Original Research Article

Comparative Study of Foetal Outcome in IUGR Pregnancies by Various Parameters of Doppler Flow Velocimetry of Umbilical Artery and Middle Cerebral Artery

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Abstract

Background: Intra uterine growth restriction is said to be present in those babies whose birth weight is below the 10th percentile of the average for the gestational age. Approximately 15-20 % babies born worldwide are low birth weight babies and IUGR comprises one third of these low birth babies. Once IUGR is confirmed on USG, further monitoring is done by Doppler velocitometry of Umbilical and middle cerebral artery. The aim of this study was to determine the relationship of various Doppler parameters in predicting adverse fetal outcome in Intrauterine Growth-Restricted (IUGR) pregnancies.**Methods**: This was a prospective cross-sectional study of 52 clinically IUGR pregnancies on the basis of USG biometry study at 28–40 weeks of gestation. These IUGR pregnancies were followed till delivery. The NICU admission of >48 hrs were taken as adverse perinatal outcome. The various parameters of Doppler velocitometry of umbilical artery (UA) and middle cerebral artery (MCA) such as Systolic–Diastolic Ratio (UA S/D), UA Pulsatility Index (PI), the Middle Cerebral Artery (MCA) PI, Ratio of MCA PI to UA PI and the Ratio of MCA S/D to UA S/D were screened for their sensitivity, specificity, positive and negative predictive values, percentage of true and false negative. Those various parameters of Doppler findings were also compared with the NICU admission/adverse fetal outcome.**Results***:*Doppler velocitometry of umbilical and middle cerebral artery are very effective in monitoring the IUGR pregnancies. Out of various parameters The MCA PI/UA PI ratio had the highest sensitivity of 80 % and specificity of 96.7 % with positive predictive value of 94 and negative predictive value of 88.57 respectively in determining adverse perinatal outcome. In our study PI ratio of Middle Cerebral Artery and Umbilical artery is highly significant for predicting poor perinatal outcome (77.8 %) p value of 0.000 (< 0.01) with Odds Ratio 16.333 (3.954, 67.473) with 95% Confidence Interval.**Conclusion**: The doppler evaluation of umbilical and middle cerebral artery is very important in monitoring the growth restricted fetus and helps to determine the optimal time for delivery. There were not a single intrauterine fetal demise (IUFD) in the IUGR cases in our study. The PI ratio of Middle Cerebral Artery and Umbilical artery is the most important parameter of doppler evaluation in prdicting adverse perinatal outcome.

Keywords: Intrauterine growth restriction (IUGR), Umbilical artery (UA), Middle cerebral artery (MCA).

Introduction

Intra Uterine Growth Restriction (IUGR) is said to be present in those babies whose birth weight is below the 10th percentile of the average for the gestational age[1]. Growth restriction can occur in preterm, term or post-term babies[2].Low birth weight continues to be a significant public health problem globally and is associated with a range of both short- and long-term consequences. Overall, it is estimated that 15% to 20% of all births worldwide are LBW, representing more than 20 million births a year. IUGR comprises about one third of low birth babies and a major cause of perinatal morbidity and mortality[3,4].The etiology of IUGR can be maternal, fetal and placental. The cause is unknown in about 40 % cases. It can be symmetrical (early onset, 20%) or asymmetrical (late onset, 80%). Symmetrical IUGR has poor prognosis as compared to asymmetrical IUGR[5].Serial measurement of symphysis fundal height (SFH) should be done at each antenatal visit from 24 weeks onward to detect IUGR clinically. A lag of 3 cm or more suggests growth restriction with a sensitivity of (30-80%)[6].However the confirmatory test of IUGR is fetal biometry on USG. It is extremely helpful not only to diagnose the growth restriction but also to identify a fetus of symmetrical or asymmetrical one[7].Once IUGR is confirmed on USG, further management is done with Doppler velocitometry of umbilical and middle cerebral artery[8].

Doppler Principle Doppler Effect is a change in the perceived frequency of sound emitted by a moving source. The effect was first described by Christian Doppler in the 1843. Ultrasound images of flow, whether color flow or spectral Doppler, are essentially obtained from measurements of movement. In ultrasound scanners, a series of pulses is transmitted to detect movement of blood. Echoes from stationary tissue are the same from pulse to pulse. Echoes from moving scatterers exhibit slight differences in the time for the signal to be returned to the receiver. These differences can be measured as a direct time difference or, more usually, in terms of a phase shift from which the 'Doppler frequency' is obtained. They are then processed to produce either a color flow display or a Doppler sonogram[9].

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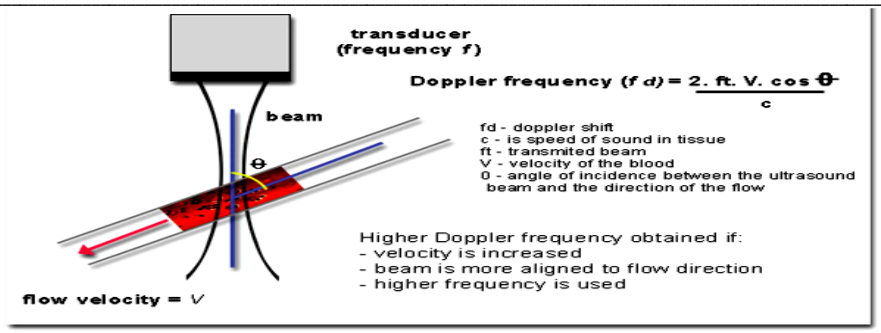

Fig 1:**Doppler ultrasound measuring the movement of the scatterers through the beam as a phase change in the received signal. The resulting Doppler frequency can be used to measure velocity if the beam/flow angle is known.**

The size of the Doppler signal is dependent on:

(1) Blood velocity: As velocity increases, so does the Doppler frequency.

(2) Ultrasound frequency: higher ultrasound frequencies give increased Doppler frequency. As in B-mode, lower ultrasound frequencies have better penetration.

(3) The choice of frequency is a compromise between better sensitivity to flow or better penetration.

(4) The angle of insonation: The Doppler frequency increases as the Doppler ultrasound beam becomes more aligned to the flow direction (the angle *q* between the beam and the direction of flow becomes smaller). This is of the utmost importance in the use of Doppler ultrasound. The implications are illustrated schematically below[10].

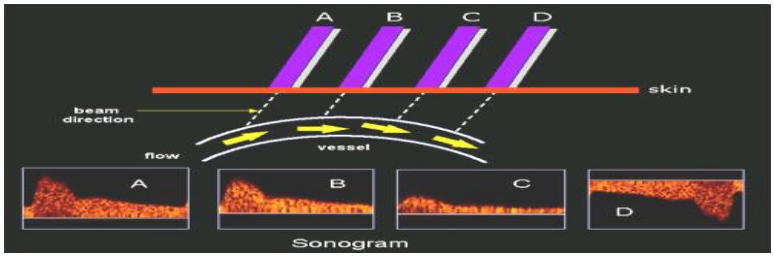

Fig 2: **Effect of the Doppler angle in the sonogram. (A) higher-frequency Doppler signal is obtained if the beam is aligned more to the direction of flow. In the diagram, beam (A) is more aligned than (B) and produces higher-frequency Doppler signals. The beam/flow angle at (C) is almost 90° and there is a very poor Doppler signal. The flow at (D) is away from the beam and there is a negative signal.**

Doppler Velocimetry Study of Middle Cerebral Artery and Umbilical Artery in IUGR

40% of the combined fetal ventricular output is directed to the placenta by two Umbilical Arteries (UA).The assessment of the Umbilical blood flow provides information on the blood perfusion of the fetoplacental unit as the high vascular impedance detected in first trimester gradually decreases[11]. In the evaluation of the fetal cerebral circulation, the Middle Cerebral Artery (MCA) is the most accessible vessel and therefore the vessel of choice. It is the main branch of the Circle of Willis and carries 80% of the blood flow to the ipsilateral cerebral hemisphere. The Middle Cerebral Artery (MCA) Pulsitatiliy Index (PI)/ Umbilical Artery (UA) PI has the highest predictive value in determining IUGR by a sensitivity of 84% and a diagnostic accuracy of 87%.[12] The index study is about to compare the various parameters of umbilical and middle cerebral artery to monitor the confirmed IUGR pregnancies in terms of their perinatal outcome.

Aims and Objectives

1. To determine the role of Umbilical and Middle Cerebral Artery Doppler Flow velocitometry in predicting adverse fetal outcome in Intra Uterine Growth Restriction (IUGR) fetus occurring during pregnancy
2. To compare various parameters of Umbilical and middle cerebral artery Doppler velocitometry in evaluating the perinatal outcome of IUGR patients.

Methods

The study area, design and period

The study is a prospective cohort study of 52 cases of intrauterine growth restriction (IUGR) babies who underwent doppler velocito-metry in the intrauterine period followed by NICU admission between September 2017 to March 2020 in the Department of Radio-Diagnosis , Labour Room and Neo-Natal Intensive Care Unit (NICU) of a tertiary care hospital of Pune which is fully equipped with state of art technology in the health care management. The study was approved by the Institutional Ethical committee.

Population

Source population : All pregnant patients who reported or referred to the antenatal opd for checkup.

Study population : All pregnant patients who were suspected to have IUGR babies on clinical examination in the antenatal opd.

Eligibility

Inclusion criteria: Pregnant pateints suspected to have IUGR on clinical examination were referred to Radiology department for evaluation of fetel biometry and doppler parameters. Only those patients were included in which IUGR was confirmed on biomerty after ruling out of wrong date. These patients were followed up regularly till delivery

Exclusion criteria: All cases with radiologically disproven IUGR, congenital malformations, fetal aneuploidy or twin pregnancies were excluded from the study

Equipment: Doppler examinations of 114 clinically IUGR suspected pregnant patient with singleton pregnancy of more than ($\geq$ 28) weeks of gestation were performed with 4-9MHz curvilinear transducer (Philips Affinitti 70).

Technique: All patients gave written informed consent in accordance of PCPNDT act. The study was conducted in accordance with the approval and recommendations of our institutional Ethical Review Board.Measurements of the Doppler signal were obtained from the middle section of the Middle Cerebral Artery and from the umbilical artery the Doppler signal was taken from a free loop (between the thigh of the fetus). Measurements were obtained during periods of fetal apnea, and the angle of insonation was maintained as close to 0° as possible when interrogating the MCA.The Pulsatility Index (PI) and Resistance Index (RI) for the MCA and Umbilical Artery Doppler values were calculated apart from fetal biometry and other related sonographic scan including liquor estimation.The measurements were performed weekly in cases with abnormal Doppler values or at the time of the next growth scan. The last measurements before delivery were used for our analysis.

Precaution

Cerebroplacental Doppler ratio measurements alone were not used for clinical management. In addition to Doppler evaluations, these cases with IUGR were monitored with twice-weekly nonstress tests and biophysical profiles. When a case with abnormal Doppler findings was identified, the patient was admitted and continuous monitoring of the patient and fetus was started. The IUGR fetuses were delivered because of either arrested fetal growth or abnormal biophysical profile test results. No fetus was delivered on the basis of Doppler parameter findings except for two cases where the decision deliver was taken by obstetrician on the basis of reversal of flow in Umbilical artery.

Operational definitions

IUGR: Intra Uterine Growth Restricted babies are those, whose birth weight lies below the 10th percentile for that gestational age.

Abnormal Doppler findings

1. S/D ratio of Middle Cerebral Artery/Umbilical Artery < 1 of IUGR fetus was considered abnormal. Reversed diastolic flow in Umbilical artery indicate the presence of fetal hypoxemia and the need to deliver the fetus and so was considered abnormal.
2. PI Index of Umbilical Artery more than 1 was considered abnormal.
3. PI Index of Middle Cerebral Artery less than 1 was considered abnormal.
4. PI ratio of Middle Cerebral Artery/Umbilical artery < 1 of IUGR fetus was considered abnormal.

Data collection tools and procedure

Data were collected by the nursing staff at the time of opd visits. Information such as gravid, parity, antenatal history of, past history was collected at the time of first visit. The same history was being verified by the obstetrician at the time of filling of antenatal card which is being made at after anomaly scan. On detection of IUGR clinically, they were referred to Department of Radiology for confirmation. Once IUGR is confirmed, close monitoring of those pregnancies were done in terms of Doppler velocitometry of umbilical and middle cerebral artery and delivered at appropriate time.

Fetal Outcome

All NICU admission of IUGR baby immediately after birth of more than 48 hrs for treatment was taken as adverse perinatal outcome. Major adverse outcomes were perinatal deaths - including intrauterine and early neonatal deaths. The causes of death were hypoxic ischemic encephalopathy, intraventricular hemorrhage, periventricular leukomalacia, pulmonary hemorrhage and necrotizing enterocolitis.

Statistical planning

The Doppler flow velocitometry of umbilical and middle cerebral artery were screened for their sensitivity, specificity, predictive value of positive and negative test, percentage of true and false negative. Data of NICU admission/ adverse outcome of IUGR pregnancies were analyzed using SPPS version 18.0.Pearson's chi-square test was used for comparison of variables. Crude odd ratio was analyzed by using Bivariate binary logistic regression analysis and the level of significance of association was determined at p value < 0.05.

Results

In our study there were 114 suspected IUGR pregnancies. All these 114 patients were send to Department of Radiology for fetal biometry and Doppler velocitometry of umbilical and middle cerebral artery. Only 52 patients were found to be IUGR and remaining 62 patients although found to clinically IUGR but radiologically no IUGR was detected and was excluded from the study.These 52 patients underwent Doppler analysis of umbilical artery (UA) and Middle cerebral artery (MCA) in terms of S/D, PI and their ratio in the antenatal period and statistically studied. The fetal outcome is shown in Table 1.A total no of 20 babies were kept in NICU for more than 48 Hrs for further monitoring/management.

Table 1: Fetal outcome in R/O NICU admission

S.No	Parameter	Frequency	Percent
1	NICU admission (< 48 hrs)	32	61.54
2	NICU admission (> 48 hrs)	20	38.46
	Total	52	100

A total of 42 neonates were admitted in NICU. Out of which 22 neonates were send back to their mother within 48 hrs of NICU admission and remaining 20 neonates remained in the NICU for more than 48 hrs for further management. There were 02 neonatal deaths.

1. S/D Ratio of Umbilical Artery of IUGR fetus in predicting NICU admission / adverse fetal outcome

All 52 mothers who were found to have IUGR babies underwent Doppler of umbilical artery. A S/D Ratio Of Umbilical Artery >3 was very specific in Predicting IUGR .The sensitivity and specificity of U/A S/D in predicting IUGR and adverse outcome was 57 and 93.54 respectively with positive predictive value of 85.71 and negative predictive value of 76.31. The percentage of false negative and false positive was 42 & 6.45 respectively.

Table 2: Cross tabulation for evaluation of S/D Ratio of Umbilical Artery and NICU admission / adverse fetal outcome

S.No	U/A-S/D	NICU admission >48 hrs	< 48 hrs	total	P value	OR (95 % CI)
1	> 3	09(63.6%)	04(36.4%)	13	0.031	5.73(1.46,22.51)
2	<3	11(28.2%)	28(71.8%)	39		
	Total	**20**	**32**	**52**		

63.6% of the pregnancies with S/D ratio of more than 3 of the Umbilical Artery were admitted in NICU with poor perinatal outcome in our study.

2. PI Value of Umbilical Artery of IUGR fetus in predicting NICU admission / adverse fetal outcome

The sensitivity and specificity of PI of U/A in predicting IUGR and adverse outcome was 75 and 87 respectively with positive predictive

value of 75 and negative predictive value of 75. The percentage of false negative and false positive was 42 & 12.9 respectively.

Table 3: **Cross tabulation for Evaluation of Pulsatility Index (PI) of Umbilical Artery and NICU admission/ adverse fetal outcome**

S.No	PI of U/A	NICU admission >48 hrs< 48 hrs	total	P value	OR (95 % CI)
1	> 1	12 (75%) 04 (25 %)	16	0.002	7.5 (1.88, 29.91)
2	< 1	08 (22.2%) 28(77.8%)	36		
	Total	**20 32**	**52**		

75% of pregnancies with Umbilical Artery PI value of more than 1 were admitted in NICU with poor perinatal outcome/IUGR.

3. PI Value of Middle Cerebral Artery of IUGR fetus in predicting NICU admission / adverse fetal outcome

The sensitivity and specificity of PI of MCA in predicting IUGR and adverse outcome was 70 and 81.25 respectively with positive predictive value of 70 and negative predictive value of 81.25. The percentage of false negative and false positive was 30 & 18.75 respectively.

Table 4: **Cross tabulation for Evaluation of Pulsatility Index (PI) of MCA and NICU admission / adverse fetal outcome**

S.No	PI of MCA	NICU admission >48 hrs< 48 hrs	total	P value	OR (95 % CI)
1	<1	12 (60%) 08 (40 %)	20	0.012	4.5 (1.355, 14.944)
2	>= 1	08 (25%) 24 (75%)	32		
	Total	**20 32**	**52**		

60% of patients with PI of Middle Cerebral artery, less than 1 had poor perinatal outcome in our study.

4. S/D ratio of Middle Cerebral Artery/Umbilical Artery < 1 of IUGR fetus in predicting NICU admission / poor perinatal outcome).

The sensitivity and specificity of S/D ratio of MCA/UA in predicting IUGR and adverse outcome was 68.42 and 81.81 respectively with positive predictive value of 68.42 and negative predictive value of 81.81. The percentage of false negative and false positive was 31.57 & 18.18 respectively.

Table 5: Cross tabulation for evaluation of S/D Ratio of MCA/UA and NICU admission / adverse fetal outcome

SN	S/D of MCA & UA	NICU admission >48 hrs< 48 hrs	total	P value	OR (95 % CI)
1	<1	14(70%) 06(30%)	20	0.001	10.11(2.74, 37.28)
2	>= 1	06(18.8%) 26(81.3%)	32		
	Total	**20 32**	**52**		

70% of pregnancies with S/D Ratio of Middle Cerebral artery and Umbilical Artery, less than 1 had poor perinatal outcome

5. PI ratio of Middle Cerebral Artery/Umbilical artery < 1 of IUGR fetus in predicting NICU admission / poor perinatal outcome.

The sensitivity and specificity of PI ratio of MCA/UA in predicting IUGR and adverse outcome was 80 and 96.7 respectively with positive predictive value of 94 and negative predictive value of 88.57. The percentage of false negative and false positive was 20 & 3.3 respectively.

Table 6: **Cross tabulation for Evaluation of Pulsatility Index (PI) of MCA/UA and NICU admission / adverse fetal outcome**

S.No	PI of MCA	NICU admission >48 hrs< 48 hrs	total	P value	OR (95 % CI)
1	<1	14(77.8%) 04(22.2%)	18	0.000	16.33(3.954,67.473)
2	>= 1	06(17.6%) 28(82.4%)	34		
	Total	**20 32**	**52**		

77.8 % of the pregnancies with PI ratio of Middle Cerebral Artery and Umbilical artery had poor perinatal outcome. p value of 0.000 (< 0.01) in our study is highly significant for predicting poor perinatal outcome / IUGR if the Pulsatility index Ratio(PI Ratio) of MCA (Middle Cerebral Artery) and UA (Umbilical artery) is less than 1. The Odds Ratio of Pulsatility index Ratio (PI Ratio) of MCA (Middle Cerebral Artery) and UA (Umbilical artery) less than 1 being predictive of IUGR would be 16.333 with 95% Confidence Interval based on our study.

Discussion

A total of 114 patients whom IUGR was suspected, it was actually present in 52 patients on the basis of fetal biometry. Incidence of IUGR in clinically suspected high risk cases in our hospital 46.42 %. During the period of our study a total of 1500 deliveries took place in our hospital out of which 52 pregnancy were IUGR. Hence the percentage of IUGR in our hospital was only 3.47 (National incidence of IUGR is approximately 30%) and it is attributed to better socio economic condition, better education and excellent medical facilities available to armed forces population.

IUGR is a pathological condition strongly related to the development and function of the uteroplacental and fetoplacental circulations. An adequate fetal circulation is necessary for normal fetal growth. To facilitate this, remarkable changes occur in the maternal, placental and fetal vasculatures.UA velocimetry correlates with hemodynamic changes in the fetoplacental circulation. With an increase in the number of tertiary stem villi and arterial channels, as the fetoplacental compartment develops the impedance in the UA decreases. A diastolic component in the UA flow velocity waveform (FVW) appears during the early second trimester, i.e, at 15 weeks' gestation, and progressively increases with an increase in the gestational age. A mature UA FVW is usually achieved by 28- 30 weeks. The normal UA waveform pattern shows low impedance and high diastolic flow with a low PI.F et al MCA is a low resistance circulation throughout pregnancy and accounts for 7% of fetal cardiac output. The MCA seems to react earlier and is more sensitive to hypoxia and ischemia. The MCA impedance varies during gestation according, with a parabolic pattern during pregnancy and does not change significantly after delivery. Increase in diastolic flow with decreased Pulsatility index shows the brain sparing taking place

in compromised fetuses[13]Gramellini et al calculated the C/U ratio and found that it remained constant in the last 10 weeks of pregnancy. We, therefore used a single cut-off value of 1.08 for all cases of 28-40 weeks of gestation. Above this value, Doppler velocimetry was considered normal and below it, abnormal. Using this cut-off value, we could divide the study population into two groups: those with a normal ratio and those with an abnormal ratio[14].Cerebral placental ratio is constant during pregnancy especially after 30 weeks and suggested 1 as the cut off value; all values less than 1 are considered abnormal. This ratio is shown to have higher sensitivity (100%) when compared with Pulsatility index of MCA alone (50%) for 5 min APGAR score according to study by Ozcan et al[15].In our study, we found that the cerebral placental (C/U) ratio was a better predictor of SGA newborns and adverse perinatal outcome than either the MCA PI or UA PI taken alone. The C/U ratio demonstrated 96.87% specificity and 94% PPV in diagnosing IUGR and predicting adverse perinatal outcome as against 75% specificity and PPV of UA PI and 70% specificity and PPV of MCA PI. The NPV of the C/U ratio were comparable to those of MCA PI, but much higher than those of UA PI.In our study of Umbilical artery S/D ratio, although sensitivity of only 57, but was highly specific with specificity of 93.54 in predicting IUGR especially in case of the reversed diastolic flow. Out of two patients who were having reverse diastolic flow in the Umbilical artery, both resulted in intra uterine death (1135 gm, 1240 gm) , before taking up the case for LSCS. We took all NICU admission of IUGR baby of more than 48 hrs for treatment as significant for considering for adverse perinatal outcome (minor/major) and S/D ratio of middle cerebral and umbilical artery was studied for predicting the same with specificity of 81.81 % and NPV of 81.81%.Thus although all the Doppler parameter may be considered important in the prediction and follow up in the IUGR pregnancies, the ratio of MCA PI and UA PI (Cerebro Placental Ratio) was found to be more specific with very high PPV and NPV , as per our study in predicting IUGR and its complication.

Diagnostic Accuracy of Doppler in predicting IUGR and adverse perinatal outcome

Our study for the screening test of UA PI for IUGR with specificity of 87%, Positive Predictive Value (PPV) of 75% and Negative Predictive Value (NPV) of 75 % can be compared with the study ofGramellini et al[14] with similar results i.e. specificity of 90.7%, PPV of 72.7% and NPV of 86.7 %. PPV of UA PI of our study was higher (75%) than Fong et al[16] study (54.0%) because of PI more than 1 in more than 28 weeks pregnancy was uniformly considered as abnormal in our study where as in Fong et al study, it was considered as per gestational age nomogram (mean+/- 2SD). Sensitivity of UA PI in the study by Lakhkar et al[17] (50%) is similar to our study (52%).Our study of MCA PI with sensitivity of 70% and NPV of 81.25% can also be compared with the study of Fong et al having sensitivity of 72.4% and NPV of 85.7%. PPV of MCA PI of our study was higher (70%) than Fong et al study (37.7%) due to the lower number of patients evaluated. Our study for the screening test of MCA PI in predicting IUGR with specificity of 81.25% and PPV of 70% can be compared with the study of lakhkar et al[17] with similar results i.e. specificity of 90.9% and PPV of 88.2%.In the analysis of adverse perinatal outcome in terms of NICU admission results of Fong et al can be compared with our results. We found that ratio of Pl of MCA/UA is more sensitive than MCA Pl alone in predicting adverse neonatal outcome in contrast to Fong et al. Probably the difference is due to the smaller size of our sample.Similarly Gramellini et al[14] who studied the cerebro-umbilical ratio as a predictor of adverse perinatal outcome gave the sensitivity, specificity, positive predictive value and negative predictive value of Pl Ratio of MCA and UA as depicted in the table. We obtained a higher sensitivity for MCA Pl/ UA PI (80%) compared to Gramellini et al (68%). Screening test for S/D Ratio of MCA/UA of our study has sensitivity of 68.42%, specificity of 81.81% PPV of 68.42% and NPV of 81.81% and can be compared to the study by Lakhkar et al[17] with sensitivity of 55.5%, specificity of 72.7% PPV of 76.9% and NPV of 50%.

Summary and Conclusion

IUGR is a serious condition in which extensive monitoring of the fetus is required. Perinatal outcome is poor with early onset FGR (34 weeks) compared to late onset of FGR (>34 weeks). Decision for early delivery may result in neonatal deaths due to complications. On the other hand, delay in delivery may result in IUFD. So, correct diagnosis and timed intervention are essential. The introduction of Doppler technology has provided an opportunity for repetitive noninvasive hemodynamic monitoring in such pregnancies. There is ample evidence that Doppler indices from the fetal circulation can reliably predict adverse perinatal outcome in an obstetric patient population who have a high prevalence of fetal growth restriction. Compared to other methods of fetal monitoring, Doppler has proved to be more sensitive in detecting fetal compromise early and aids in the appropriate timing of delivery. The Doppler evaluation of the fetal circulation plays an important role in monitoring the growth restricted fetus and thereby helps to determine the optimal time for delivery. Fetal Doppler indices, in particular ratios that include measurements obtained from the cerebral circulation, the PI index of Umbilical Artery (UA), S/D ratio of UA, PI index of Middle cerebral Artery (MCA) and ratio of PI of MCA and UA along with ratio of S/D of MCA and UA help in the prediction of neonatal morbidity. Therefore, the use of Intra Uterine Doppler is highly recommended in the monitoring and management of the Growth-Restricted fetus.

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