ORIGINAL RESEARCH

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Correlation Between Fetal Middle Cerebral Artery and Umbilical Artery Doppler Ratio at 38-40 weeks of Gestation with Fetal Distress and Adverse Perinatal Outcome

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ABSTRACT

Background and Objectives: The study aimed to determine the correlation between fetal middle cerebral artery and umbilical artery doppler ratio with fetal distress at 38-40weeks of gestation.

Materials and Methods: In this prospective observational study, 100 pregnant patients between 38-40 weeks of gestational age with no complications were selected from April 2020 to October 2021.They were subjected to Doppler ultrasonography and all the indices such as Middle cerebral artery, Umbilical artery, and Cerebroplacental (C/U) ratio were noted. The patients were followed till delivery and monitored for maternal, fetal, and neonatal outcomes.

Results: The mean cerebroplacental ratio was 1.33. there was a significant association between the low C/U ratio with caesarean section and poor perinatal outcome in terms of APGAR <7 at 5minutes, meconium liquor, respiratory distress syndrome, neonatal death, and NICU admission. There was a significant association of low middle cerebral artery PI (p=0.0004), high umbilical artery PI (P=<0.0001), and low C/U ratio (p=<0.0001) with fetal distress. The C/U ratio cut-off ≤1.33 led to sensitivity, specificity, PPV, and NPV of 82.86, 78.46, 67.4, and 89.5%, respectively. There was a linear relationship between birth weight (p=0.10) and postdelivery cord pH(<0.0001) with a C/U ratio. Hence, although sensitivity of cerebroplacental ratio and umbilical artery PI are comparable, the specificity of cerebroplacental ratio is higher than that of umbilical artery PI.

Conclusion: It may be concluded that the Cerebroplacental ratio is a better predictor of fetal distress and adverse perinatal outcome than the individual pulsatility index of middle cerebral artery and umbilical artery taken alone.

Keywords: Cerebroplacental ratio, Colour doppler, Pulsatility Index, Umbilical artery, Middle cerebral artery

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INTRODUCTION

Fetal hypoxia is one of the major causes of high perinatal morbidity and mortality rates.[1–3] During fetal life, oxygen supply is entirely dependent on maternal respiration and circulation, placental perfusion, gas exchange across the placenta, and umbilical and fetal circulations. Complications occurring at any of these levels may result in decreased oxygen concentration in fetal arterial blood (hypoxemia) and ultimately in the tissues (hypoxia).[4]

In fetal hypoxemia, there is central redistribution of blood flow allowing increased blood flow to the brain, heart, and adrenals and decreased blood flow to the peripheral and placental circulations, known as the "Brain-sparing effect". There are different prenatal tests to determine the optimal

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fetal oxygen supply such as biophysical profile, amniotic fluid index (AFI), non-stress test (NST), contraction stress test (CST), and Doppler assessment of umbilical and middle cerebral arteries.[5-7]

Ultrasonographic fetal assessment with bi-dimensional colour doppler would help to diagnose structural anomalies, rhythm abnormalities, and disordered fetal circulation.[8]

Colour doppler ultrasound is used to assess the flow in the umbilical artery (UA) and fetal middle cerebral artery (MCA). Hence, by knowing the modifiable risk factors affecting fetal distress is of great importance in deciding the optimum time and mode of delivery and thus improving the perinatal outcome.

The pulsatility index (PI) is used to calculate the cerebroplacental ratio which is an indicator for fetal oxygenation.[9-11]

The cerebroplacental ratio (C/U) is calculated as the ratio of pulsatility index of MCA to UA doppler and has been hypothesized to be more accurate than its components.

MATERIALS AND METHODS

A prospective observational study was conducted in a tertiary care hospital over a period of one year after taking due permission from the Institutional Ethical Committee (IEC).

100 pregnant females between 38 to 40 weeks of gestational age over a period of one year were included. Written informed consent was taken from all the patients. A detailed history and examination with investigations were done as per standard hospital protocol.

The inclusion criteria were women with singleton pregnancy at 38-40 weeks of gestational age without any complications. Those patients refusing to give consent or in labor or with any chromosomal and structural disorders were excluded from the study. All women were subjected to Doppler ultrasonography at 38-40weeks of gestational age and flow velocity waveforms were obtained.

In the Colour doppler ultrasonography, all the indices were noted. The umbilical artery waveforms was detected at free loop part of cord and middle cerebral artery was determined at a transverse section of fetal head at the level of lesser wing of sphenoid bone. All women were followed up till delivery.

The cerebroplacental ratio (C/U) which was obtained was then compared with adverse perinatal outcome especially fetal hypoxia (fetal distress).

All the women were monitored for outcomes in the form of non-reactive NST, mode of delivery (normal vaginal delivery-induced/spontaneous/ instrumental delivery/ caesarean section)

The fetal outcomes were recorded in terms of presence of meconium stained liquor, intrauterine fetal growth retardation (IUGR) and perinatal death and neonatal outcomes such as APGAR score of less than 7 at 5 minutes, neonatal intensive care admission, acidosis on blood gas analysis, birth weight less than 10th percentile, need for resuscitation at birth were recorded.

STATISTICAL ANALYSIS

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, version 21.0.

The association of the variables which were quantitative were analyzed using the Independent t-test.

The association of the variables which were qualitative were analyzed using the Chi-Square test.

RESULTS

In our study, the incidence of primigravida (60%) was more than that of multigravida (40%), shown in **Table 1**. The results of color doppler are demonstrated in **Table 2**

The incidence of Reactive NST(83%) was more than that of Non-Reactive NST(17%). The mode of delivery in our study was more by normal deliveries(60%) than by LSCS (40%). Among normal deliveries, induction was required in 36% than by spontaneous progression(24%).

Table 1. Distribution of parity of study subjects

Parity	Frequency	Percentage
Primi	60	60.00%
Multi	40	40.00%
Total	100	100.00%

Table 2. Colour Doppler Results

Doppler Findings	Mean	SD	SD
Middle Cerebral Artery PI	1.38	0.3	0.7-2.3
Umblical Artery PI	1.04	0.3	0.65-2.2
C/U Ratio	1.43	0.51	0.39-2.8

Table 3. Distribution of the fetal outcome of study subjects

Fetal Outcome	Frequency	Percentage
Birth Weight (kg)		
<10th Percentile	24	24.00%
>10th Percentile	76	76.00%
APGAR Score at 1 minute		
<7	35	35.00%
>=7	65	65.00%
APGAR Score at 5 minutes		
<7	4	4.00%
>=7	96	96.00%
NICU requirement		
No	62	62.00%
Yes	38	38.00%

In the newborn, immediate fetal outcomes were studied by birth weight and APGAR scores at 1 minute and 5 minutes. 24 babies had birth weight less than 10 percentile. APGAR score was less than 7 at 1 minute in 35 babies and 4 babies had an APGAR score of less than 7 at 5minutes **(Table 3).**

NICU admission was required in 38 babies. Fetal complications like meconium-stained liquor (34), sepsis (1), respiratory distress (6) were seen. 10 babies required assisted resuscitation in the form of assisted respiration (8) and extensive support in the form of Intubation and mechanical ventilation or continuous positive airway pressure (CPAP) support (2). There was no case of necrotizing enterocolitis and neonatal intracranial abnormalities observed in our study.

Table 4. Association of C/U ratio with complications

Complication	Mean	SD	Range	P Value
Mode of delivery				
LSCS(n=40)	1.26	0.48	0.41-2.65	0.005*
Normal delivery (n=60)	1.55	0.49	0.39-2.8	
APGAR Score at 5 minutes				
<7(n=4)	0.76	0.33	0.41-1.07	0.006*
>=7(n=96)	1.46	0.49	0.39-2.8	
NICU admission				
Not required(n=62)	1.64	0.42	0.39-2.8	<.0001
Required(n=38)	1.09	0.45	0.41-2.62	
Meconium Liquor				
No(n=66)	1.65	0.41	0.39-2.8	<.0001
Yes(n=6)	1.01	0.4	0.41-2.03	
Respiratory distress syndrome				
No(n=94)	1.47	0.5	0.39-2.8	0.002
Yes(n=6)	0.81	0.2	0.56-1.07	
Neonatal death				
No(n-98)	1.45	0.49	0.39-2.8	0.007
Yes(n=2)	0.48	0.1	0.41-0.56	
NST				
Non-reactive(n=17)	1.04	0.37	0.53-1.75	0.0003
Reactive(n=83)	1.51	0.5	0.39-2.8	

Table 5. Receiver operating characteristic curve of doppler findings for predicting adverse outcome

Variables	MCA PI	UA PI	C/U ratio
Area under the ROC curve (AUC)	0.733	0.802	0.841
Standard Error	0.053	0.0445	0.0429
95% Confidence interval	0.635 to 0.816	0.711 to 0.875	0.754 to 0.906
P Value	<0.00001	<0.0001	<0.0001
Cut off	≤1.3	>0.97	≤1.33
Sensitivity (95% CI)	80%(63.1-91.6%)	82.86%(66.4 - 93.4%)	82.6%(66.4 -93.4)
Specificity(95% CI)	56.92%(44.0 - 69.2%)	70.77%(58.2 - 81.4%)	78.46%(66.5 - 87.7%)
PPV(95% CI)	50%(36.3-63.7%)	60.4%(45.3 - 74.2%)	67.4%(51.5 - 80.9%)
NPV(95% CI)	84.1%(69.9 - 93.4%)	88.5%(76.6 - 95.6%)	89.5%(78.5 - 96.0%)
Diagnostic accuracy	65.00%	75.00%	80.00%

Table 4 shows significant association between the low fetal MCA and UA Doppler ratio with caesarean section and poor perinatal outcome in terms of APGAR <7 at 5minutes, meconium liquor, respiratory distress syndrome, neonatal death, and NICU admission.

The C/U ratio cut-off ≤1.33 led to sensitivity, specificity, PPV, and NPV of 82.86, 78.46, 67.4, and 89.5%, respectively **(Table 5).**

In our study, fetal distress was present in 12%. Among that, 11% was seen in patients with a C/U ratio ≤1.33 and 1% in patients with a C/U ratio>1.33

The study showed significant association of the C/U ratio with fetal distress (p=0.0002) **(Table 6).**

In the present study, adverse fetal outcomes were seen in 35% of babies. Out of 100 patients, MCA PI was low (≤1.3)

Table 6. Association of C/U ratio with fetal distress

C/U ratio	Fetal distress ab-sent(n=88)	Fetal distress present(n=12)	Total	P Value
≤1.33	30 (73.17%)	11 (26.83%)	41 (100%)	0.0002
>1.33	58 (98.31%)	1 (1.69%)	59 (100%)	
Total	88 (88%)	12 (12%)	100 (100%)	

Table 7. Association of doppler findings with the outcomes

Doppler Findings	Adverse (n=35)	Uneverful (n=65)	Total	P Value
MCA PI				
>1.3	7(15.91%)	37 (84.09%)	44 (100%)	0.0004
≤1.3	28 (50%)	28 (50%)	56 (100%)	
Mean	1.22	1.46	1.38	0.0004
SD	0.29	0.34	0.34	
UA PI				
≤0.97	6(11.54%)	46(88.46%)	52(100%)	<.0001
>0.97	29(60.42%)	19 (39.58%)	48 (100%)	
Mean	1.23	0.94	1.04	<.0001
SD	0.32	0.24	0.3	
C/U Ratio				
>1.33	7(11.86%)	52(88.14%)	59(100%)	<.0001
≤1.33	28(68.29%)	13(31.71%)	41 (100%)	
Mean	1.06	1.63	1.43	<.0001
SD	0.35	0.47	0.51	

in 56% of patients, out of which 50% (n=28) had an adverse perinatal outcome. UA PI was raised (>0.97) in 48% of patients, out of which 60% (n=29) had adverse perinatal outcomes. C/U ratio was low (≤1.33) in 41% of patients, out of which 68% (n=28) had an adverse perinatal outcome. Hence, in our study, all three low middle cerebral artery PI (p=0.0004), high umbilical artery PI (P=<0.0001), and low C/U ratio (p=<0.0001) were statistically significant **(Table 7).**

There was a linear relationship seen between birth weight (p=0.10) and postdelivery cord pH(<0.0001) with a C/U ratio **(Table 8).**

In the present study, the cut off of the C/U ratio obtained was 1.33 **[Figure 1]**. Comparison of results of Sensitivity, Specificity, Positive predictive value(PPV), Negative predictive value (NPV) of C/U ratio in predicting adverse perinatal outcome with other studies are shown in **Table 9.**

DISCUSSION

Fetal hypoxia is one of the major causes of high perinatal morbidity and mortality rates.[1–3] The doppler ultrasonography

Table 8. Correlation of C/U ratio with birth weight, NICU care duration, postdelivery cord pH

Variables	Birth weight(kg)	NICU care (in days)	Post Delivery cord pH
C/U Ratio			
Correlation coefficient	0.255	-0.476	0.523
P Value	0.010	0.003	<0.0001

Table 9. Comparison of Cerebroplacental ratio (C/U) in predicting the adverse perinatal outcome

	Present study	Gramellini D et al[12]	BN Lakhkar et al[13]	Bano et al[14]
Sensitivity	82.86%	68%	47.2%	83.3%
Specificity	78.46%	98.4%	86.3%	100%
PPV	67.4%	94.4%	85%	100%
NPV	89.5%	88%	50%	94.3%

can give access to fetal circulation. The integration of flow velocity waveforms obtained from colour doppler may help us to know the cause of fetal hypoxia. Thus, knowing the modifiable risk factors affecting fetal distress is of great importance in deciding the optimum time and mode of delivery and thus improving the perinatal outcome.

The aim of this study was to study the correlation between fetal middle cerebral artery and umbilical artery doppler ratio with fetal distress at 38-40weeks of gestation.

In our study, 12% had fetal distress and among that C/U ratio was low in 11%. The C/U ratio cut-off point was ≤1.33 with sensitivity, specificity, PPV, and NPV of 82.86, 78.46, 67.4, and 89.5%, respectively.

In our study, the incidence of adverse perinatal outcomes was 35% which was consistent with the study of Bligh LN et al[15] (38.3%).

In our study, neonatal outcomes were comparable to the study of Gaikwad PR et al[16] in terms of NICU admission

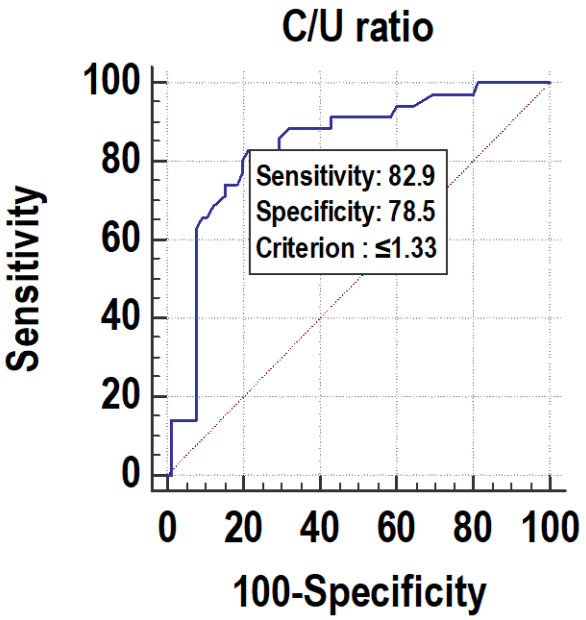

Figure 1. Receiver operating characteristic curve of C/U ratio for predicting adverse outcome

(38% vs 40%), meconium liquor (34% vs 45.9%), birth weight less than 10 percentile (24% vs 34%) and neonatal death (2% vs 8%).

The sensitivity of the UA PI in the present study was 82.86%. UA flow velocity waveforms tells about the placental circulation. In presence of placental insufficiency, changes are seen in feto-placental circulation, hence diastolic flow decreases, and PI increases.

According to Gramellini D et al.[12] the sensitivity of UA PI in predicting the adverse perinatal outcome was 65.5% whereas K W Fong et al.[17] showed sensitivity of UA PI was 82.1%. The study by Narula et al.[18] reported a sensitivity of 94% for combined indices of the umbilical artery whereas the study by Bano et al.[14] showed that the sensitivity of UA PI in predicting the perinatal outcome was 79.2%

In our study, the sensitivity of MCA PI was 80%. The MCA carries more than 80% of cerebral blood flow.[19] In fetal hypoxemia, brain-sparing effect occurs and plays a major role in fetal adaptation to oxygen deprivation.[20-22] wherein after this there will be an increase in end-diastolic flow which causes a decrease in PI.

The study by Gramellini D et al.[12] showed that the sensitivity of MCA PI in predicting the perinatal outcome was 54.4% whereas K W Fong et al[17] showed that the sensitivity of MCA PI was 72.4%.

The sensitivity and specificity of the C/U ratio in predicting perinatal outcome in the present study were 82.86% and 78.46% respectively. In the present study, the cut off of the C/U ratio obtained was 1.33. The difference can be due to smaller study subjects and differences in perinatal mortality and morbidity rates in Western countries compared to India.

Our study results were confirmed by the study of Gramellini D et al,[12] the C/U ratio is a better predictor than that of Umbilical artery PI and Middle cerebral artery PI individually.

STRENGTHS AND LIMITATIONS

The strengths of our study is that it is prospective study and the participant has no additional risk factors for a poor outcome. A compressive doppler assessment were performed and along with fetal doppler indices, expected fetal weight, biophysical score, cord blood gas measurement and NST were also taken, hence we could have a better correlation.

The limitations were doppler assessment results were not blinded, giving rise to the possibility that this knowledge could have influenced subsequent clinical intervention and treatment effect however intervention in the form of induction was only taken according to the protocol of the hospital and not on the basis of C/U ratio.

Another possible limitation of our study could be relatively small number of participants.

CONCLUSION

Cerebroplacental ratio (C/U) gives us information about both the placental insufficiency as well as the fetal response to the resulting hypoxia.

Therefore, it can be said that the Cerebroplacental ratio is a better predictor of fetal distress and adverse perinatal outcome than the individual pulsatility index of middle cerebral artery and umbilical artery taken alone.

Hence, although sensitivity of cerebroplacental ratio and umbilical artery PI are comparable, the specificity of cerebroplacental ratio is higher than that of umbilical artery PI.

It can be concluded that the Cerebroplacental ratio is a better predictor of feal distress and adverse perinatal outcomes.

END NOTE

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