjects recruited, the mean age was 28.8±3.0 years, the mean BMI was 27.2±2.4 Kg/m2, the mean gestational age was 35.7±1.5 weeks and regarding the parity 70% of the women were PG and 30% were multipara.

The current study showed that among patients with IUGR, 20 (66.7.0%) had low CPR, 10 (33.3%) had normal CPR, while in patients without IUGR, 11 (36.7%) had low CPR, 19 (63.3%) had normal CPR. This shows that Low CPR was statistically significantly more frequent among IUGR research categorical group.

Alaa Ebrashy *et al.*, also reported abnormal cerebroplacental ratio in 41.8 % cases of preeclampsia without IUGR and 84.2 % cases of preeclampsia with IUGR. Our study corresponds with this study[7].

Najam *et al.*, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for detection of IUGR for umbilical artery Doppler were 48.15, 80.67, 53.06, and 77.41 %, while that for MCA Doppler were 59.25, 88.89, 72.72, and 81.35 %. Forabnormal C/U ratio, the values were 85.18, 89.72, 80.70 %, and 92.30. So, CPR is most sensitive with higher PPV for detection of IUGR. Those research findings could be justified by the fact that cerebroplacental ratio analyses two different flow indices in an integrated manner that represents the fetoplacental vascular status in a more representive manner[15].

Abnormal CPR has been associated with an increased risk of perinatal complications, especially in IUGR fetuses from PE pregnancy those findings are justified by the fact that placental vascular pathology causing hypoperfusion of the fetus necessitates the trigger of brain spaing effect casing the abnormalities in cerebroplacental ratio[16].

CPR could be used to identify fetuses that have a higher risk of hemodynamic pathological changes before birth, CPR being considered as a marker of placental hypoperfusion and reduced placental functional reserve[9].

There is reduced resistance within fetal circulation once the pregnancy progresses to term. However resistance within middle cerebral artery should remain higher than in the umbilical artery. Therefore, CPR should be greater than 1-1.1 in an uncomplicated pregnancy[17].

The current study showed that among patients with IUGR, 19 (63.3%) had CS for fetal distress, 14 (46.7%) had neonate with low APGAR, 13 (43.3%) had neonatal meconium aspiration, 6 (20.0%) had neonatal Hypoxic ischemic Encephalopathy, 16 (53.3%)had neonate need NICU admission, 3 (10.0%) had neonatal death, 1 (3.3%) had neonatal still birth, while in patients without IUGR, 11 (36.7%) had CS for fetal distress, 6 (20.0%) had neonate with low APGAR, 5 (16.7%) had neonatal meconium aspiration, 1 (3.3%) had neonatal Hypoxic ischemic Encephalopathy, 7 (23.3%) had neonate need NICU admission, 1 (3.3%) had neonatal death, 0 (0.0%) had neonatal still birth. This shows that Poor outcomes were more frequent among IUGR group; the differences were statistically signfciant except Hypoxic ischemic encephalopathy, death and still birth. Those research findings coud be justified by the fact that pregnancies affected by placental vascular hypo perfusion issues have lower capability to withstand normal hypoxic challenges that could arise during the physiological process of delivery[24].

Abnormal CPR has been associated with an increased risk of perinatal complications, especially in IUGR fetuses from PE pregnancy[16].

The current study showed that 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.

Also Eser *et al.* (2011), found statically significant positive correlation between abnormal CPR with fetal distress as *P* value =0.0008, *P* value =0.004, respectively, the results showed that CP ratio had 34.7 % sensitivity and 96 % specificity to detect Fetal distress, with positive predictive value 96 % and negative predictive value 12%[8].

The current study showed that low CPR in IUGR group had 85.7% sensitivity, 50.0% Specificity, 66.7% Diagnostic accuracy, 60.0% positive predictive value and 80.0% negative predictive value to predict low APGAR, while the low CPR in non-IUGR group had 83.3% sensitivity, 75.0% Specificity, 76.7% Diagnostic accuracy, 45.5% positive predictive value and 94.7% negative predictive value to predict low APGAR. So, Low CPR had moderate diagnostic characteristics in predicting low APGAR in study groups.

On the other hand Eser *et al.* (2011), in their cross sectional study that included 185 women, that studied the predictive value of CP ratio in prediction of neonatal outcomes in preeclampsia. showed no significant positive correlation between abnormal CP ratio and poor Apgar score, as *P* value =0.1, showed no significant positive correlation between abnormal CP ratio and poor Apgar score, as *P* value =0.1, The results showed that CP ratio had 42.8% sensitivity and 74.3% specificity, 9.7% positive predictive value and 94.1% negative predictive value, 9.7% positive predictive value and 94.1% negative predictive value to predict newborns with Apgar 5min < 7, but didn't study APGAR 1 min[8].

The current study showed that low CPR in IUGR group had 100.0% sensitivity, 58.8% Specificity, 76.7% Diagnostic accuracy, 65.0% positive predictive value and 100.0% negative predictive value to predict meconium aspiration, while the low CPR in non-IUGR group had 80.0% sensitivity, 72.0% Specificity, 73.3% Diagnostic accuracy, 36.4% positive predictive value and 94.7%

negative predictive value to predict meconium aspiration. So, Low CPR had high sensitivity and low specificity in predicting meconium aspiration in study groups.

The current study showed that low CPR in IUGR group had 100.0% sensitivity, 41.7% Specificity, 53.3% Diagnostic accuracy, 30.0% positive predictive value and 100.0% negative predictive value to predict hypoxic ischemic encephalopathy, while the low CPR in non-IUGR group had 100.0% sensitivity, 65.5% Specificity, 66.7% Diagnostic accuracy, 9.1% positive predictive value and 100.0% negative predictive value to predict hypoxic ischemic encephalopathy. So, Low CPR had high sensitivity and low specificity in predicting hypoxic ischemic encephalopathy in study groups.

These results agreed with the results obtained by Eser *et al.* (2011), that show significant positive correlation between abnormal CPR with fetuses with NICU admission, as P value =0.0006, P value =0.0009, respectively, also Smitha *et al.* (2014) showed significant positive correlation as P value <0.001[8].

Shahinaj *et al.* (2010), in their prospective observational study that included 738 singleton pregnancies, that studied The value of the CP ratio in the prediction of neonatal outcome in patient with preeclampsia, found positive correlation and statistically significant between abnormal CP ratio and Neonatal death as P value <.0001, the result showed that CP ratio had 97.7% sensitivity and 66.0% specificity to predict Neonatal death, with positive predictive value 16.5 % and negative predictive value 99.7%.

The current study showed that low CPR in IUGR group had 100.0% sensitivity, 34.5% Specificity, 36.7% Diagnostic accuracy, 5.0% positive predictive value and 100.0% negative predictive value to predict still birth, while the low CPR in non-IUGR group had 63.3% Specificity and 36.7% Diagnostic accuracy to predict still birth. So, Low CPR had high sensitivity and low specificity in predicting still birth in IUGR group.

A prior meta-analysis with the aim to evaluate usage of cerebroplacental ratio in predictability of adverse perinatal clinical outcome. The research data have revealed and displayed that abnormal cerebroplacental ratio could predict the requirement for operative mode of delivery necessary for foetal distress [P value < 0.001], low pH [P value = 0.005] and low Apgar scoring [P value = 0.10], foetal or neonatal death [relative risk = 2.49, 95% confidence interval= 1.00-6.20], besides NICU admission [P value = 0.14]. The research team of investigators from the data analysis have revealed and displayed a statistically significant correlation as regards all outcomes except the low pH. Those research findings show great similarity and harmony to the current research study findings[13].

CONCLUSION

Cerebro -placental ratio has high predictive value of perinatal outcome in high risk pregnancy with intrauterine growth restriction.

CONFLICT OF INTEREST

There are no conflicts of interest.

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