ORIGINAL RESEARCH ARTICLE

Assessment of Accuracy of Color Doppler in Predicting FGR

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A B S T R A C T

Introduction: Prediction of risk is the cornerstone of antenatal care. Early prenatal diagnosis of FGR aids in decision making concerning the timing and the route of delivery thereby reducing the perinatal risk. Circulatory changes, reflected in certain fetal Doppler waveforms, predict adverse perinatal outcome. The present work aimed to study the waveforms and color flow of umbilical artery, uterine artery and middle cerebral artery and accuracy of Color Doppler in predicting FGR.

Material and Methods: A total of 100 clinically suspected FGR subjects were enrolled for the purpose of this study Ultrasound examination by Color Doppler carried out serially every three weeks starting from 30 weeks till delivery on Color Doppler machine Chi-square test and Independent Samples t-test was used for statistical analysis. Receiver-Operator curve analysis was performed to find out appropriate cut-off points for prediction of FGR.

Results: For color Doppler, the uterine artery RI was found to be most efficient from the point of view of early detection, it had a sensitivity of 84.6%, specificity of 82.9% and diagnostic accuracy of 84% even at 30 week interval. Uterine artery PI was found to be 76.9% sensitive, 82.9% specific and had 79% diagnostic accuracy at 30 weeks. Umbilical artery RI was found to be 80% sensitive, 74.3% specific and had a diagnostic accuracy of 78% at 30 weeks whereas Umbilical artery SD ratio was 70.8% sensitive and 65.7% specific and had a diagnostic accuracy of 69% at 33 weeks interval. MCA RI had only 60% sensitivity and 71.4% specificity at 36 weeks interval whereas MCA PI had 66.2% sensitivity and 68.6% specificity at 36 weeks interval. MCA PSV was not found to be a useful tool as it did not produce a significant difference between two groups.

Conclusion: Doppler measurements for uterine artery showed higher efficacy as compared to umbilical artery and middle cerebral artery findings. Among different umbilical artery measurements, umbilical artery RI was observed to be the most efficient even at early stage (30 weeks). The findings in this study suggested Color Doppler findings have their significance for finding FGR even at the earliest stage (30 weeks).

Key words: Doppler Ultrasound; Fetal Growth; Perinatal Outcome

INTRODUCTION

Introduction of Doppler ultrasound in medicine has offered a great advantage. The first Doppler ultrasound study of the fetus was reported by Fitzgerald DE, Drumm JE in 1977.[1] Nowadays, Doppler ultrasound velocimetry of uteroplacental umbilical and fetal vessels has become established method of antenatal monitoring, allowing the noninvasive assessment of fetal circulation. Its indices provide important information on the hemodynamics of the vascular area under study. Circulatory changes, reflected in certain fetal Doppler waveforms, predict adverse perinatal outcome.[2]

Prediction of risk is the cornerstone of antenatal care. Early prenatal diagnosis of FGR aids in decision making concerning the timing and the route of delivery thereby reducing the perinatal risk. Ultrasound evaluation of fetal growth and impedance to blood flow in fetal vessels are the cornerstone for diagnosis, prognosis and management.[3] The present work aimed to study the waveforms and color flow of umbilical artery, uterine artery and middle cerebral artery and accuracy of Color Doppler in predicting FGR.

MATERIAL AND METHODS

A total of 100 clinically suspected FGR subjects were enrolled for the purpose of this study from the departments of Obstetrics and Gynecology, Radiology and Pediatrics, Era's Lucknow Medical College and Hospital, Lucknow after informed consent in patient's language. The study was carried over a period of 18 months. This study was approved by Institutional Review Board and Institutional Ethical Committee. Women with singleton pregnancies with fundal height being less than the period of gestation by 4 weeks or more and women with certainty of last menstrual period with previous 3 menstrual cycles (after withdrawal of oral contraceptive pills) were included in the study. Women with Congenital malformations of the fetus were excluded

from the study. A detailed history and examination was done as per the proforma. Ultrasound examination by Color Doppler carried out serially every three weeks starting from 30 weeks till delivery on Color Doppler machine LOGIQ-5-GE machine using 3.5 MHz probe after getting the PNDT forms F and G duly explained and signed by the doctor and the patient. Subsequently confirmation of FGR was done by assessing the newborn parameters for growth restriction.

Doppler ulrasound was performed using the macro convex probe (3-5 MHz). 4 MHz ultrasound with pulsed wave Doppler mode and color flow mapping with simultaneous real-time B-mode ultrasound imaging was used to locate and record the umbilical, uterine and middle cerebral artery waveforms.

The recordings were made with an angle of insonation being 30-60 degrees and when at least 4 waves of equal height appeared on the screen. Findings were recorded under Color Doppler as per the designed proforma and tabulated.

STATISTICAL ANALYSIS

After collection of data the clinical data was correlated with radiological findings using statistical package for social sciences version 15.0. Chi-square test was used to compare the proportions while Independent Samples "t"-test was used to compare the parametric variables in two groups. Receiver-Operator curve analysis was performed to find out appropriate cut-off points for prediction of FGR.

RESULTS

Color Doppler examination involved assessment of blood flow in umbilical, uterine and middle cerebral arteries (table-1).

SN	Time interval	Non-FGR Group (n=35)				FGR Group (n=65)				Statistical Significance	
		Mean	SD	95%CI		Mean	SD	95%CI		"t"	"p"
				Lower	Upper			Lower	Upper		
1.	30 wk	0.66	0.05	0.01	0.64	0.75	0.10	0.01	0.72	4.975	<0.001
2.	33 wk	0.69	0.11	0.02	0.65	0.81	0.18	0.02	0.76	3.616	<0.001
3.	36 wk	0.61	0.07	0.01	0.58	0.70	0.12	0.01	0.67	4.504	<0.001
4.	39 wk	0.65	0.08	0.01	0.62	0.77	0.13	0.02	0.74	5.461	<0.001
Correlation with time		-0.152				-0.028					

Table-1: Umbilical Artery Resistive Index in two groups at different time intervals

SN	Time interval	Non-FGR Group (n=35)				FGR Group (n=65)				Statistical Significance	
		Mean	SD	95%CI		Mean	SD	95%CI		"t"	"p"
				Lower	Upper			Lower	Upper		
1.	30 wk	2.93	0.80	0.13	2.66	3.47	0.67	0.08	3.30	12.635	0.001
2.	33 wk	2.75	0.73	0.12	2.50	3.48	0.78	0.10	3.29	20.744	<0.001
3.	36 wk	2.61	0.73	0.12	2.36	3.21	0.64	0.08	3.05	17.970	<0.001
4.	39 wk	2.44	0.71	0.12	2.20	3.19	0.77	0.10	3.00	22.936	<0.001
Correlation with time		-0.208				-0.163					

Table-2: Umbilical Artery SD Ratio in two groups at different time intervals

SN	Time interval	Non-FGR Group (n=35)			FGR Group (n=65)			Statistical Significance	
		Mean	SD	95%CI	Mean	SD	95%CI	"t"	"p"
1.	30 wk	0.47	0.07	0.44-0.49	0.63	0.10	0.61-0.66	8.438	<0.001
2.	33 wk	0.43	0.07	0.41-0.46	0.63	0.10	0.61-0.66	10.272	<0.001
3.	36 wk	0.43	0.07	0.40-0.45	0.64	0.11	0.61-0.66	10.714	<0.001
4.	39 wk	0.42	0.07	0.40-0.45	0.64	0.11	0.61-0.66	11.041	<0.001
Correlation with time		r=-0.227			r=0.033			Overall r=-0.026	

Table-3: Resistive Index in two groups at different time intervals

SN	Time interval	Non-FGR Group (n=35)				FGR Group (n=65)				Statistical Significance	
		Mean	SD	95%CI		Mean	SD	95%CI		"t"	"p"
				Lower	Upper			Lower	Upper		
1.	30 wk	46.16	11.29	1.91	42.28	47.90	8.99	1.11	45.67	0.842	0.402
2.	33 wk	48.13	12.12	2.05	43.97	49.24	9.93	1.23	46.78	0.490	0.625
3.	36 wk	51.69	13.70	2.32	46.98	55.26	13.01	1.61	52.04	1.288	0.201
4.	39 wk	60.81	16.22	2.74	55.23	60.03	15.49	1.92	56.19	0.235	0.815
Correlation with time		0.360				0.369					

Table-4: Middle Cerebral Artery PSV in two groups at different time intervals

SN	Method	Gestational Age (Weeks)	Sens	Spec	PPV	NPV	Diagnostic Accuracy
1.	Uterine artery RI	30	84.6	82.9	90.2	74.4	84.0
2.	Uterine artery PI	30	76.9	82.9	89.3	65.9	79.0
3.	Umbilical artery RI	30	80.0	74.3	85.2	66.7	78.0
4.	Umbilical artery SD Ratio	33	70.8	65.7	79.3	54.8	69.0
5.	MCA RI	36	60.0	71.4	79.6	49.0	64.0
6.	MCA PI	36	66.2	68.6	79.6	52.2	67.0
7.	MCA PSV:		Values almost the same in all observed gestational ages, hence not explored further				

Table-5: Diagnostic Efficacy of Color Doppler techniques at different gestational ages

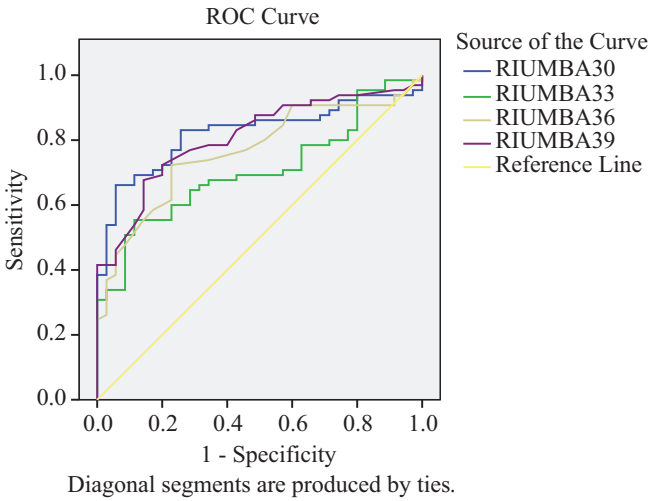

Figure-1: Receiver Operator Curve Analysis to find out appropriate cut-off of Umbilical Artery Resistive Index for FGR detection

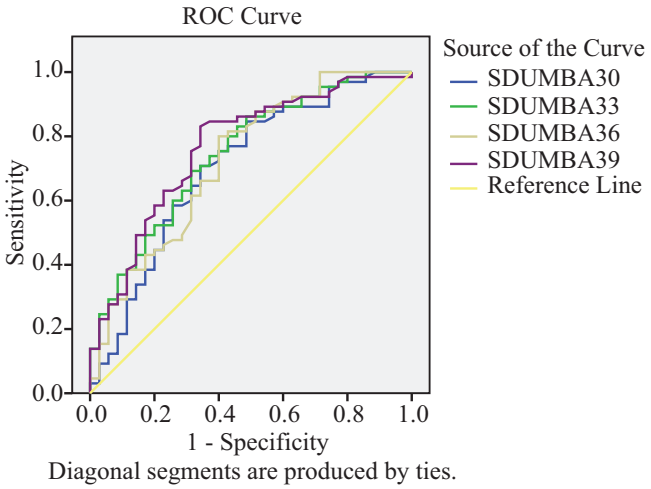

Figure-2: Receiver Operator Curve Analysis to find out appropriate cut-off of Umbilical Artery SD Ratio for FGR detection

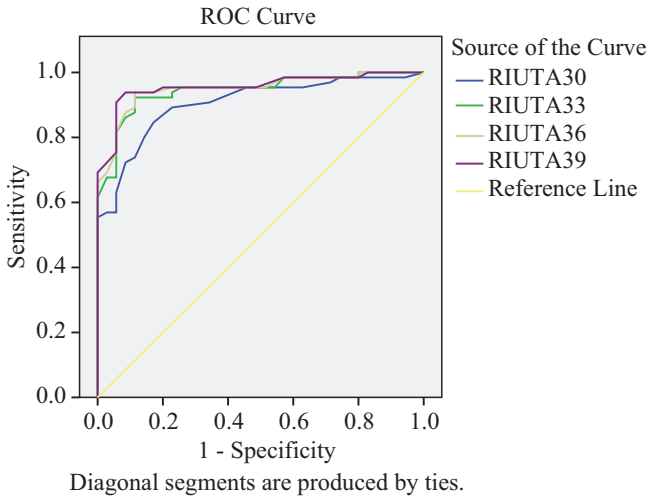

Figure-3: Receiver Operator Curve Analysis to find out appropriate cut-off of RI for FGR detection

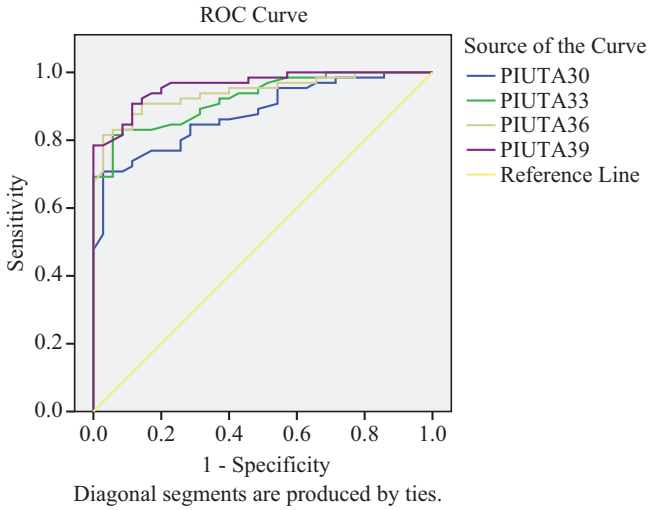

Figure-4: Receiver Operator Curve Analysis to find out appropriate cut-off of uterine artery PI for FGR detection

I. Umbilical Artery

Statistically significant difference in RI of two groups was seen at all time intervals (table 1). The mean RI in non-FGR group was maximum at 33 weeks (0.69±0.11) and thereafter it started showed a decline at 36 weeks and finally reached to 0.65±0.08 at 39 weeks. In FGR group, the mean RI was maximum at 33 weeks (0.81±0.18) and minimum at 36 weeks (0.70±0.12). At 39 weeks, the mean RI in FGR group was 0.77±0.13. A very weak to almost negligible inverse correlation between RI and time was observed in both the groups (figure-1).

Umbilical Artery Resistive Index for FGR detection

Receiver operator curve analysis to find out appropriate cut-off of Umbilical Artery Resistive Index for FGR detection (figure 1) showed maximum area under curve at 30 weeks (0.822) while minimum area under curve was seen at 33 weeks. At 30 week the cut-off value of 0.68 was predicted to

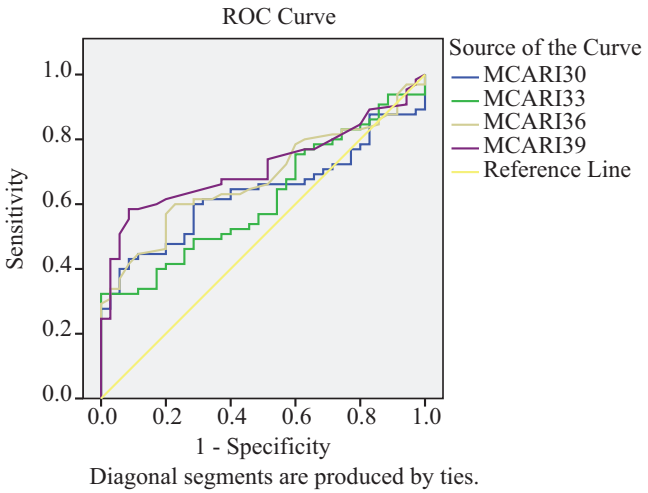

Figure-5: Receiver Operator Curve Analysis to find out appropriate cut-off of MCA RI for FGR detection

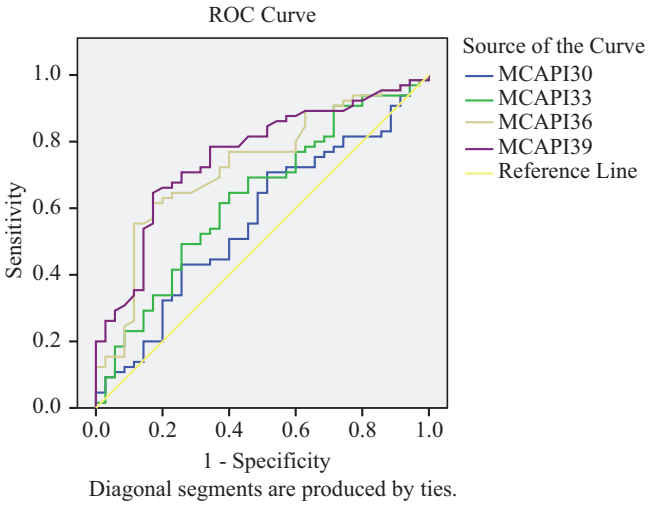

Figure-6: Receiver Operator Curve Analysis to find out appropriate cut-off of MCA PI for FGR detection

be 83.1% sensitive and 74.3% specific. Considering the early detectability and maximum accuracy, the 30 weeks cut-off was evaluated for diagnostic accuracy.

Table 2 shows umbilical artery SD ratio in two groups at different time intervals. Statistically significant difference in SD ratio of two groups was seen at all time intervals. The mean SD ratio in non-FGR group was maximum at 30 weeks (2.93±0.80) and thereafter it showed a decline to finally reach to 2.44±0.71 at 39 weeks. In FGR group, the mean SD ratio was maximum at 36 weeks (3.48±0.78) and minimum at 39 weeks (3.19±0.77). A very weak to almost negligible inverse correlation between SD ratio and time was observed in both the groups.

Receiver operator curve analysis to find out appropriate cut-off of Umbilical Artery SD Ratio for FGR detection (figure 2) showed maximum area under curve at 39 weeks (0.767) while minimum area under curve was seen at 30 weeks (0.706). At 33 weeks the cut-off value of 3.13 was predicted to be 70.8% sensitive and 65.7% specific.

Considering the early detectability, the 33 weeks cut-off was evaluated for diagnostic accuracy.

II. Uterine Artery

Mean resistive index in uterine artery amongst non-FGR group was found to be significantly lower as compared to FGR group at all gestational ages (table 3). In non-FGR group with the progression of labor, the RI was found to be decreasing mildly (r=-0.227) whereas in FGR group correlation with gestational age was almost negligible (r=0.033). In non-FGR group, minimum mean value was seen at 39 weeks (0.42±0.07; 95% CI 0.40-0.45) and maximum value was observed at 30 wks (0.47±0.07; 95% CI 0.44-0.49) while in FGR group minimum value was observed at 30 and 33 weeks (0.63±0.10; 95% CI 0.61-0.66) while maximum value was observed at 36 and 39 weeks (0.64±0.11; 95% CI 0.61-0.66).

Calculation of cut-off with the help of receiver-operator curve (ROC) analysis at different gestational ages is shown in figure 3.

Area under curve was maximum at 39 weeks (0.956) and minimum at 30 weeks (0.904). At 30 weeks the regressed value of >0.54 had 84.6% sensitivity and 82.9% specificity. At 33 weeks the cut-off value of >0.535 had 86.2% sensitivity and 91.4% specificity. At 36 weeks too the cut-off value of >0.535 had 86.2% sensitivity and 91.4% specificity. At 39 weeks the cut-off value of >0.525 had 90.8% sensitivity and 94.3% specificity.

As the cut-off values at different time intervals had adequate sensitivity and specificity, the value that can differentiate earliest *i.e.* at 30 weeks time interval was tested for diagnostic efficacy in current series.

Receiver operator curve analysis showed maximum area under curve at 39 weeks (0.962) while minimum area under curve was seen at 30 weeks (figure 4). At 30 weeks the cut-off value of 1.03 was predicted to be 76.9% sensitive and 82.9% specific. At 33 wk the cut-off value of 0.905 was regressed to be 83.1% sensitive and 91.4% specific. At 36 weeks the cut-off value of 0.96 was regressed to be 83.1% sensitive and 94.3% specific. The 39 weeks cut off value of 0.925 was found to be 84.6% sensitive and 91.4% specific.

Considering the early detectability and adequate accuracy, the 30 weeks cut-off was evaluated for diagnostic accuracy.

III. Middle Cerebral Artery

Statistically significant difference in Middle Cerebral Artery Resistive Index in two groups was seen at all time intervals (table 3). The mean RI in non-FGR group was maximum at 33 weeks (0.91±0.15) and thereafter it showed a decline to finally reach to 0.83±0.10 at 39 weeks. In FGR group, the mean RI was maximum at 33 weeks (1.04±0.30) and minimum at 36 weeks (0.95±0.26). A very weak to almost negligible inverse correlation between RI and time was observed in both the groups.

Receiver operator curve analysis showed maximum area under curve at 39 weeks (0.716) while minimum area under curve was seen at 30 weeks (0.646) (figure 5). At 36 weeks the cut-off value of 0.86 was predicted to be 61.6% sensitive and 71.4% specific.

The 36 weeks cut-off was evaluated further for diagnostic

accuracy.

Receiver operator curve analysis showed maximum area under curve at 39 weeks (0.757) while minimum area under curve was seen at 30 weeks (0.565) (figure 6). At 36 weeks the cut-off value of 1.88 was predicted to be 67.7% sensitive and 65.7% specific. The 36 weeks cut-off was evaluated further for diagnostic accuracy.

No statistically significant difference between two groups was observed as regards PSV at different time intervals (table 4). The mean PSV in both the groups was minimum at 30 weeks and maximum at 39 weeks. In both the groups a mild positive correlation between time and PSV was observed. As no significant differences were observed between two groups at different time intervals, hence they were not further explored.

Table 5 shows diagnostic efficacy of color doppler techniques at different gestational ages. The uterine artery RI was found to be most efficient from the point of view of early detection, it had a sensitivity of 84.6%, specificity of 82.9% and diagnostic accuracy of 84% even at 30 week interval. Uterine artery PI was found to be 76.9% sensitive, 82.9% specific and had 79% diagnostic accuracy at 30 weeks.

Umbilical artery RI was found to be 80% sensitive, 74.3% specific and had a diagnostic accuracy of 78% at 30 weeks whereas Umbilical artery SD ratio was 70.8% sensitive and 65.7% specific and had a diagnostic accuracy of 69% at 33 weeks interval.

MCA RI had only 60% sensitivity and 71.4% specificity at 36 weeks interval whereas MCA PI had 66.2% sensitivity and 68.6% specificity at 36 weeks interval. MCA PSV was not found to be a useful tool as it did not produce a significant difference between two groups.

DISCUSSION

In the present study, statistically significant difference in mean umbilical artery RI of two groups at all time intervals was observed. A very weak to almost negligible inverse correlation between RI and time was observed in both the groups. The 30 week RI >0.68 showed to be 80.0% sensitive, 74.3% specific with a positive predictive value of 85.2% and a negative predictive value of 66.7%. Overall diagnostic efficacy of the test was found to be 78%. North et al[4] reported a sensitivity of 47% and specificity of 91% for prediction of FGR. In present study, a relatively higher diagnostic efficacy was achieved, though the specificity was lower as compared to that of North yet the sensitivity was quite high. In the study of Kurmanavicius et al[5] the 95% percentile value of RI for umbilical artery resistive index at 30 weeks was found to be around 0.9.

Statistically significant difference in umbilical artery SD ratio of two groups was seen at all time intervals. A very weak to almost negligible inverse correlation between SD ratio and time was observed in both the groups. The higher sensitivity of the present study against lower specificity could be because we have taken a relatively relaxed criteria for inclusion, thereby increasing the sensitivity while compromising the specificity to some extent.

The 33 weeks SD ratio >3.13 showed to be 70.8% sensitive, 65.7% specific with a positive predictive value of 79.3% and a negative predictive value of 54.8%. Overall diagnostic efficacy of the test was found to be 69%.

The umbilical artery SD ratio was found to be 66.6% sensitive and 45.4% specific for adverse perinatal outcome by Lakhkar et al.[6] The present study reports a better efficacy as compared to that reported by Lakhkar et al.[6] Byun et al[7] reported that poor perinatal outcome was significantly increased in subjects with abnormal umbilical S/D ratio.

Among Color Doppler investigations, mean resistive index in uterine artery amongst non-FGR group was found to be significantly lower as compared to FGR group at all gestational ages. In non-FGR group with the progression of pregnancy, the RI was found to be decreasing. At 30 weeks RI value >0.535 was found to be 84.6% sensitive, 82.9% specific with a positive predictive value of 90.2% and a negative predictive value of 74.4%. Overall diagnostic efficacy was assessed to be 84%.

Kurmanavicius et al[5] in their study have shown resistive index to be decreasing slightly with increasing gestational age between 30 to 38 weeks of gestation. In present study too, a slight decrease in RI was seen in from 30 to 39 weeks. Our results are in close proximity with the results of Lakhkar et al[6] who reported a mean value of 0.49 in normal and 0.65 in abnormal pregnancy group at 28 weeks and 0.45 in normal and 0.64 in abnormal pregnancy at 34 weeks. In present study, at 30 weeks the mean value in non-FGR group was 0.47 and the same in FGR group was 0.63. The value decreased to 0.42 at 39 week in FGR group but in FGR group it was found to be 0.64 showing a slight increment. Dugoff et al[8] in their study showed that women with a high uterine artery mean RI (≥75th percentile) even at first trimester were 5.5 times more likely to have IUGR as compared to lower uterine artery mean RI. Chung et al[9] that a uterine artery RI value >0.6 between 26 to 28 weeks' gestation was an evidence of abnormal Doppler velocimetry and had an increased incidence of abnormal pregnancy including FGR.

In a study by Gomez et al[10] sequential changes in uterine artery blood flow pattern between the first and second trimesters of gestation in relation to pregnancy outcome were studied. They observed that mean uterine artery PI showed a significant linear decrease within each of the two intervals considered. In present study too, in the non-FGR group, a linear decrease in PI was seen (r=-0.408). They showed that compared with pregnancies with a normal outcome, complicated pregnancies showed a significantly higher mean PI in each of the two intervals studied. In present study too, at each time interval the mean PI of FGR group was found to be significantly higher as compared to that of non FGR group ($p<0.001$). Lakhkar et al[6] too have showed a significant difference in mean PI of non-FGR and FGR groups. In their study too mean PI in normal pregnancy group showed a continuous decrease from 28 weeks to 38 weeks while in FGR group the mean PI remained almost stable as in our study. Llurba et al[11] showed that PI had a sensitivity of 73% in detection of IUGR. In present study, we found a sensitivity

of above 76% for 30 week PI value. Olofsson et al[12] in their study too showed that uterine artery PI was significantly more often abnormally high in the pregnancy associated with FGR.

For Middle cerebral artery statistically significant difference in RI of two groups was seen at all time intervals. A very weak to almost negligible inverse correlation between RI and time was observed in both the groups. The 36 weeks RI >0.86 showed to be 60.0% sensitive, 71.4% specific with a positive predictive value of 79.6% and a negative predictive value of 49.0%. Overall diagnostic efficacy of the test was found to be 64%.

The 95th percentile MCA RI at 36 week as obtained by Tarzamni et al[13] was obtained to be 0.88 which is too close to the calculated cut-off value in present study. Kurmanavicius et al[5] too reported a 95th percentile value above 0.81 for MCA RI, thereby indicating that all these findings were suggestive of a similar pattern.

Statistically significant difference in PI of two groups was seen at all time intervals except at 30 weeks. A weak negative correlation between time and PI was observed in non-FGR group whereas in FGR group the correlation was almost negligible. It was observed that the differences between two groups were maximum at 39 weeks.

The 36 weeks PI >1.88 showed to be 66.2% sensitive, 68.6% specific with a positive predictive value of 79.6% and a negative predictive value of 52.2%. Overall diagnostic efficacy of the test was found to be 67%.

Tarzamni et al[14] reported a 90th percentile value of MCA PI at 36 weeks to be 2.20 which is well above the cut-off level in the present study. However, in present study it had a limited success for both resistance index and pulsatility index. It emerged as a late marker for FGR.

Middle cerebral artery PSV did not show a significant difference between two groups, hence it was not explored further. Mari G et al[15] observed that low MCA-PI.MCA-PSV might be valuable in clinical assessment of FGR fetuses that have abnormal UA Doppler. Similar views have been expressed by Qahtani et al.[16]

The outcome in terms of mode of delivery revealed a significantly higher incidence of caesarean delivery in FGR group as compared to non-FGR group. The reason for this could be imminent fetal distress. Though the proportion of FGR babies admitted to NICU was significantly higher as compared to non-FGR group, yet no significant difference was observed between two groups in terms of neonatal death. This indicates that with prognosis of FGR and adequate availability of hospital facilities, the FGR babies could be managed perinataly for a better outcome.

However, the utility of Color Doppler findings especially for uterine artery showed a promising efficacy at early gestational age of 30 weeks itself. The utility of MCA findings could not be of much use as they detect only late abnormalities and that too with only a limited precision. Umbilical artery resistive index was also a promising marker at early gestational age.

CONCLUSION

Doppler measurements for uterine artery showed higher efficacy as compared to umbilical artery and middle cerebral artery findings. The uterine artery RI was found to be 84.6% sensitive and 82.9% specific even at 30 weeks. Among different umbilical artery measurements, umbilical artery RI was observed to be the most efficient even at early stage (30 weeks). The findings in this study suggested Color Doppler findings have their significance for finding FGR even at the earliest stage (30 weeks). In present study we observed that the cut-off values obtained by us were in close proximity with the findings in other studies yet a normative database preparation is essential to obtain more precise results.

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