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Original Research Article

Role of Doppler Velocimetry and Placental Thickness in Evaluation of IUGR

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Abstract:

Objectives: The present study was to evaluate the role of Doppler velocimetry of umbilical artery and middle cerebral artery for non-anomalous fetus with suspected IUGR. And to evaluate the placental thickness in suspected cases of IUGR.

Methods: A detailed clinical history, fetal biometry, amniotic fluid assessment and color Doppler study were performed on S10 voluson with a curvilinear transducer, having a variable frequency of 1.0-5.0 MHz. The ratio between the pulsatility index (PI) of the middle cerebral artery (MCA) and the umbilical artery (UA) PI, known as the MCA/Umb A PI ratio or Cerebral-umbilical ratio, was calculated. In our study, a single cutoff value of 1.0[21] for the MCA/Umb A PI ratio was utilized. Velocimetry was deemed normal if the ratio was above this threshold and abnormal if it fell below it. Placental thickness was assessed at the level of umbilical cord insertion, with the maximum thickness recorded in cross-section.

Results: In umbilical artery, PI and RI of IUGR fetuses were significantly higher than that of normal fetuses (1.508±0.581 vs 1.053±0.233; p=0.001, 0.857±0.238 vs 0.668±0.125; p=0.001). In middle cerebral artery PI and RI of middle cerebral artery was significantly lower than that of normal fetuses (1.206±0.380 vs 1.607±0.319; p<0.001, 0.597±0.122 vs 0.704±0.138; p=0.002). Cerebro-placental ratio(CPR) of IUGR fetuses were significantly lower than that of normal fetuses (0.848±0.335 vs 1.609±0.526; p<0.001). Among the total of 70 patients assessed, 50 fetuses were diagnosed with intrauterine growth restriction (IUGR), while 20 did not exhibit IUGR. Within the group of 50 fetuses with IUGR, 34 were classified as having asymmetric IUGR, and the remaining 16 fetuses were categorized as having symmetric IUGR.

Conclusions: Cerebro-Placental Ratio (CPR) is the superior predictor of IUGR in comparison to PI or RI values of MCA or UA. The PI of the umbilical artery has higher diagnostic accuracy as compared to the RI of umbilical artery and PI and RI of middle cerebral artery. Since PI and RI of MCA has least diagnostic accuracy in predicting IUGR, it is recommended to be used along with other Doppler indices in the setting of suspected IUGR.

Key words: Doppler velocimetry, Placental thickness, IUGR.

Introduction

Intrauterine growth restriction (IUGR) prevails as a severe public health concern. Globally, it is the second-most significant cause of perinatal death and morbidity after premature deliveries [1]. An inability of a fetus to reach its genetically set potential growth is referred to as IUGR. When the

birth weight of a fetus is less than the 10th percentile, IUGR is diagnosed [2].

Depending on the population under investigation and the definition chosen, the total incidence of IUGR varies. Research suggests that IUGR may impact as many as 25% of births in low- and middle-income nations and 3–9% of deliveries in developed nations [3]. Bangladesh (50%, 39%), India (28%, 21%), and Pakistan (25%, 18%) have the most significant national incidences of LBW and IUGR-LBW, respectively [4,5]. Women in the lowest quartile of low pre-pregnancy weight and pregnancy weight increase were shown to be most at risk of having an IUGR baby [6].

Nowadays, IUGR classification is based on ultrasonic biometry technology. The hemodynamic flow of the fetal arteries is measured by comparing the flow indices and patterns of regular and IUGR patients with Doppler velocimetry. The umbilical artery has been the subject of the most outstanding research in Doppler velocimetry due to its accessibility and substantial association with fetal outcomes.

The proposed method seeks to determine the optimal delivery window by integrating Doppler velocimetry and biophysical profile, reducing the risk of adverse perinatal outcomes [7,8].

Placental insufficiency is the main contributing factor to intrauterine growth restriction. Many growth-restricted fetuses may also be hypoxemic. Reducing cardiac output and heart rate, a rise in arterial pressure and the resulting afterload, and the redistribution of blood flow due to selective peripheral vasoconstriction can sum up the fetal hemodynamic adaptation to hypoxia [4,9]. The reversed flow of the ductus venosus has been implicated in the pulsations of the umbilical vein [16].Fetal venous Doppler tests constitute vital diagnostic methods that have the potential to influence how IUGR fetuses are treated. An obvious strategy to maximize delivery timing is continuously monitoring the venous flow velocity waveforms in IUGR fetuses. When managing IUGR fetuses severely, the gestational age, biophysical profile scores, and longitudinal multi-vessel monitoring may provide a clear indicator for treatment [9,10].

Sustaining a healthy fetus during pregnancy requires average placental growth. The decreased placental function adversely affects fetal growth, resulting in IUGR. Small placentas have been linked to intrauterine growth restriction, gestational diabetes mellitus, chromosomal abnormalities, and preeclampsia [11].

Small for gestational age newborns at term were more connected with excellent rates of fetal abnormalities and neonatal morbidity and mortality [17]. IUGR is linked to a less than 2.5 cm placental thickness, whereas thick placentas are linked to maternaldiabetes mellitus, fetal hydrops, and intrauterine fetal infections [12].

Identifying risk factors for decreased fetal growth is the first step in prenatal screening for IUGR. Sequential ultrasonography or anatomical reference point measurements of fetal size are performed when the fetus is determined to be at riskfor IUGR. Fetal biometry shows that IUGR fetuses have smaller livers due to decreased glycogen storage and smaller abdominal circumferences because of the loss of abdominal adipose tissue. When there is a reduction in oxygen and nutrition delivery from the placenta, the fetus redistributes blood to the brain at the expense of liver glycogen and fat reserves. This leads to average fetal brain growth and a decrease in the expansion of the abdomen circumference [13,14].

Objectives

1. To evaluate role of Doppler velocimetry of umbilical artery and middle cerebral artery for non-anomalous fetus with suspected IUGR.
2. To evaluate the placental thickness in suspected cases of IUGR.

Material & methods

Study design: This prospective, observational, hospital-based study was designed to assess the role of Doppler velocimetry and placental thickness in the evaluation of intrauterine growth restriction (IUGR). This study was conducted in the Departmentof Radiodiagnosis, Kalinga Institute of Medical Sciences, Bhubaneswar from 19th July 2022 to 28th January 2024. For this study, we got ethical approval (letter no. KIIT/KIMS/IEC/983/2022 dated 18/07/2022) from Institutional Ethics Committee, Kalinga Institute of Medical Sciences, Bhubaneswar, prior to study initiation. The patient information sheet, explaining the purpose and details of the study vis-à-vis the benefits and the potential risks for the participants, was provided in the local vernacular language, i.e., Odia, to each patient screened for eligibility as well as the close relatives accompanied them. Written informed consent was obtained from all the study participants prior to their enrolment. The consent was taken under Pre-Conception and Pre-Natal Diagnostic Technique (PC-PNDT) Act,1944.

Study population:

Pregnant women, presenting at Obstetrics and Gynecology OPD, Kalinga Institute of Medical Sciences, Bhubaneswar, for routine check-up, were screened for their eligibility for this study. The convenience sampling method was applied for this study. The inclusion and exclusion criteria of the study were as follows:

Inclusion criteria:

1. Primigravida with singleton pregnancy.
2. Pregnant women diagnosed as suspected IUGR in the late 2nd and 3rd trimester based on symphysis fundal height (SFH) if less than 10th percentileand referred to the department of Radio diagnosis for the evaluation.
3. Patient who agreed to provide written informed consent for the study.
4. Pregnant women who underwent delivery in our hospital and is discharged from our hospital.

Exclusion criteria:

1. Patients with twin pregnancy.
2. Patients with multiple pregnancy.
3. Pregnant women with normal SFH.
4. Congenital malformations and chromosomal abnormalities detected during screening.
5. Patient who did not provide the consent.
6. Patient who did not undergo delivery at KIMS.

Study procedure:

Seventy pregnant (primigravida) women with singleton pregnancy suspected for IUGR were sent to the Department of Radiodiagnosis, Kalinga Institute of Medical Sciences, Bhubaneswar. They were included in this prospective, observational study. The diagnoses generated by the principal investigator were confirmed by the guide and co-guide of this research. The patient information sheet, explaining the purpose and details of the study vis-à-vis the benefits and the potential risks for the participants, was provided in the local vernacular language, i.e., Odia, to each patient screened for eligibility. Written informed consent was obtained from all the study participants prior to their enrolment.

After obtaining detailed clinical history, fetal biometry, amniotic fluid assessment and color Doppler study was performed on S10 voluson with a curvilinear transducer, having a variable frequency of 1.0-5.0 MHz. Clinical follow up and repeat color Doppler study was performed in cases where its clinically indicated to know the usefulness of Doppler.

Doppler Ultrasound Technique

- **Concentrating on the Umbilical Artery for Doppler Assessment:**

Using a duplex scanner, the umbilical artery (cord) was detected, appearing as twin parallel white lines within the amniotic fluid. The pulsed Doppler beam's range gate was positioned over the vessel, and the sample volume was adjusted to extend just beyond the vessel's limit. Typically, the umbilical cord was found near the fetal abdominal wall. The Doppler probe was adjusted to capture the highest quality signal representing arterial flow. Once optimal signals were achieved, the probe was held steady, and the spectral tracing image was frozen to record the waveform. The height of the maximum frequency outline in the flow velocity waveform depended on the angle between the Doppler beam and the examined vessel (i.e., the angle of insonation). A smaller angle resulted in a higher frequency recorded in the flow velocity waveform, so the angle was kept below 60 degrees to minimize this effect, to confirm the possible appearance of end diastolic zero velocities, the waveform was examined from at least two different angles of insonation and from different segments of the umbilical cord.

- **Middle Cerebral Artery**

Color flow imaging enables the identification of the middle cerebral arteries. The initial step involved obtaining the plane for biparietal diameter (BPD) measurements. While staying in the same plane, the ultrasound probe was moved towards the base of the brain until the sphenoid bone was visible and the circle of Willis was located. The middle cerebral artery (MCA) conveniently runs along the greater wing of the sphenoid bone and is easily visualized using color Doppler imaging. The MCA, located in the near field, was then examined approximately 1 cm distal to its origin from the internal carotid artery.

The pulsatility index (PI), along with the presence or absence of end-diastolic flow and reverse diastolic flow, were observed and documented. The umbilical artery (UA) PI served as an indicator in monitoring the progressive absence of end-diastolic or reverse diastolic flow, as it continues to reflect changes in resistance.

The ratio between the pulsatility index (PI) of the middle cerebral artery (MCA) and the umbilical artery (UA) PI, known as the MCA/Umb A PI ratio or Cerebral-umbilical ratio, was calculated. In our study, a single cutoff value of 1.0 [15] for the MCA/Umb A PI ratio was utilized. Velocimetry was deemed normal if the ratio was above this threshold and abnormal if it fell below it.

Placental Thickness

Placental thickness was assessed at the level of umbilical cord insertion, with the maximum thickness recorded in cross-section. Measurements were precise to 1 mm, taken at the placenta's greatest thickness, perpendicular to the uterine wall. The assessment excluded the uterine myometrium and retroplacental veins. A cut off 25mm was taken to determine whether the fetus had IUGR.

Statistical Analysis

All the data were tabulated, compared and analyzed using software STATA version 15.1, Statacorp Texas, USA. The data were expressed as either mean ± standard deviation or median (inter-quartile

range). Appropriate statistical tests were applied for the assessment of the role of Doppler velocimetry and placental thickness in the evaluation of IUGR.

Observations and Results

This prospective, observational, hospital-based study of 70 antenatal patients with IUGR was done after considering inclusion and exclusion criteria. Flow velocity waveforms of the umbilical and middle cerebral arteries along with placental thickness were obtained from all the cases and were analysed.

Patient Demographics

All our patients ranged from 20-40 years. Majority of the patients 24 (34.3%) were in 20-25 and 26-30 years of age group each. The average age of the patient was 28.49 years, around 22 (31.4%) patients were seen in the age group of more than 30 years.

Gestational Age Distribution in Doppler Examination

In our study group of 70 antenatal mothers, the gestational age at the time of Doppler examination ranged between 28-39weeks.

None of the antenatal mothers were assessed prior to 28 weeks of gestation. Among those examined, 37 cases (52.9%) were in 31-35week gestational age group, 18 cases (25.7%) were in 28-30 weeks, and 15 cases (21.4%) were in the 36-40 week bracket.

Clinical Presentation and Indication for Doppler Study

Among the group of 70 pregnant women enrolled in the study, the clinical presentations and indications for Doppler examinations are delineated below.

Distribution of Patients According to Confirmed Iugr Status

On the basis of estimated birth weight and birth weight after delivery out of a total 70 IUGR suspected clinically, 50(71.4%) were confirmed to have IUGR while 20(28.6%) did not turn out to be IUGR. We have considered those patients who were confirmed to have IUGR as Group I and those patients who were confirmed not to have IUGR as Group II.

Umbilical Artery Doppler Study

Umbilical artery PI was elevated in 54 patients (77.1%) and was normal in 16 (22.9%) patients

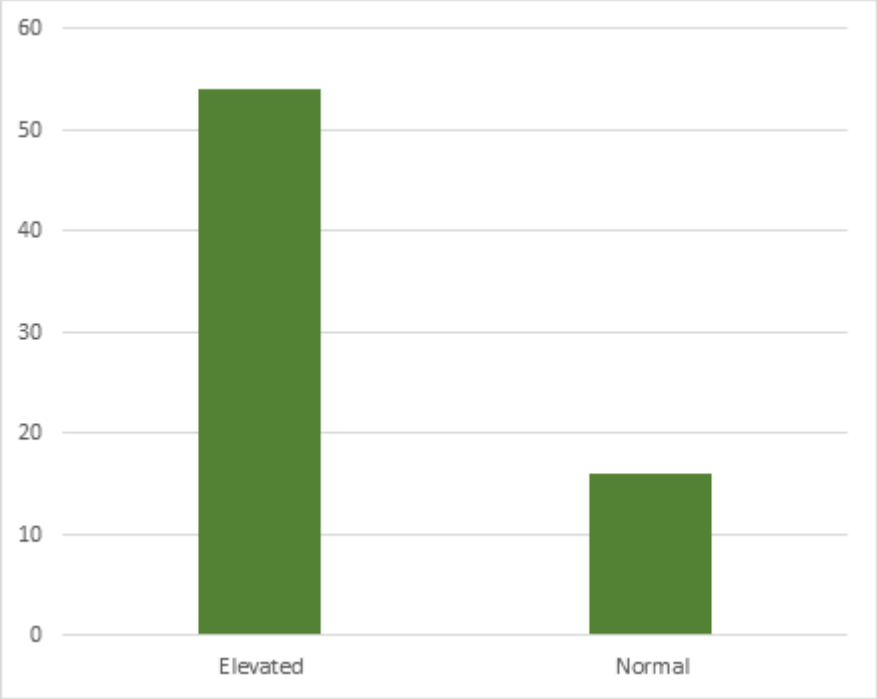

Figure 1: Umbilical artery PI Doppler study Findings

Umbilical artery RI was elevated in 44 patients (62.9%) and was normal in 26 patients (37.1%)

Figure 2: Umbilical artery RI Doppler study Findings

Umbilical Artery End Diastolic Velocity Flow Pattern

Table 1: Absent or reversal of end diastolic flow in umbilical artery

End Diastolic Flow Pattern	Number	Percentage
Absent	4	5.7%
Reversal	2	2.9%
Positive Diastolic Flow	64	91.4%
Total	**70**	**100%**

Four fetuses (5.7%) showed absence and 2 fetuses (2.9%) showed reversal of end diastolic artery flow with the total of 64 fetuses (91.4%) showing normal positive diastolic flow.

Fetal Middle Cerebral Artery Doppler Study

Table 2: MCA PI values on Doppler examination

PI	Number	Percentage
Decreased	46	65.7
Normal	24	34.3
Total	**70**	**100**

About 46 (65.7%) of the 70 fetuses had decreased pulsatility index and 24 (34.3%) had normal Middle cerebral artery pulsatility index

Table 3: Findings of middle cerebral artery RI on Doppler examination

RI	Number	Percentage
Decreased	41	58.6
Normal	29	41.4
Total	**70**	**100**

About 41 fetuses(58.6%) had decreased pulsatility index and 29 fetuses (41.4%) had normal middle cerebral artery pulsatility index.

Table 4: Ratio of PI of MCA to PI of umbilical artery

MCA/UmbA PI	Number	Percentage
MCA/umbA PI(<1.0)[21]	52	74.3
Normal	18	25.7
Total	**70**	**100**

About 52 fetuses (74.3%) had decreased MCA/UmbA PI and 18 fetuses (25.7%) had normal MCA/UmbA PI.

Placental Thickness Estimation

Table 5: Placental thickness measurement on Ultrasound

Placental Thickness	Number	Percentage
Decreased	42	60.0
Normal	28	40.0
Total	**70**	**100**

About 42 fetuses (60%) had decreased placental thickness and 28 fetuses (40%) had normal placental thickness.

TABLE 6: Diagnostic efficacy of Doppler indices in evaluation of IUGR

Dopplex Index	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
UmbA PI	41	13	9	7	82%	65%	85.4%	59%	77.1%
UmbA RI	39	15	5	11	78%	75%	88.6%	57.6%	77.1%
MCA PI	37	11	9	13	74%	55%	80.4%	45.5%	68.5%
MCA RI	33	12	8	17	66%	60%	80.4%	41.3%	64.2%
MCA /UmbAPI	46	16	4	4	92%	80%	92%	80%	88.5%

Table 7: Diagnostic efficacy of Placental thickness in evaluation of IUGR

Placental Thickness Evaluation		TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
Placental Thickness	35	18	2	15	70.00%	90.0%	94.50%	54.50%	75.70%

Table 8: Comparison of mean value of Doppler indices between Group I and Group II

S.No	Type of Wave Form		Umbilical Artery		Middle Cerebral Artery		
			RI	PI	RI	PI	CPR
1	GroupI (IUGR)	Mean	0.857	1.508	0.597	1.206	0.848
		Standard Deviation	0.238	0.581	0.122	0.38	0.335
2	GroupII (No IUGR)	Mean	0.668	1.053	0.704	1.607	1.609
		Standard Deviation	0.125	0.233	0.138	0.319	0.526
Test of Significance(P-value)			0.001	0.001	0.002	<0.001	<0.001

In umbilical artery, PI and RI of IUGR fetuses were significantly higher than that of normal fetuses (1.508±0.581 vs 1.053±0.233; p=0.001, 0.857±0.238 vs 0.668±0.125; p=0.001). In middle cerebral artery PI and RI of middle cerebral artery was significantly lower than that of normal fetuses (1.206±0.380 vs 1.607±0.319; p<0.001, 0.597±0.122 vs 0.704±0.138; p=0.002). Cerebro-placental ratio(CPR) of IUGR fetuses were significantly lower than that of normal fetuses (0.848±0.335 vs 1.609±0.526; p<0.001).

Table 9: Comparison of Placental thickness, Estimated fetal weight and Birth weight between Group I and Group II .

S.No			Estimated Fetal Weight	Birth Weight	Placental Thickness
1	GroupI(IUGR)	Mean	1589	1715	25
		Standard Deviation	497	496	4.27
2	GroupII(No IUGR)	Mean	2124	2485	32.1
		Standard Deviation	370	207	2.78
Test of Significance(P-value)			<0.001	<0.001	<0.001

In IUGR fetuses, the estimated fetal weight was notably lower compared to that of normal fetuses (1589±497 vs. 2124±370; p<0.001). Additionally, the birth weight of IUGR fetuses was significantly reduced compared to normal fetuses (1715±496 vs. 2485±207; p<0.001). Furthermore, the placental thickness in IUGR fetuses was observed to be markedly diminished compared to normal fetuses (25±4.27 vs. 32.1±2.78; p<0.001).

Type of Iugr

Among the total of 70 patients assessed, 50 fetuses were diagnosed with intrauterine growth restriction (IUGR), while 20 did not exhibit IUGR. Within the group of 50 fetuses with IUGR, 34 were classified as having asymmetric IUGR, and the remaining 16 fetuses were categorized as having symmetric IUGR.

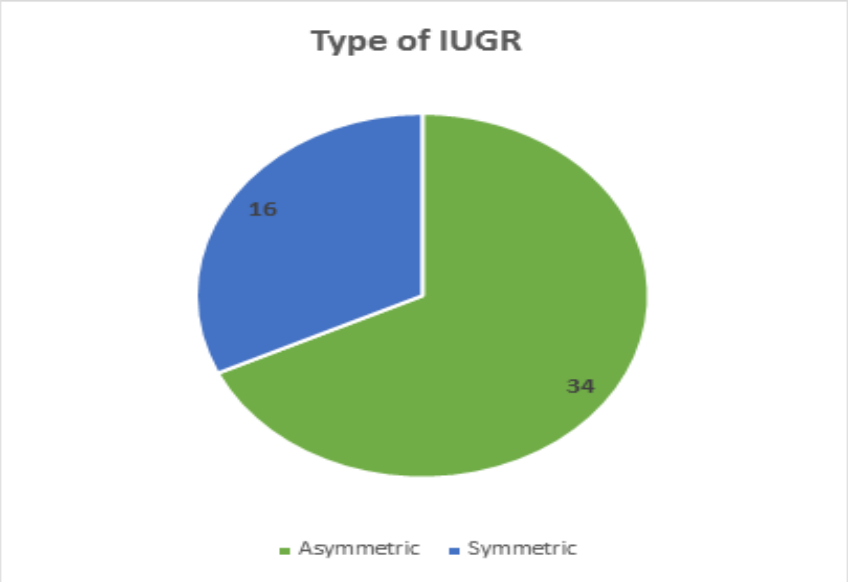

Figure 3: **Type of IUGR**

Discussions

Intrauterine growth restriction (IUGR) arises from a multitude of factors affecting various pathways. Doppler flow velocimetry and analysis of placental thickness emerge as valuable tools in resolving this diagnostic challenge.

We conducted color Doppler and evaluated placental thickness in a cohort of 70 pregnant women suspected of carrying fetuses with intrauterine growth restriction (IUGR), based on clinical indications and grayscale ultrasound findings.

Age Incidence

The research findings indicated a noteworthy proportion of pregnant women belonging to the age ranges of 20 to 25 years (24 cases, 34.3%) and 26 to 30 years (24 cases, 34.3%), with an average age of 28.49 years. This trend is likely indicative of the heightened prevalence of pregnancies within these specific age brackets.

Distribution of gestational age

In our study, all patients underwent Doppler studies in the late second and third trimesters of their pregnancies, with 37 cases (52.9%) undergoing investigation between 31 and 35 weeks of gestation. The earliest study occurred at the 28th week of gestation. Thus, most pregnancies were monitored between 31 and 35 weeks, a critical period during which the fetus would have initiated sufficient lung maturity, potentially enabling survival outside the uterus.

Etiology of IUGR

Anemia complicated about 15 (21.4%) of the cases in our study. Hypertensive disorders were present in 31 cases (44.3%) of pregnancies complicated by IUGR. Bad obstetric history was identified as a cause in 6 (8.6%) of cases. Approximately 18 cases (25.7%) of the study group had IUGR without any detectable cause.

Umbilical Artery

For the diagnosis of intrauterine growth restriction, umbilical artery PI value >95th percentile was 82% sensitive, 65% specific with positive and negative predictive value of 85.4% and 59% respectively. A cut off value >95th percentile the sensitivity and positive predictive value increased but specificity and negative predictive value decreased.

The variation observed could be explained by the fact that the umbilical artery reflects the fetoplacental system, primarily indicating placental resistance. In our study, the higher prevalence of pregnancy-induced hypertension (PIH) cases might potentially account for the difference compared to other studies. The significant difference of sensitivity PPV and NPV between our study and Moawad et al.[63] is probably due to low sample size(n=23) of the later study.

The umbilical artery RI value >95th percentile was 78% sensitive ,75% specific with positive and

negative predictive value of 88.6% and 57.6% respectively in our study.

Fetal Blood Circulation and Redistribution

Over the past 20 years, there has been a notable advancement in the utilization and integration of MCA (middle cerebral artery) and CPR (cerebral perfusion) Doppler measurements in clinical settings. As MCA carries approximately 80% of fetal cerebral blood and is conveniently accessible through ultrasound, it has emerged as the preferred vessel for evaluating fetal intracranial perfusion, establishing itself as the gold standard in this regard. Our study showed middle cerebral artery PI <5th percentile was 74% sensitive, 55% specific with positive and negative predictive value of 80.4% and 45.5% respectively. The following table compare the results of the present study with other studies.

Our present study findings are in concordance with Singh s et al [17] study. The notable variations in sensitivity, positive predictive value (PPV), and negative predictive value (NPV) between our study and that of Moawad et al. [10] are likely attributed to the smaller sample size (n=23) in the latter study.

Our study showed middle cerebral artery RI <5th percentile was 66% sensitive, 60% specific with positive and negative predictive value of 80.4% and 41.3% respectively.

The redistribution calculated from the ratio of the PI in the MCA to PI in the umbilical artery (value less than 1.0) showed 92% sensitivity, 80% specific with a positive and negative predictive value of 92% and 80% respectively. These values are in concordance with Munikumari et al. [18] and EL-Kady et al. [19]. The notable variations in sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) between our study and that of Moawad et al. [16] are likely attributed to the smaller sample size (n=23) in the latter study.

Our study's diagnostic accuracy aligns with that of Munikumari et al. [18], demonstrating a 90% accuracy for MCA/UmbA PI, 88% for UA PI, and 66% for MCA PI consistent with Munikumari et al. [18] findings, our study also confirms that optimal outcomes are achieved when utilizing the MCA/UmbA PI ratio, rather than assessing the pulsatility indices of the middle cerebral artery and umbilical artery individually.

Placental Thickness in Iugr

The placenta sustains the feto-maternal circulation through the umbilical cord, crucial for typical fetal growth and development. A properly developed and functioning placenta is vital for supporting the needs of the growing fetus. Throughout the fetal growth process, the placenta enlarges to fulfill its essential roles. When fetal growth is impaired, it's often attributed to irregular placental function, which can be detected through the measurement of abnormal placental parameters.

The thickness of the placenta is closely linked to fetal development and can play a role in the perinatal outcome. The placenta is about 3 cm thick and 15-25 cm in diameter [20].

Typically, placental thickness increases as gestational age progresses. However, our study revealed a decrease in placental thickness among fetuses confirmed to have intrauterine growth restriction (IUGR). In our investigation, placental thickness demonstrated a sensitivity of 70% and specificity of 90%, with positive predictive and negative predictive values of 94.5% and 54.5%, respectively. These findings align with a study conducted by Rafique et al. [21], which reported a sensitivity of 86.30%, specificity of 86.70%, positive predictive value of 75%, and negative predictive value of 92% for determining IUGR based on placental thickness. The diagnostic accuracy of our study is 75.7% while that of Rafique et al. [21] is 86.4%.

This suggests that placental thickness serves as a reliable indicator for predicting IUGR. Based on the preceding discussion, it's evident that a decrease in placental thickness correlates with IUGR. Therefore, we can infer that below-average placental thickness ought to be considered as a marker for identifying IUGR.

Limitation of the study:

- Our study was covered a small sample size.
- There is not a universally accepted threshold for abnormal placental thickness in IUGR.
- A normal placental thickness doesn't guarantee a healthy pregnancy, as IUGR can still occur despite seemingly adequate thickness, emphasizing the necessity for further assessments.
- The accuracy of measurements depends on ultrasound technique and image quality, with variations in placental location or maternal factors potentially affecting the measurement.

Conclusions

The present study concluded that the Cerebro-Placental Ratio (CPR) is the superior predictor of IUGR in comparison to PI or RI values of MCA or UA. The PI of the umbilical artery has higher diagnostic accuracy as compared to the RI of umbilical artery and PI and RI of middle cerebral artery. Since PI and RI of MCA has least diagnostic accuracy in predicting IUGR, it is recommended to be used along with other Doppler indices in the setting of suspected IUGR.

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