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

AbdelMonem Mohamed Zakaria
Obstetrics & Gynecology Department, Faculty of Medicine, Al-Azhar University, Egypt

AbdelMonsef Abdel Ghaffar Mostafa
Obstetrics & Gynecology Department, Faculty of Medicine, Al-Azhar University, Egypt

Khalid Abdel Hakim Shehata
Resident of Obstetrics and Gynecology Sohag Teaching Hospital, Egypt
*Corresponding author email: khaledshehata2025@gmail.com

***Abstract*---**Background: Antenatal surveillance using Doppler ultrasound velocimetry of the uteroplacental umbilical and fetus arteries has been commonplace. The cerebroplacental ratio has been investigated as a way to predict newborn outcomes. Aim and objectives: In this research, we wanted to see whether the cerebro-placental ratio may help predict perinatal outcomes in high-risk gestation with intrauterine growth restriction. Subjects and methods: This was case-control research done at Al-Hussein University Hospital's Department of Obstetrics and Gynecology; The obstetric color Doppler investigation might be examined in two groups of 100 high-risk pregnant wome: Group I - study group: 50 high risk pregnant women with IUGR and Group II - control group: 50 high risk pregnant women without IUGR. Results: CPR achieved significance at cutoff point of 1.03 for predicting IUGR with sensitivity of 87.2% and specificity of 71.6% with PPV 83% and NPV 79%. Conclusion: Intrauterine growth restriction in high-risk gestations, the cerebral-placental ratio has a significant prognostic value for perinatal outcome.

***Keywords*---**cerebro-placental ratio, growth restriction, high-risk pregnancies, intrauterine, perinatal outcome.

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Introduction

Sonographic measured fetus weight < 10th percent for gestation age is classified as intrauterine growth restriction (IUGR). [1] IUGR is "one of the most prevalent and difficult disorders in contemporary obstetrics," as per the American College of Obstetricians and Gynecologists.[2] Given the different published criteria, low detecting rate, limited preventative or therapeutic options, several related morbidities, and higher risk of perinatal death linked with IUGR, this classification is comprehensible. In maturity, suboptimal development is connected to reduced intellectual performance and disorders like hypertension and obesity.[3] Accurate identification of the genuinely growth-restricted embryo, selection of adequate fetus monitoring, and delivery time optimization are all current issues in the clinical treatment of IUGR. Despite the possibility of a difficult course, IUGR identification and antepartum monitoring may enhance outcomes.[4]

It is critical to generate and assess the confidence of proofs in the existing literature regarding the use of umbilical artery and middle cerebral artery Doppler velocimetry for non-anomalous fetus with suspect IUGR, as well as to provide guidelines for antepartum management of these gestation, especially for singleton pregnancies.[5] Although it is accepted that using general population charts vs tailored charts to define tiny for gestation age (birthweight < 10th percent for gestation age) is a significant problem, this is not the topic of this clinical opinion.6 The placenta provides the sole nutritional support for the baby. The placenta's capacity to supply appropriate nutrients to the baby is hampered with IUGR, resulting in growth difficulties.[7] Any failure to adjust to these changes leads to the formation of aberrant vascular resistance patterns, which may lead to fetal well-being being jeopardized and, eventually, IUGR.[8] The purpose of this research is to see how effective these Doppler indicators are in our settings in third trimester pregnancies. The goal of the research was to see whether the cerebro-placental ratio might help predict perinatal outcomes in high-risk gestation with intrauterine growth restriction.

Patients and Methods

From May 2021 to May 2022, case control research was done at Al-Hussein University Hospital's department of Obstetrics and Gynecology. The research was performed at Al-Hussein University Hospital's Department of Obstetrics and Gynecology. The obstetric color Doppler study could be evaluated in 100 high risk pregnant women were placed in to two groups: Group I - study group: 50 high risk pregnant women with IUGR. Group II - control group: 50 high risk pregnant women who did not have IUGR.

Inclusion Criteria of study group

Singleton with a mother who is over 20 years old. Pregnant women in their third trimester, high-risk pregnancies such as pregnancy-induced hypertension (PIH), smokers, sure of their last menstrual period (LMP) date, and IUGR assessment by sonographic predicted fetus weight less than the 10th percent for gestation age are all at hazard.

Inclusion Criteria of control group

Singleton with a mother who is over 20 years old. Pregnant women in their third trimester, high-risk pregnancies such as pregnancy-induced hypertension (PIH), smokers, sure of their last menstrual period (LMP) date, and by sonographic assessed fetus weight for gestation age, there was no IUGR diagnosis.

Exclusion Criteria for both group

Gestational diabetes mellitus, the current fetus has a congenital abnormality, multiple fetal pregnancy and unsure LMP date.

Ethical Considerations

The research was reported to the El-Hussien University Hospital's Department of Obstetrics and Gynecology's ethics committee for clearance.

Study Tools

All cases subjected to the following:

- Consent: The ethics committee decided that all participants in the trial would obtain both oral and written informed permission once the study's specifics were explained to them.
- Obstetric history: Last menstrual period date to determine weeks of gestation, singleton viable fetus and exclude gestational diabetes.
- Medical and operative history: Chronic hypertension, renal disorder, asthma, diabetes, herpes simplex infection and previous section or myomectomy
- Physical examination included: General evaluation: Vital markers: blood pressure, temp, heartbeat, and body mass index. Abdominal examination: Scar of previous operation
- All participants then ultrasound Doppler study: In the first trimester or early 2nd trimester, gestation age was determined using the accurate estimates from the last menstrual history and ultrasonography (USG) or regular fetus biometrics. Close to the transducer, Doppler velocimetry was done on the umbilical artery and the middle cerebral artery. In a free-floating loop of the mid region of the umbilical cord distant from the placental and fetus cord insertion, Doppler velocimetry of the umbilical arteries was done. Color flow Doppler was used to examine the umbilical cord, and flow velocity waveforms were acquired from each artery. The middle cerebral artery was detected in the Sylvian fissure emerging from the Circle of Willis employing color flow Doppler. A flow velocity waveform was acquired using a Doppler sample implanted in the first third of the middle cerebral artery. In the absence of fetal respiration or moving, pulsed wave Doppler ultrasonography examinations were undertaken.
- Ultrasonographic scanning: The following were assessed trans-abdominally utilizing a Medison R5 Ultrasound device with a 3.5 MHz Convex probe: Biometry of the fetus: BPD (biparietal diameter), AC (abdominal circumference), FL (femur length), GA (gestational age), F (fetal age) Weight: Doppler examinations of the following arteries were performed to measure

fetal weight: Color Doppler ultrasonography and Pulsed wave Doppler were used to assess the umbilical artery and the middle cerebral artery (MCA). All Doppler tests were conducted utilizing a Medison R5 ultrasound device with a 3.5 MHz Convex probe is used. The machine's built-in software programs computed the Doppler indices. S/D ratio (systolic/diastolic ratio) The simplest of all indicators is the systolic/diastolic ratio, which is written as S/D, where S is the peak systolic rate and D is the end diastolic rate. RI (resistance index): The disparity between the peak systolic and end diastolic velocity is examined using this index, also defined as Pourcelot's ratio, and is stated as:

RI = (S – D)/S
Pulsatility index (PI): This index is calculated as follows:
PI = (S – D)/velocity $_{mean}$

Cerebroplacental ratio (CPR) (PI ratio of the middle cerebral artery to the umbilical artery) was calculated. On the graph, the (CPR) ratio is displayed; < 5th percent was declared irregular. Figure 1

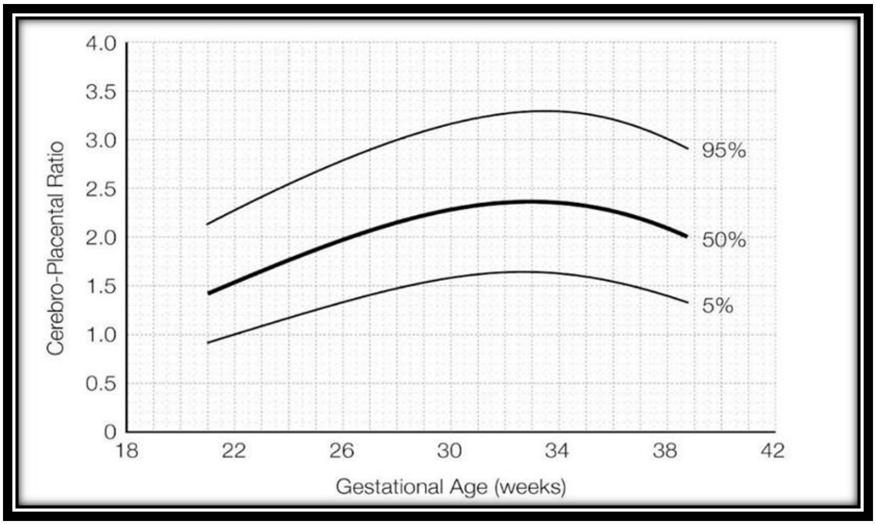

Figure 1. CPR Reference values (Ebbing et al., 2007)

Neonatal assessment

Data was collected with regard to perinatal outcome.

Included outcome variables are

Low APGAR score (1min, 5 min APGAR score less than 7).

Neonatal evaluation using the APGAR score

The Apgar score system is a valuable clinical tool for identifying infants who need resuscitation as well as assessing the success of any resuscitative efforts. Newborn Mortality and NICU Admission: When the foregoing issues were not present, the pregnancy outcome was classified as Uneventful or Favorable. The outcome of each gestation was determined by reviewing labor ward and newborn critical care unit records, when needed. Fetal discomfort, meconium aspiration, and stillbirth are all treated with CS.

Statistical Analysis

SPSS 22.0 for Windows was utilized to gather, tabulate, and statistical analysis of the all data (SPSS Inc., Chicago, IL, USA). The Shapiro Walk test was performed to determine whether the data had a normal distribution. Frequencies and relative proportions were employed to depict qualitative data. The difference between qualitative data was calculated using the Chi square test (x2) and Fisher exact as specified. For parametric data, mean± SD (standard deviation) was utilized, while for non-parametric data, median and range were used. All statistical comparisons were done utilizing a two-tailed significance level. P-values≤ 0.05 indicate a substantial variation, p<0.001 denotes a very substantial distinction, and P> 0.05 denotes a non-significant distinction.

Results

Table 1
Cerebro-placental ratio between the two studied groups

	Cases (n=50)	Controls (n=50)	T	p
CPR Mean ± SD	1.01 ± 0.215	1.1 ± 0.228	2.1	.039

This table shows that CPR was substantially reduced in subjects compared to controls. Table (1)

Table 2
Fetal biometry between the two studied groups

	Cases (n=50)	Controls (n=50)	T	p
Biparietal diameter Mean ± SD	73.62 ± 4.65	77.16 ± 3.86	2.97	.004
Abdominal circumference Mean ± SD	23.51 ± 3.92	25.32 ± 3.68	2.38	.019
Femur length Mean ± SD	54.58 ± 3.98	56.4 ± 3.49	2.43	.017

This table shows that fetus biometrics were substantially reduced in subjects compared to controls. Table (2)

Table 3
Neonatal characteristics between the two studied groups

	Cases (n=50)	Controls (n=50)	t/ x^2	p
GA (weeks) Mean ± SD	37.39 ± 1.08	37.86 ± 0.927	2.34	.022
Birth weight (kg) Mean ± SD	2.47 ± 0.845	3.08 ± 0.563	3.97	.000
Apgar at 1 min Mean ± SD	6.32 ± 2.37	7.23 ± 0.918	2.53	.012
Apgar at 5 min Mean ± SD	8.81 ± 2.75	9.7 ± 1.09	2.13	.036

In terms of neonatal features, there is a substantial variation between the groups. As a result, as compared to controls, GA, birth weight, and APGAR at 1 and 5 minutes were considerably lower in cases. Table (3)

Table 4
Correlation between CPR with other parameters in cases group

	CPR	
	r	p
GA	.300	.062
Birth weight	.371	.006
APGAR at 1 min	.332	.009
Umbilical RI	-.315	.012
Middle cerebral RI	.421	.003

This table shows that there a substantial positive connection between CPR with birth weight, APGAR at 1 min and middle cerebral artery RI while there a significant negative correlation between CPR and umbilical artery RI. Table (4)

Table 5
Neonatal outcome between the two studied groups

	Cases (n=50)	Controls (n=50)	x^2	p
Low APGAR	23 (46%)	9 (18%)	9	.003
Fetal distress	30 (60%)	17 (34%)	6.78	.009
Meconium aspiration	20 (40%)	8 (16%)	7.14	.008
Hypoxic ischemic encephalopathy	7 (14%)	1 (2%)	4.89	.027
Admitted to NICU	27 (54%)	10 (20%)	12	.000
Stillbirth	2 (4%)	0	2.04	.153
Death	5 (10%)	1 (2%)	2.84	.092

There is a substantial variance in the groups in term of low APGAR, fetal distress, meconium aspiration, hypoxic ischemic encephalopathy and NICU admission. Table (5)

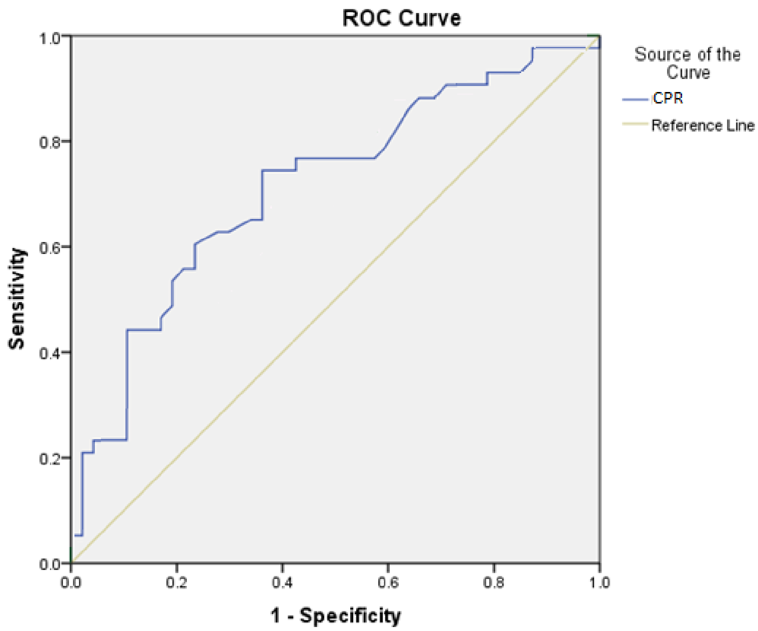

Figure 2. ROC curve of CPR as a predictive for IUGR.

Variables	AUC	S.E.	Sig.	95% Confidence Interval
CPR <1.03	.714	.055	.000*	0.607 - 0.821

Variables	Sensitivity	Specificity	PPV	NPV
CPR	73.6%	87.2%	62%	79%

CPR achieved significance at cutoff point of 1.03 for predicting IUGR with sensitivity of 87.2% and specificity of 71.6% with PPV 83% and NPV 79%. Figure.2

Table 6
Diagnostic value of CPR in predicating low APGAR

IUGR	Value	95% CI
Sensitivity	86.957%	66.411% - 97.225%
Specificity	48.148%	28.667% - 68.050%
Positive Predictive Value (PPV)	58.824%	49.006% - 67.986%
Negative Predictive Value (NPV)	81.25%	58.440% - 93.033%
LR+	1.677	1.128 - 2.493
LR-	0.271	0.088 - 0.835
Accuracy	66%	51.235% - 78.795%
Non-IUGR	Value	95% CI

Sensitivity	77.778%	39.991% - 97.186%
Specificity	70.732%	54.463% - 83.87%
Positive Predictive Value (PPV)	36.842%	24.43% - 51.281%
Negative Predictive Value (NPV)	93.548%	80.785% - 98.04%
LR+	2.657	1.473 – 4.795
LR-	0.314	0.091 - 1.084
Accuracy	72%	57.509% - 83.769%

This table shows that low CPR has accuracy of 66% in predicting low APGAR among IUGR group, while low CPR has accuracy of 72% in predicting low APGAR among non-IUGR group. Table (6)

Table 7
Diagnostic value of CPR in predicating neonatal death

IUGR	Value	95% CI
Sensitivity	100%	47.818% - 100%
Specificity	35.556%	21.686% - 51.22%
Positive Predictive Value (PPV)	14.706%	12.187% - 17.641%
Negative Predictive Value (NPV)	100%	---
LR+	1.552	1.249 - 1.928
LR-	0	---
Accuracy	42%	28.188% - 56.794%
Non-IUGR	Value	95% CI
Sensitivity	100%	2.5% - 100%
Specificity	63.265%	48.288% - 76.578%
Positive Predictive Value (PPV)	5.263%	3.705% - 7.427%
Negative Predictive Value (NPV)	100%	---
LR+	2.722	1.885 – 3.931
LR-	0	---
Accuracy	64%	49.193% - 77.084%

This table shows that low CPR has accuracy of 42% in predicting neonatal death among IUGR group, while low CPR has accuracy of 64% in predicting neonatal death among non-IUGR group. Table (7)

Discussion

In this research, we wanted to see whether the cerebro-placental ratio may help predict perinatal outcomes in high-risk gestation with intrauterine growth restriction (IUGR). This was case-control research done at Al-Hussein University Hospital's Department of Obstetrics and Gynecology; The obstetric color Doppler research might be examined in two groups of 100 high-risk pregnant women: Group I - study group: 50 high risk pregnant women with IUGR and Group II - control group: 50 high risk pregnant women without IUGR. Analysis of our findings revealed that the mean age of case group was 27.33 ± 4.28years, and in control group was 25.77 ± 4.54, and as regard BMI; in case group was 28.4 ± 4.1, and in control women was 27.53 ± 3.31, In terms of maternal age, BMI, and parity, there is no substantial variation between the groups. In accordance with what we've discovered, the research of El-Kady et al., [9] aimed to assess In high-risk gestation with intrauterine growth restriction, the cerebro-placental ratio has a role in predicting neonatal outcomes and reported Mean±SD of age in case group was 28.8±3.0, and in control group was 29.2±2.8, and there were no substantial variation between investigated groups as regard demographic characteristics.

Bharatnur et al., [10] showed that the average age of the patients in this study was 28.89 years (SD- 4.54 years). Nulliparous women made up 64.75 percent of the population. The examination of the fetus's cerebral blood flow has been an integral aspect of the evaluation of high-risk gestations. The middle cerebral artery (MCA) has been widely investigated, and Doppler records of the MCA are now routinely used in the treatment of embryos at risk of placental impairment and fetus anemia. Clinical therapy of IUGR is mostly focused on waveform analysis, specifically the pulsatility index (PI), with a low PI indicating transfer of cardiac output to the brain.[11] The MCA peak systolic velocity (PSV) is primarily utilized to predict and treat infant anemia. In a sample of IUGR fetuses, however, A higher MCA-PSV level was displayed to be a stronger predictor of perinatal death than a reduced MCA-PI6 level. Serial Doppler measures, including the MCA, are frequently required for the observation of fetuses at risk.[12]

Nearly adherent to our findings, Tolu et al., [13], The research comprised 170 expecting moms who were dealing with growth-restricted babies, with 133 having normal umbilical artery Doppler investigations and 37 having abnormal umbilical artery Doppler studies. Perinatal mortality occurred in four (3%) of normal and nine (24.3%) of abnormal umbilical artery Doppler investigations (value = 0.001). Twenty-five percent of normal umbilical arteries and twenty-four percent of dysfunctional umbilical arteries Neonatal critical care hospitalization was necessary in the Doppler study neonates (value = 0.002). When compared to growth-restricted fetuses with normal umbilical artery Doppler flow, growth-restricted babies with aberrant Doppler flow were twice more likely to need newborn intensive care unit admission, P-value 0.002, (OR = 2.059,95 percent CI 1.449–2.926).

While the study of Contro et al., [14] 53 cases and 1000 controls were obtained retrospectively. The dependent variable in the regression line was log10 UtA-PI, which was a function of both gestation age and IUGR. In both groups, UtA-PI declined with gestation age. UtA-PI was greater in the IUGR group from 20 weeks onwards, and the variance with controls grew as gestation age progressed. In fact, the UtA-PI ratio between patients and controls was 1.84 at 20 weeks, while it was 2.05. by 30 weeks. Finally, in the IUGR group, the weight at birth was negatively associated to the UtA-PI levels. Moreover, in the study done by El Ktatny et al., [15] which aimed to assess the potential utility of (CPR) at 34-37 weeks of pregnancy in identifying the perinatal prognosis of FGR pregnancies, they reported that mean UAD PI was 1.06±0.45 as it ranged from 0.47 to 2.5 and it was normal in 50% of cases and abnormal in the other 50%. The mean MCD PI was 1.33±0.38 as it ranged from 0.71 to 2 and it was abnormal in 52.5% of cases and normal in 47.5% of cases.

In the current study, the Mean ± SD of CPR in IUGR group was 1.01 ± 0.215, while in control group was 1.1 ± 0.228, CPR was significantly lower in subjects compared to controls. In accordance with our findings, the study of El-Kady et al., [9] noted that in women with IUGR, 20 (66.7%) had low CPR, while 10 (33.3%) had regular CPR. In women without IUGR, 11 (36.7%) had low CPR, while 19 (63.3%) had normal CPR. This reveals that within the IUGR study category group, Low CPR was statistically substantially more common. Ebrashy et al., [16] In 41.8 percent of preeclampsia patients without IUGR and 84.2 percent of preeclampsia cases with IUGR, the cerebro-placental ratio was abnormal. Bernstein et al., [17] showed that when compared to index values of lean body mass, fetus fat and lean body mass have distinct development profiles, and measuring fetus fat may give a more sensitive and specific technique of diagnosing aberrant fetus growth due to an accelerated growth rate in late pregnancy. In the study on our hands, as regard fetal biometry, we found that fetal biometry significant lower in subjects compared to controls.

In accordance with what we discovered, Larciprete et al., [18] reported that In IUGR fetuses, the abdominal circumference and humerus were considerably lower than in controls. The majority of the SCTT readings in the two groups were distinct. The SSFM (3.6 ± 1.1 vs. 2.6 ± 0.7 mm; P = 0.011), the AFM (5.1 ± 0.7 vs. 4 ± 1 mm; P = 0.01), the MAFM (3.5 ± 0.9 vs. 2.2 ± 0.8 cm2; P < 0.01) and MALM (2.1 ± 0.4 vs. 1.7 ± 0.5 cm2; P = 0.029) were all considerably higher in normal-developing fetuses than in those. In addition of our findings, we found that there is a substantial variation in the groups in term of neonatal characteristics. Interestingly, in our research, we demonstrated that there a substantial positive connection between CPR with birth weight, APGAR at 1 min and middle cerebral artery RI while there a substantial negative connection between CPR and umbilical artery RI. There is a substantial variation in the groups in term of low APGAR, fetal distress, meconium aspiration, hypoxic ischemic encephalopathy and NICU admission. The weight at birth of the newborns, the Apgar score at 1 and 5 minutes, the need for admittance to the NICU, the length of stay in the NICU, and perinatal mortality were all examined in Sengodan and Mathiyalagan's,[19] research.

The NPV of CPR was shown to be considerably great in a prospective cohort research done by Natthicha and Chusana,[20] and hence It might be used to identify pregnant women who would benefit from continuous fetal heart rate recording. Finally, in the present study, CPR achieved significance at cutoff point of 1.03 for predicting IUGR with sensitivity of 87.2% and specificity of 71.6% with PPV 83% and NPV 79%. The El-Kady et al., [9] study showed that to predict hypoxic ischemic encephalopathy, the low CPR in the IUGR group had 100.0 percent sensitivity, 41.7 percent specificity, 53.3 percent diagnostic accuracy, 30.0 percent PPV, and 100.0 percent NPV, whereas the low CPR in the non-IUGR group had 100.0 percent sensitivity, 65.5 percent specificity, 66.7 percent diagnosing accuracy, 9.1 percent PPV, and 100.0 percent NPV. So, Low CPR had high sensitivity and low specificity in predicting hypoxic ischemic encephalopathy in study groups.

These findings corroborated those that found a substantial positive connection between inadequate CPR and NICU admission in fetuses, with P values of 0.0006 and 0.0009, respectively. Limitations of the study, for all women, the equipment and software utilized for estimate remain the same. The study's findings may not be applicable to other centers, particularly if they lack a specialized obstetric ultrasonography center where obstetricians do prenatal ultrasound exams. Finally, other from delivery, no other appropriate intervention for IUGR pregnancies has been authorized at this time. Low CPR was formerly utilized as a measure for changes in brain or placental blood vessels to indicate poor neonatal outcome, especially in late-onset IUGR. UCR had a comparable predictive accuracy to CPR in our research, but had a stronger connection with unfavorable outcome characteristics.

Conclusion

Aside from delivery, there is currently no other effective intervention for IUGR pregnancies. Low CPR was linked to an adverse gestation outcome in our research, particularly when combined with IUGR. In high-risk gestations with intrauterine growth restriction, the cerebral-placental ratio has a significant prognostic value for perinatal outcome.

Conflict of interest: no conflicts of interest.

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