

Usefulness of Color Doppler evaluation of Cerebral –Umbilical pulsatility index ratio in the diagnosis of clinically suspected IUGR

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Abstract

Background :Intrauterine growth retardation (IUGR) is defined as growth at the 10th or less percentile for weight of all fetuses at the gestational age. It also refers to a condition in which a fetus is unable to achieve its genetically determined potential size.It has long been recognized that abnormal fetoplacental and uteroplacental development and function is associated with Intrauterine growth retardation.Ultrasonography with doppler velocimetry is a rapid , noninvasive and has provided a new efficient tool for this purpose.

Objective:To evaluate the pulsatility index (PI) of the umbilical artery(UA) and that of the MiddleCerebral Artery(MCA), as well as the ratio of the MCA PI to the UA PI (C/U ratio)in the diagnosis of clinically suspected IUGR .

Methods:This prospective study was carried out in the department of Obstetrics and Gynaecology of Chattogram Maa-O-Shishu Hospital Medical College within a period of June2019 –December 2019 on 50 patients aged between 16-35 years who were clinically suspected as cases of IUGR or provisionally USG diagnosed cases of IUGR.

Results:The highest incidence of IUGR was found in the age group between 21-15 years. The mean gestational age at birth was 36.02 ± 1.83 weeks. According to cerebro –umbilical pulsatility index(PI) value, thirty -three cases (66%) were diagnosed as abnormal (C/U ratio <1.08) and 17 cases (34%) as normal flow pattern. Mean gestational age at birth was $35.63 \pm$ weeks in case of abnormal cerebro-umbilical (C/U) ratio group while the mean birth weight was 1.65 ± 0.307 kg in .Perinatal findings showed that 34were small for gestational age (SGA) and 16 had normal birth weight. UA PI and MCA PI show sensitivity of 37.5% and 50% and specificity of 83.33% and 85% respectively. The validity tests such as sensitivity, specificity, positive predictive value and negative value and diagnostic accuracy of Cerebral –Umbilical pulsatility ratio C/U(PI) for diagnosis of IUGR were 91%,87%,93%,82% and 90% respectively.

Conclusion: The sensitivity and specificity of Umbilical artery PI and Middle cerebral artery pulsatility index vary in diagnosing IUGR and predicting Fetal compromise. Among the Doppler indices, the C/U ratio is an useful modality in diagnosing IUGR and adverse perinatal outcome than the UA PI and MCA PI alone. Moreover, it also may be helpful to determine the optimum time of delivery in complicated pregnancies.

Key Words: Umbilical Artery, Middle Cerebral Artery, Cerebro-Umbilical Pulsatility index, IUGR.

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I. Introduction:

Intrauterine growth retardation is a syndrome characterized by failure of the fetus to reach its normal growth potential. It is the second leading cause of perinatal death and is associated with significant morbidity including increased rates of meconium aspiration, hypoglycemia, respiratory distress syndrome, intrapartum asphyxia, developmental delay and still birth(1)

The average incidence of IUGR is nearly 8% in the general population and 6%-30% in developing countries. Factors like placental insufficiency, pre-eclampsia, chronic hypertension, cardiovascular disease, diabetes, renal disease, anaemia 75%-80%, maternal condition not associated with placental insufficiency such as severe malnutrition, smoking, Alcohol ingestion, Haemoglobinopathies 5%, Fetal chromosomal abnormalities 5%, Multifactorial fetal abnormalities 2%-3%, fetal infections 1%(2). 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 vasculature. (3). An inability to adapt to these changes result in the development of abnormal vascular resistance patterns, which might consecutively lead to the compromise of fetal well-being and ultimately IUGR (4). Doppler velocimetry is a rapid non-invasive test that provides valuable information about the hemodynamic situation of the fetus (5). In fetal growth retardation the umbilical and intracranial arteries are the vessels most commonly examined (6). There is significant association between the Doppler waveform analysis and clinical outcome. The availability of Doppler studies led to better obstetric decision making(7). The present study was aimed to correlate clinical as well as Doppler findings in IUGR to decide the optimum time of intervention. Our objective was to evaluate the usefulness of the pulsatility index (PI) of the umbilical artery and that of the middle cerebral artery (MCA), as well as the ratio of the MCA PI to the UA PI (C/U) ratio, or CPR (Cerebro-umbilical pulsatility index ratio) in the diagnosis of IUGR and to see its adverse perinatal outcome.

Methods:

This prospective observational study was conducted in Chattagram Maa-O-Shishu Hospital Medical College from June 2019 to December 2019. The study included 50 women with singleton IUGR pregnancy after 28 weeks. Informed written consent was taken and proper counseling was done in accordance with the inclusion criteria. Ethical approval was taken from the ethical committee of the institute beforehand.

Inclusion Criteria:

- Known date of last menstrual period.
- Suspected IUGR with pregnancy induced hypertension (PIH), Oligohydramnios, anaemia and constitutional.
- Clinical discrepancy of fundal height being less than the period of gestation by four weeks or more.
- Ultrasonography showing fetal weight less than 10th percentile of their gestational age based on femur length (FL), biparietal diameter (BPD) and abdominal circumference (AC)
- Normal fetal anatomy.

Exclusion Criteria:

Following women were excluded from the study:

- Women with a congenital malformation in the present fetus.
- A multifetal pregnancy
- Mistaken dates.

Detailed history was taken and clinical examination was recorded in all the cases. Gestational age was determined either from the last menstrual period if certain or from the earliest ultrasonography in the first trimester (8).

The fetal biometry included assessment of biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL) as well as fetal weight was estimated by Hadlock formula. Amniotic fluid index (AFI) was calculated by adding the vertical depth of the largest pocket in each of the four quadrants. The middle cerebral artery and the umbilical artery were identified and flow velocity were obtained. The PI of the umbilical artery and the middle cerebral artery were noted and the ratio of the MCA PI and UA PI (C/U ratio) was calculated. The patients with decreased middle cerebral artery PI and reduced, absent or reversed diastolic flow in the umbilical artery were admitted for further evaluation and delivery. Patients who were given conservative treatment were monitored by closed fetal surveillance consisted of bed rest, daily fetal movement count (DFMC), non-stress test and biweekly amniotic fluid estimation and Doppler velocimetry. The following criteria were considered for decision regarding termination-1) Absent end diastolic flow, reverse end diastolic flow, 2) Abnormal fetal heart tracing. 3) Worsening of maternal condition. 4) Gestational age of more than 34 weeks with high resistance diastolic flow. 5) Severe fetal growth restriction with AFI less than five. Women were divided into four groups of 28-30 weeks, 31-33 weeks, 34-37 weeks, 38

weeks of gestation or more . Steroids were administered to all the women between 28 and 34 weeks to enhance fetal lung maturity. All the women were followed up and data were collected regarding mode of delivery, gestational age at birth, birth weight, 5 min APGAR score, number of fetal and perinatal deaths, neonatal complications and admission to NICU. The reference value of umbilical artery Pulsatility index (PI) > 1.42 and middle cerebral artery Pulsatility Index (PI) < 1.5 is according to Arduini D et al (9) and MCA/UA PI ratio are according to Gramellini et el (1), Giancarlo Mari et el (10) and Ifrad et el (11). The cerebro umbilical PI ratio remains constant in the last 10 weeks of pregnancy and, therefore, a single cut off value of 1.08 is considered normal. Below that value , velocimetry was considered abnormal (11)
 C/U ratio= MCA PI/ UA PI; Normal:>1.08, Abnormal:<1.08.

All the data obtained were analyzed by using the Microsoft Excel software. Statistical analysis of data was done after compiling and tabulation of data. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated and compared with other studies.

II. Results

Table1: Maternal characteristics of study population

Maternal Characteristics	N	Percentage
Age group (years)		
16-20	5	10%
21-25	23	46%
26-30	18	36%
31-35	4	8%
Parity		
Primiparous	23	46%
Multiparous	27	54%
Pregnancy Complications		
Oligohydramnios	15	30%
Severe Pre -Eclampsia	16	32%
APH	3	6%
Anaemia	3	6%
Constitutional	8	16%
BOH	2	4%
Post term pregnancy	3	6%
Mode of Delivery		
Full term spontaneous vaginal delivery	3	6%
Induced Vaginal Delivery	8	16%
Caesarian Section(LSCS)	39	78%
Indications for LSCS		
Fetal Distress	17	43.58%
Severe Pre-Eclampsia	13	33.33%
Others	9	24.32%

Demographic characteristics of the study population are depicted in table 1. In present study, out of 50 pregnancies, 46% were primiparous and 54% were multiparous. All the subjects were divided into 4 age groups.

The maximum 46% were within 21-25 year age group and minimum 10% was within 16-20 year age group. The mean age of the subjects was 25.28 years. In our study, preclampsia was the most common cause of IUGR (32% n=16) followed by Oligohydramnios (30% n=15). There were 8 cases who were constitutionally small (16% n=8) and severe anaemia (6% n=3) was present in 3 cases. The study population in the present study was between 30 -41 weeks of gestation with mean gestational age in study group being 36.02wks±SD1.83 as some patients needed termination due to severe pre eclampsia while some spontaneously progressed to normal labour. Mean gestational age of women with abnormal C/U(PI) was 35.63wks±1.673SD. Majority of the patients (78% n=39) had to undergo caesarian section. Most common indication being fetal distress and severe pre eclampsia with severe oligohydramnios. APGAR SCORE <7 at 5 min was observed in 30 babies (60%) Admission to NICU was 65% (n=32). Most of the babies were in the range from 1.2-2.5 kg . 65% of the live births needed admission in NICU. 1 Still birth and 6 neonatal deaths were observed (Table II). Mean birth weight was 1.65kg±0.307SD in the abnormal C/U (PI) ratio and so as the adverse perinatal outcome (Table III) .

Neonatal hyperbilirubinaemia and respiratory distress syndrome were the common complications . there was no cases reported for necrotizing enterocolitis. There were 1 case for intracranial haemorrhage and 1 for hypoxic ischemic encephalopathy were recorded. There was no case reported for necrotizing enterocolitis. AEDV was found in 6 patients, REDF was seen in 2 patients and 2 patients had brain sparing effect in Doppler study. All these Fetuses had poor perinatal outcome. One of the subjects with reversed end diastolic velocity (REDV)

of umbilical artery with decreased MCA values had still birth and another had died in NICU. There were 3 cases with (AEDV) of UA with decreased MCA values and high diastolic flow in MCA and 3 with AEDV with normal MCA values, all of them were terminated by LSCS and had live births. All of them were admitted to the NICU. Out of 9 babies, 6 of the neonates died within 24 hours and rest of the 3 were survived and discharged.

Table 2: Neonatal Characteristics of study population (N=50)

Neonatal Characteristics	N	Percentage
Outcome		
Live birth	49	98%
Still Birth	1	2%
Neonatal death	6	12%
Gestational age at birth		
<30	1	2%
30-33	5	10%
34-37	34	68%
38->	10	20%
Maturity		
Term	22	44%
Preterm	28	46%
Birth Weight(gram)		
<1000	1	2%
1001-1500	16	32%
1501-2500	29	58%
>2500	4	8%
Birth weight <10 th percentile	33	66%
5 min APGAR SCORE <7	30	60%
Admission at NICU	32	65%
Duration of stay in NICU >24 hours	28	56%
Neonatal complications	25	51%
Mean birth weight (1.65 kg)		

Table III: adverse perinatal outcome

Adverse Outcome	Abnormal C/U PI ratio	Normal C/U PI Ratio
Still Birth	1	0
Neonatal death	6	0
Retinopathy of prematurity	1	0
Intracranial Haemorrhage	1	0
Hypoxic ischemic encephalopathy	1	0
Hyperbilirubinaemia	8	3
Early onset neonatal sepsis	2	0
Respiratory distress syndrome	6	3
5 min APGAR SCORE <7	30	4
Admission at NICU	28	4
LSCS for fetal distress	26	13

Table IV: distribution of normal and abnormal C/U PI ratio findings (n=50)

PI Ratio	Number	Percentage
Normal (>1.08)	17	34%
Abnormal (<1.08)	33	66%
Total	50	100

Out of 50 patients who were evaluated by Doppler USG to identify the normal and abnormal cerebral umbilical pulsatility ratio, 33 (66%) were found abnormal and 17 (34%) were normal.

Table V: distribution of perinatal diagnosis of SGA determined by birth weight measurement (n=90)

Perinatal findings	Number	Percentage
SGA	34	68%
Normal	16	32%
Total	50	100

Out of 50 patients, 34(68%) had small for gestational age (SGA) and 16 (32%) had normal birth weight baby. Validity of the tests were confirmed by calculating sensitivity, specificity, positive predictive value, negative predictive value and accuracy by using standard formulae (Table VI and VII)

Table VI: Sensitivity, specificity, accuracy, positive predictive value and negative predictive value of the Colour Doppler evaluation of cerebral- umbilical pulsatility ratio for diagnosis of SGA.

VALIDITY TEST	Percentage
Sensitivity	91.17%
Specificity	87.5%
Accuracy	90%
Positive predictive value	93%
Negative predictive value	82%

Table VII: Colour Doppler evaluation of cerebral- umbilical pulsatility ratio correlation with small for gestational age (n=50)

C/U Pulsatility Ratio	Small for gestational age determined by birth weight measurement		Total
	SGA present	SGA absent	
Abnormal PI ratio	31 (True Positive)	2 (False Positive)	33
Normal PI ratio	3 (FalseNegative)	14 (True Negative)	17
Total	34	16	50

III. Discussion :

IUGR is a pathological condition which is strongly related to the development and function of the uteroplacental and fetoplacental circulation. Umbilical artery (UA) velocimetry correlates with the hemodynamic changes in the fetoplacental circulation. In normal pregnancy, UA flow velocity waveform patterns shows low impedance and high diastolic flow with a low PI the MCA shows high resistance and low diastolic flow with an increase in the pulsatility index. In chronic fetal hypoxia, the blood volume in the fetal circulation is redistributed in the favour of vitally important organs eg heart, kidney and brain. Vasodilatation of the MCA with an increase in diastolic flow through it, results in decrease in its PI. The resulting hyperperfusion is pathological.

The prevalence of IUGR in clinically suspect cases of fetal growth restriction was 68% as observed in the present study. The higher prevalence of iugr in this study could be attributed to the fact that the pregnancies included in this study were already diagnosed as clinically suspected iugr.

In our study, out of 50 cases, 23(46%) were primiparous and 27(54%) were multiparous. Mode of delivery were more towards LSCS and highest indications of LSCS were for fetal distress 43.58% and then for severe PE 33.33% which is similar to the study conducted by Harneet et al (12) and Geeta et al (13). In our study, mean birth weight is 1650 gram while the mean birth weight were 2119 gram and 2030 gram respectively in the studies conducted by them.

Our aim was to establish the usefulness of C/U PI ratio in diagnosis of IUGR. Validity test was done by calculating sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy. These findings were compared with previously published relevant studies conducted by Gremellini et al (1), Fong et al (14), Lakhar et al (15), Bano et al (16) that was shown in the Table VIII.

Table VIII: Comparison with other studies

	Author	Sensitivity	Specificity	PPV	NPV
UA PI	Gramellini et al	64%	70.02%	72.7%	66.7%
	Lakhar et al	50%	59%	66.6%	41.9%
	Fong et al	44.7%	86.6%	54%	86.7%
	Bano et al	46.7%	93.3%	87.5%	63.6%
	Present Study	37.5%	83.33%	80%	42.85%
MCA PI	Gramellini et al	24%	100%	100%	77.3%
	Lakhar et al	41.6%	90.9%	88.2%	48.7%
	Fong et al	72.4%	58%	37.7%	85.7%
	Bano et al	8.9%	100%	100%	52.3%
	Present Study	50%	85%	83%	53.14%
MCA/UA PI	Gramellini et al	68%	98.4%	94.4%	88%
	Lakhar et al	47.2%	86.3%	85%	50%
	Fong et al	51.3%	80.6%	48.1%	82.5%
	Bano et al	44.4%	100%	100%	64.3%
	Present Study	91.17%	87.5%	93%	82%

Regarding UA (PI), our study showed sensitivity of 37.5% which is comparable with the studies performed by Lakhar et al, Fong et al and Bano et al where they showed the UA PI to be 50%, 44.7% and 46.7% respectively. They concluded that UA PI can be used to identify IUGR. In our study, though the specificity and PPV of MCA PI were 85% and 83%, the sensitivity and NPV were 50% and 53.14% which is consistent with the

studies conducted by Bano where they found specificity , PPV were 100% and 100% sensitivity and NPV were much lower 8.9% and 52.3% respectively. Therefore a normal MCA PI may not be an indicator of fetal well-being. We observed perinatal death in one pregnancy which had shown a change in the MCA PI from abnormal to normal. This suggests ,in severe fetal hypoxia, the brain sparing effect breaks down due to acidemia or brain edema and the low MCA PI becomes normal. Therefore ,MCA PI alone is not a reliable indicator . In the diagnosis of IUGR ,Bano et al ,Lakhar et al and Gramellini et al found the sensitivity of UA PI were higher than the sensitivity of MCA PI . This relatively higher sensitivity of the UA PI is probably because it directly reflects the resistance in the placental vascular bed(16).

As MCA /UA ratio incorporates data not only on placental status but also on fetal response, an abnormal MCA/UA PI Doppler ratio is strongly correlated with worse fetal prognosis. In our study CPR had a high specificity and positive predictive value of (87.5% and 93%) which is similar to Gramellini et al, Lakhar et al ,Bano et al and Deepti et al(17) where they showed specificity of 98.4%,86.3%,100% and 86.9% respectively. One study Rochelson et al (18) had shown that a C/U PI ratio of less than 1.08 had a sensitivity of 68%, specificity 98.4%, positive predictive value 94.4%, negative predictive value 88.8% and diagnostic accuracy 90% for predicting adverse perinatal outcomes of IUGR. Gramellini et al (1) using C/U PI ratio of less than 1.08 found sensitivity of 83.3%, specificity 100%, positive predictive value 94.3% and diagnostic accuracy 95.6% for predicting adverse perinatal outcomes in IUGR their findings are consistent with ours.

Limitations: The limitations of the present study were its sample size and the duration of study which is 6 months period.

IV. Conclusion

The sensitivity and specificity of Umbilical artery PI and Middle cerebral artery pulsatility index vary in diagnosing IUGR and predicting fetal compromise. Among the Doppler indices, the evaluation of C/U ratio is a useful modality for diagnosis of IUGR and a good predictor for adverse perinatal outcome than the UA(PI) and MCA(PI) alone. Moreover, it also may be helpful to determine the optimum timing of delivery. The findings of present study must be viewed in context with a high risk population with clinical suspicion of IUGR. Further cross-sectional studies on a larger population are recommended for pregnant women with different risk levels.

Disclosure: All the authors declared no competing interest.

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