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UMBILICOCEREBRAL (UCR) VS. CEREBROPLACENTAL RATIO (CPR) IN PREDICTION OF PERINATAL OUTCOME IN HIGH-RISK PREGNANCY

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Abstract

Background: Purpose Aim of our study was to compare the prognostic value of the Umbilical-to-Cerebral ratio (UCR) directly to the Cerebroplacental ratio (CPR) in the prediction of poor perinatal outcomes in pregnancies complicated by Fetal Growth Restriction (FGR).

Methods: A retrospective study was carried out on pregnant women with either a small-for-gestational-age (SGA) fetus or that were diagnosed with FGR. Doppler measurements of the two subgroups were assessed, and the correlation between CPR, UCR, and relevant outcome parameters was evaluated by performing linear regression analysis, binary logistic analysis, and receiver operator characteristic (ROC) curves. Outcomes of interest were mode of delivery, acidosis, preterm delivery, gestational age at birth as well as birthweight and centiles.

Results: Boxplots and Scatterplots illustrated the different distribution of CPR and UCR leading to deviant correlational relationships with adverse outcome parameters. In almost all parameters examined, UCR showed a higher independent association with preterm delivery (OR: 5.85, CI 2.23–15.34), APGAR score<7 (OR: 3.52; CI 1.58–7.85) as well as weight under the 10th centile (OR: 2.04; CI 0.97–4.28) in binary logistic regression compared to CPR, which was only associated with preterm delivery (OR: 0.38; CI 0.22–0.66) and APGAR score<7 (OR: 0.27; CI 0.06–1.13). When combined with different ultrasound parameters to differentiate between SGA and FGR during pregnancy, odds ratios for UCR were highly significant compared to odds ratios for CPR (OR: 0.065, 0.168–0.901; p=0.027; OR: 0.810, 0.369–1.781; p=0.601). ROC curves plotted for CPR and UCR showed almost identical moderate prediction performance.

Conclusion: These findings indicate that the UCR should be prospectively examined as a prognostic tool while keeping the statistical characteristics and challenges of reversing the ratio in mind.

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Keywords: Cerebroplacental ratio, Umbilicocerebral ratio, Fetal Growth Restriction, Perinatal outcome, Doppler

INTRODUCTION

Ultrasound Fetal Growth Restriction (FGR) is a serious obstetric complication affecting 5–10% of pregnancies worldwide [1]. It is associated with an increased risk of adverse perinatal outcome, such as premature birth, fetal hypoxia, neonatal acidosis, low APGAR score or intrauterine death [2-3]

There are multiple causes for FGR—they can be of fetal, placental or maternal origin such as preeclampsia. Ultimately, they lead to the same endpoint: insufficient uteroplacental perfusion and restricted fetal nutrition which is reflected by abnormal Doppler parameters [4] (UA PI, mean cerebral artery (MCA), as well as an increased ductus venosus (DV) pulsatility. To estimate the optimal timing of delivery, it is essential to use prediction parameters with high sensitivity [6]. Cerebroplacental ratio (CPR), the ratio MCA PI/UA PI is said to reflect alterations in placental or fetal blood flow more sensitively than the UA PI or MCA PI alone [7,8].

However, recent literature indicates variable accuracy for predicting adverse outcomes with CPR, making its clinical utility controversial [9-11]. Latest publications suggest that the umbilicocerebral ratio (UCR), which is the inversion of the CPR, is a more sensitive predictor for various adverse perinatal outcome parameters [12-14].

Rationale: To the best of our knowledge, most publications report the predictive value of the CPR rather than the UCR and so far studies directly comparing the predictive potential of poor perinatal outcomes in FGR pregnancies are rare. Latest publications suggest that the umbilicocerebral ratio (UCR), which is the inversion of the CPR, is a more sensitive predictor for various adverse perinatal outcome parameters.

Aims and objectives: To compare prognostic value of UCR with CPR in predicting adverse neonatal outcomes in pregnancies complicated by FGR.

MATERIALS AND METHODS

Study Design: Single Center Retrospective Study
Study Centre: Index Medical College Hospital & Research Centre, Indore
Duration of Study: 1 Years from Approval by Ethics Committee
Sample Size: 50

Statistical analysis was done using SPSS 21.0 software. The correlation between CPR, UCR and relevant outcome parameters was evaluated by performing linear regression analysis, binary logistic analysis and receiver operator characteristic (ROC) curves. A p value <0.05 was considered statistically significant

Inclusion criteria: Only singleton SGA and FGR pregnancy with maternal age more then 18yr were included in study: Pregnant patient between 28 and 48weeks of gestation with complete

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follow-up were included in this study
Exclusion Criteria: Maternal age below 18years were excluded. Major fetal malformation or aneuploidy, as well as fetal infection were excluded from the study

RESULTS

23 (46%) pregnancies affected by FGR and 27 (54%) SGA pregnancies were included in our study. Of all eligible cases, 4 cases of stillbirth, 2 neonatal deaths and 3 terminations of pregnancy were excluded, leaving 50 patients for final analysis.

Table 1: Maternal demographics stratified by FGR and SGA

Variables	FGR n=23 (46%)	SGA n=27 (54%)	p
Age of mother (years) median	29 [26-34]	30 [26-34]	0.656
GAscan (weeks) median	32.5 [29.7-35.6]	34.6 [31.2-37.3]	<0.001 * Significant
Diabetes (maternal)	2 (8.6%)	1 (3.7%)	0.021
Smoker	1 (4.3%)	2 (7.4%)	0.854
Hypertension, pre-eclampsia (maternal)	2 (8.7%)	1 (3.7%)	0.356
Mode of delivery			<0.001* Significant
Spontaneous vaginal	4 (17.4%)	14 (51.8%)	
Instrumental	1 (4.3%)	1 (3.7%)	
Cesarean section	19 (82.6%)	12 (44.4%)	
Premature birth (<37 week)	15 (65.2%)	6 (22.2%)	<0.001* Significant

Statistically significant p< 0.05

Table 2: Ultrasound characteristics stratified by FGR and SGA

Variables	FGR n=23 (46%)	SGA n=27 (54%)	p
GA at delivery (weeks) median	34.6 [31.5-37.4]	38.0 [37.1-39.5]	<0.001* Significant
UA PI median	1.22 [1.02-1.52]	1.02 [0.89-1.14]	<0.001* Significant
MCA PI median	1.48 [1.26-1.79]	1.65 [1.40-1.94]	0.001* Significant
UCR median	0.84 [0.60-1.23]	0.64 [0.53-0.74]	<0.001* Significant
CPR median	1.16 [0.82-1.66]	1.60 [1.35-1.90]	<0.001* Significant
MCA PSV median	50.4 [42.5-56.9]	53.2 [45.3-59.3]	0.08

Statistically significant p< 0.05

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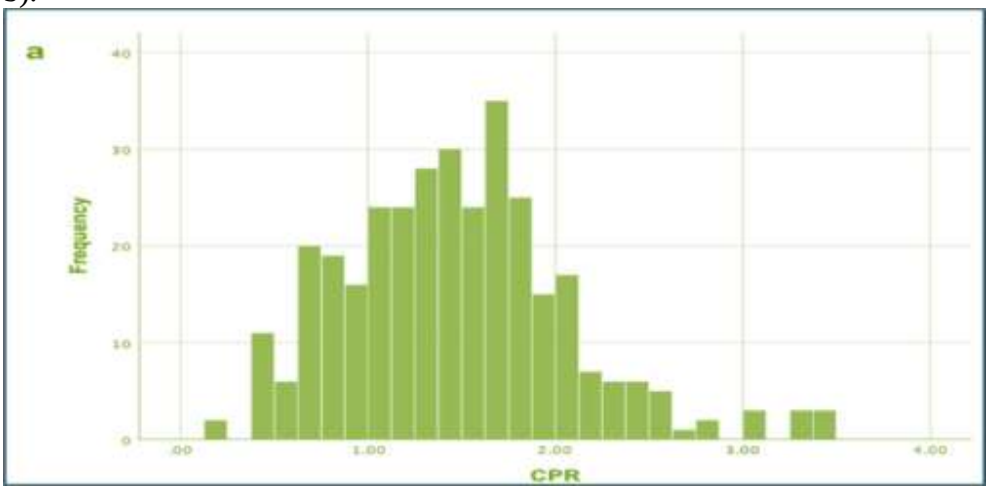
Table 3: Intrapartun outcomes stratified by FGR and SGA

Variables	FGR n=23 (46%)	SGA n=27 (54%)	p
APGAR after 5 min median	9 [8-10]	9 [9-10]	**<0.001*Significant**
Birth weight centile			
<3. Centile	10 (43.5%)	9 (33.3%)	0.108
< 10. Centile	13 (56.5%)	18 (66.7%)	0.310
Umbilical cord pH median	7.32 [7.27-7.34]	7.27 [7.25-7.34]	0.081
Birth weight (g) median	1785 [1230-2290]	2555 [2278-2805]	**<0.001*Significant**

Statistically significant p <0.05

Pregnancies affected by FGR presented a lower median CPR and conversely higher median UCR (1.17 vs. 1.62; p<0.001; 0.86 vs. 0.62; p<0.001, respectively) which can be traced back to FGR being defined by abnormal Doppler parameters. Neither ratio showed a normal distribution within either group according to the Kolmogorov–Smirnov and Shapiro–Wilk-tests.

When comparing the distributions of CPR and UCR, CPR tended towards a more symmetric distribution (Fig. a), while the values of UCR were asymmetrical with a skew to the right (Fig. b).



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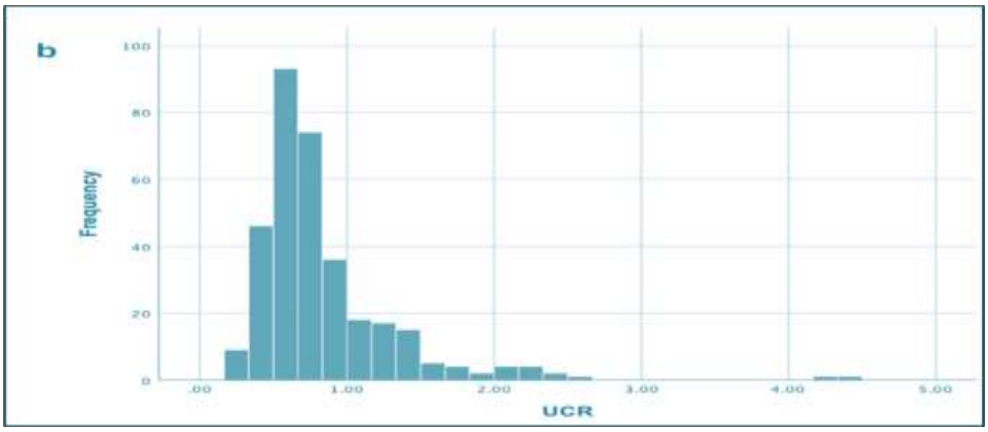

Figure 1: Boxplots of UCR and CPR show the distribution of the ratios (SI 1): UCR shows a more distinctive discrimination of abnormal values (> 1) with outliers becoming more apparent.

Table 4: Results of binary logistic regression analysis for fgr pregnancies

	Odds ratio (CI 95%)		p value	
	CPR	**UCR**	**CPR**	**UCR**
Premature birth <37	0.386 (0.224-0.666)	5,857 (2.235-15.347)	<0.001*	<0.001*
Premature birth <30	0.293 (0.119-0.721)	2,908 (1.468-5.761)	0.002*	0.001*
APGAR <7	0.273 (0.066-1.134)	3,529 (1.587-7.851)	0.040*	0.001*
Acidosis (pH<7.2)	1.142 (0.419-3.114)	1,604 (0.681-3.782)	0.799	0.327
Weight < 10th centile	0.654 (0.401-1.064)	2,047 (0.979-4.280)	0.086	0.035*
Cesarean section	0.571 (0.336-0.972)	2,964 (1.091-8.051)	0.042	0.014*

Statistically significant p <0.05

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Table 5: Logistic regression analysis for determination of FGR v/s SGA by combining CPR and UCR with different ultrasound parameters

	Odds ratio (CI 95%)	P value
UCR	0.065 (0.168-0.901)	0.027*
UA PI	0.065 (0.019-0.223)	<0.001*
MCA PI	1.194 (0.592-2.405)	0.620
MCA PSV	0.993 (0.966-1.021)	0.620
GA_scan	1.053 (0.961-1.154)	0.268
CPR	0.810 (0.369-1.781)	0.601
UA PI	0.031 (0.007-0.142)	<0.001*
MCA PI	1.991 (0.783-5.062)	0.148
MCA PSV	0.992 (0.965-1.019)	0.547
GA_scan	1.065 (0.973-1.167)	0.171

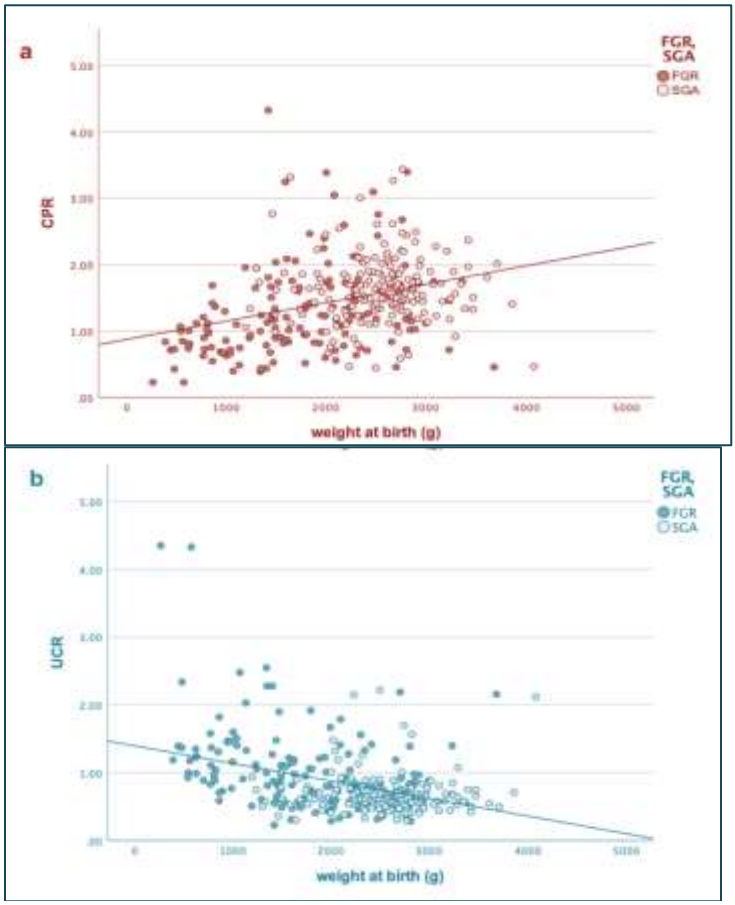

Figure 2: Scatter Plot of UCR and CPR by birth weight (g) separated by FGR and SGA.

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CPR presents a moderate non-linear relationship with weight at birth, b UCR shows a stronger linear relationship with birth weight

Table 6: Receiver operating characteristic curve (ROC) analysis: AUC, CPR and UCR screening efficacy for adverse outcome parameters

Outcome	CPR				UCR			
	AUC	Sens	Spec	Cut-off	AUC	Sens	Spec	Cut-off
Premature birth <37	0.701*	0.557	0.8	1.075	0.702*	0.604	0.745	0.875
Premature birth <30	0.723*	0.828	0.598	1.125	0.722*	0.828	0.598	0.885
APGAR <7	0.708*	0.727	0.693	0.925	0.708*	0.727	0.693	1.08
Acidosis <7.2	0.461	0.25	0.889	0.67	0.460	0.25	0.889	1.495
centile < 10	0.597	0.518	0.706	1.095	0.597	0.518	0.706	0.915
centile <3	0.538	0.456	0.667	1.005	0.538	0.456	0.667	0.995
MOD (obstetric intervention)	0.632	0.538	0.724	1.155	0.632	0.538	0.724	0.865
CS	0.651	0.547	0.727	1.155	0.651	0.547	0.727	0.865

Highest predictive accuracies of CPR nd UCR

Table 7: Multivariate logistic regression analysis for prediction of adverse outcome by combining different parameters

	Parameters#	p value	OR (CI 95%)
Premature birth <37	GA_scan	0.000*	41.195 (11.89-142.72)
	UA PI	0.000*	0.824 (0.763-0.891)
Premature birth < 30	MCA PSV	0.003*	1.142 (1.047-1.244)
	UA PI	0.00*	21.237 (4.354-103.6)
	GA_scan	0.00*	0.278 (0.165-0.468)
Cesarean section	UA PI	0.000*	14,765 (5.251-41.516)
APGAR <7	UA PI	0.038*	2.21 (1.046-4.667)
	GA_scan	0.012*	0.838 (0.730-0.962)
Weight < 10th	UA PI	0.001*	4.6 (1.904-11.113)
centile	GA_scan	0.000*	1.156 (1.081-1.236)
Weight < 3rd centile	MCA PSV	0.011*	0.973 (0.954-0.994)
	UA PI	0.041*	2.313 (1.036-5.166)
	UCR	0.003*	0.325 (0.153-0.688)

Parameters that showed highest predictive values for adverse outcome in forward stepwise analysis * Significant as P<0.05

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DISCUSSION

The results of our study demonstrated that while UCR and CPR reach similar prognostic accuracy concerning overall outcome, using UCR as a model shows better correlations with negative outcome parameters.

In our analysis, UCR showed a higher association with outcome parameters as well as more noticeable p values for most tests performed. When graphically visualizing both ratios, the presentation of UCR confirmed its ability to better model an association with high-risk pregnancies. Our main test results for the predictive accuracy of CPR were consistent with the values previously published:

CPR was associated with adverse pregnancy outcomes including preterm delivery and APGAR score below 7 [2,8,11,16,17]. CPR showed poor results in the prediction of a low umbilical cord pH. [10,11].
Our ROC analysis showed similar AUC results for adverse neonatal outcome, our cut-of values (< 1.076) were similar to the values published in recent literature (< 1.08) [10,11].

In a direct comparison of CPR and UCR, the statistical analysis of our study demonstrated that both ratios were equally associated with various outcome parameters and reached similar results regarding sensitivity and specificity in ROC analysis.

However, using the model of UCR as a prognostic marker seemed to be more compatible in the context of predicting an adverse neonatal outcome.

Consistent with our own findings, it becomes evident that with increased alteration of fetal Doppler indices the effect on the UCR grows exponentially, allowing it to distinguish the collective with a negative outcome.
Abnormal outliers become more apparent and differentiate the extent of abnormality more clearly. This may also have an impact on the different correlational relationships of UCR and CPR with numeric variables as illustrated in the scatterplots.

UCR shows a better linear correlation with parameters measured to determine a negative outcome, which makes it a better ft for prognostic assessment leading to lower p values in statistical tests.

In accordance with a previous study done by Di Mascio D et al. that deals with a low-risk collective, we believe neither ratio to be adequate as sole screening marker, but that CPR and UCR only gain clinical relevance when combined with other parameters under specific conditions indicating a high-risk collective such as FGR—where minimization of very poor outcomes without significantly increasing the rate of cesarean sections and admissions to NICU should be the primary objective. It is important to consider these limitations when implementing CPR and UCR into clinical practice.

Our research showed good results when PI UA and GA scan are combined for the prediction of adverse neonatal outcomes. We therefore propose establishing these two parameters as essential standard prediction markers for pregnancies at risk and to add other parameters such as UCR or

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CPR for further diagnosis.

CONCLUSION :

UCR offers an acceptable alternative to the Doppler parameters and ratios used in clinical practice since it is more sensitive than CPR and is a superior discriminator of Doppler values in abnormal range.
Adding UA PI and GA scan to logistic regression analysis increased the prognostic accuracy regarding negative outcomes. These findings indicate that the UCR should be prospectively examined as a prognostic tool, while keeping the statistical characteristics and challenges of reversing the ratio in mind

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