Original Research Article

Predicting IUGR by Uterine and Umbilical doppler: Though Old but Gold

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Abstract-

Introduction- The uterine and umbilical artery Doppler interrogation is an established non-invasive tool for evaluation of placental blood flow in pregnancy. The doppler studies have huge potential in detecting placental insufficiency which increases the risk of complications like preeclampsia, intrauterine growth-restriction (IUGR).This leads to early prediction and better surveillance, which ultimately results in reduction of maternal and perinatal mortality. **Objective-** This study was aimed to evaluate and compare the uterine and umbilical artery Doppler indices for early prediction of IUGR. **Method-** This prospective observational study was conducted over one year on 100 low-risk and 50 high-risk singleton pregnancies. All antenatal women were subjected to screening Doppler studies between 21-25 weeks and 31-35 weeks and followed up for subsequent development of IUGR and other pregnancy outcomes. **Results**: Out of the 150 study population, 19 mothers delivered IUGR fetus with incidence of 12.67% (5% in low-risk and 28% in high-risk women). 48 study participants had abnormal Doppler values; 43 had uterine artery and 17 had umbilical artery Doppler abnormality. 12 women had both uterine and umbilical artery Doppler abnormalities, out of these 9 developed IUGR. Out of 5 women who had bilateral persistent uterine artery diastolic notches, 3 delivered IUGR baby. For predicting IUGR in second trimester, the right uterine RI was most sensitive with highest NPV and right uterine PI was most specific. The PPV of PI of right uterine and umbilical artery was highest during the time. For IUGR prediction in third trimester, all Doppler parameters were highly specific and had good NPV. The sensitivity of all the parameters was low, the highest being 37% for left uterine RI and S/D. The PPV of umbilical artery RI (83%) was significantly higher than others. In both the trimesters the sensitivity, specificity and NPV of all the Doppler parameters was similar. The combined abnormal uterine and umbilical artery Doppler reveals a higher sensitivity (47.37%), NPV (92.81%) and PPV (75%), thus a better predictor of IUGR. **Conclusion**: The Doppler velocimetry is a useful tool for placental circulation surveillance especially in high-risk pregnancies. It is recommended to perform second trimester Doppler meticulously for early prediction and timely intervention in high-risk pregnancy. The second trimester uterine artery RI, persistent uterine artery diastolic notch, combined Doppler abnormalities of both arteries has good predictive value for growth restriction.

Keywords- uterine artery doppler, umbilical artery Doppler, IUGR, pulsatility index, resistive index.

Introduction

Despite recent advances in antenatal care, fetal growth restriction is still prevalent in about 10% of pregnancies [1]. Although definition is controversial but in most literature, birth weight below the 10th percentile for gestational age with a pathologic restriction of fetal growth is accepted as IUGR [2]. Early prediction of at risk fetus may allow focussed antenatal surveillance and optimally timed delivery, avoiding serious complications [3] and improving pregnancy outcome. In the absence of secondary preventive treatment that reverses the disease process once started, screening of intrauterine growth restriction (IUGR) has been a major research topic in contemporary obstetrics as it is a significant cause of perinatal mortality.

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The trophoblastic invasion results in remodelling of the spiral arteries into dilated, inelastic, low resistance vessels supplying huge amounts of blood to the placenta and the developing fetus in the early pregnancy.This physiological process is responsible for the development of a functional utero-placental circulation [4,5]. Impaired trophoblastic invasion of the maternal spiral arteries is associated with increased risk for subsequent development of complications of impaired placentation like intrauterine growth restriction, pre-eclampsia and placental abruption.

Fitzgerald and Drumm [6] and McCallum et al [7] first described the application of doppler studies in Obstetrics. FitzGerald and Drumm [6] observed that the shape of the blood-velocity waveform in Doppler ultrasound will change with conditions affecting the efficiency of blood supply and the method should be useful in assessing such conditions of impaired placentation. Subsequently, a number of screening studies involving evaluation of impedance to flow in the uterine and umbilical arteries have examined the potential value of Doppler in identifying pregnancies at risk of the complications of pathological placentation [8].The non-invasive Doppler interrogation of the uterine and umbilical arteries gives information on utero-placental and feto-placental circulation respectively [9]. A high mean resistance greater than 95th percentile for RI or PI in both arteries, persistence of diastolic notch in uterine

artery or absent or reversed end diastolic flow in umbilical artery depict abnormal Doppler waveforms, an indicator of at risk pregnancy for the complication of impaired placentation (IUGR).

Abnormal uterine and umbilical artery Doppler velocimetry in IUGR and adverse pregnancy outcome is well established [10-12]. Reference values of normal uterine artery Doppler indices and umbilical artery Doppler indices are well established in developed countries [13-18] but there is paucity of data in uterine artery and umbilical artery velocimetry in India. In this study we sought to determine the PSV, S/D ratio, RI, and PI values in uterine and umbilical arteries among healthy and high-risk pregnant women with singleton gestation, and to determine if there is any relationship between the Doppler indices and development of IUGR.

Material and Method

An observational and prospective study was conducted from March 2019 to February 2020 in our tertiary care centre. After obtaining the requisite ethical clearance a total of 150 Antenatal mothers with singleton pregnancy were enrolled in the study. A pragmatic sample size was calculated depending on the availability of logistics, resources and limited study period. They were divided in two groups after applying following inclusion and exclusion criteria.

Group I: 100 healthy singleton antenatal mothers.

Inclusion criteria

Antenatal mothers with singleton pregnancy

Exclusion criteria

1. Pre-existing medical disorders like Diabetes, renal disease, Epilepsy, Thrombophilia, hypertension
2. Hypertension in Previous pregnancy
3. Extreme of ages (>35 years or < 20 years)
4. Patient with congenital anomaly of fetus
5. Multiple gestations
6. Patients with unreliable LMP details and not confirmed by early ultrasound

Group II: 50 antenatal mothers with high-risk pregnancy

Inclusion criteria

1. History of IUGR, Abruptio placentae, still birth, preeclampsia or eclampsia in previous pregnancy,
2. Pre-existing medical disorders like Diabetes, renal disease, Epilepsy, Autoimmune disease, Thrombophilia, and Hypertension
4. Preeclampsia or pregnancy-induced hypertension (PIH) in present pregnancy
5. Extremes of age (>35 years or < 20 years).

Exclusion criteria

1. Patient with congenital anomaly of fetus
2. Multiple gestations
3. Patients with unreliable LMP details and not confirmed by early ultrasound

A pre-structured proforma with all the required details was filled with observations throughout the pregnancy of the study participant. Ultrasound examination was performed at 21-25 weeks and again at 31-35 weeks for both groups and uterine and umbilical artery Doppler values were recorded. All these cases were kept under surveillance for development of IUGR and other outcomes till confinement and managed according to standard protocols.

The parameters to be studied in doppler are a) Peak Systolic velocity (PSV) b) Resistive index (RI): S-D/S(S=Peak Systolic velocity D=End diastolic velocity) c) Pulsatality index (PI): S-D/mean frequency shift d) Systolic to diastolic ratio(S/D) = Systolic peak velocity/End diastolic velocity. The persistence of early diastolic notch in uterine arteries was also documented.

The uterine artery doppler was considered abnormal if PI and RI were >95th percentile for that gestation or there was persistence of early diastolic notch beyond 23 wks. Similarly umbilical artery doppler was taken to be abnormal if PI, RI and S/D was >95th percentile for that gestational age. The normal Doppler parameters for gestational age were defined by using standard reference charts from Callen's Ultrasonography in Obstetrics and Gynaecology [19] (Sixth edition, Appendix D, page 1204).Apart from the above-mentioned parameters we took uterine artery PI >1.45 in second trimester [20] and uterine artery S/D ratio above 2.6 in third trimester as abnormal [21].The technique for obtaining uterine artery and umbilical artery Doppler waveforms was as per ISUOG guidelines [22].

IUGR newborns were defined as those whose weight was below 10th centile of the average of the weight for that gestational age [23,24].

A comparative analysis of sensitivity, specificity, PPV and NPV ofsecond trimester RI, PI of both uterine arteries and PI of Umbilical artery was done for predicting IUGR. Similar comparative analysis of all thethird trimesterparameters (i.e., RI, PI and S/D) of both the umbilical and uterine artery was done for predicting IUGR.

Data was entered in Microsoft Excel Sheet. Descriptive analysis done by calculating percentages, confidence interval, mean with SD. Median and range. Appropriate statistical test applied as per the need of study. The statistical analysis was done by using the p-value (<0.5) with 95% confidence interval.

Results

In second trimester Doppler studies were done for 103 Patients in Group 1 and 51 Patients in Group 2. Subsequently 3 Patients of Group 1 and 1 Patient of Group 2 didn't come for 3rd trimester Doppler. Therefore, documentation of result, observation and analysis was done for 100 Patients in Group 1 and 50 Patients in Group 2.

Majority i.e., 91% of group 1 and 56% in group 2 were in age range of 20-29 years. Mean age in group 1 was 24.8years (range- 20-35 years) and mean age in group 2 was 26 years (range – 18-43 years).In both the groups majority were primigravida and belonged to Upper lower class (60%)as per Modified Kuppuswamy Scale.

The high-risk factors in 50 women of Group 2 were Gestational Diabetes Mellitus (GDM) (n=9), Pre-GDM (n=5), Gestational Hypertension (GHTN) (n=7), Chronic HTN (n=1), previous pregnancy loss (n=13), threatened abortion (n=1), GDM+ previous abortion (n=13), Extremes Of Ages i.e. <20 Or >35 years (n=4), Pre-GDM+ Chronic HTN (n=1), Hypertensive disorder of pregnancy (HDP) +GDM (n=2), Chronic HTN+ GDM+ Previous Abortion (n=1), Pre-GDM+ previous pregnancy loss(n=1) and GHTN+ Extremes Of Ages (n=1). Among 50 patients, 40 patients had single high-risk factors and 10 patients had more than 1 high-risk factor, commonest being GDM and Previous pregnancy loss.

The mean systolic and mean diastolic BP was 110.5 mmHg and 74.4 mmHg respectively in second trimester. The same in third trimester was 113.58 mm of Hg, 75.16 mm of Hg respectively. The mean gestational age at scan in second trimester in Group 1 was 23.2 weeks and in Group 2 was 23.56 weeks. The mean gestational age at scan in third trimester in Group 1 was 33.27 weeks and in Group 2 was 32.55 weeks.

The gestational age at the time of delivery varied from 34-40 weeks. The mean gestational age at the time of delivery was 38.48 weeks for Group 1 and 37.78 weeks for Group2. In our study, the third trimester examination and delivery interval varied from<1 week to 9 weeks. In Group 2, the delivery mostly occurred in < 1 week of Doppler examination; whereas in the Group 1 most of the patients delivered near term.

In total among 150 women, 19 mothers had IUGR fetus, thus the incidence of IUGR was 12.67% in our study. In low-risk group, incidence was 5% (n=5) and in high-risk incidence was 28% (n=14).

We did retrospective analysis of the Doppler parameters of these 19 women who delivered IUGR foetuses (Table 1).

Table1: Mean Doppler parameters in IUGR pregnancy in 2nd and 3rd trimester

	Mean Ut PSV*	Mean Ut PI	MeanUt RI	Mean Ut S/D	Mean U PSV*	Mean U PI	Mean U RI	Mean U S/D
2nd Trimester	**49.85**	0.92	0.52	2.20	36.19	1.16	0.64	3.07
Normal pregnancy	53.73	0.81	0.49	2.06	43.59	1.04	0.63	2.83
3rd Trimester	**57.23**	0.91	0.52	2.15	43.90	1.07	0.63	2.69
Normal pregnancy	59.28	0.73	0.45	1.9	47.9	0.87	0.55	2.32

Ut=Uterine artery , PSV-peak systolic velocity, PI - Pulsatility index, RI - Resistive Index, S/D - Systolic/ Diastolic ratio, U=Umbilical artery, *=cm/s

Out of 150 antenatal women, 48 (32%) had abnormal doppler values; 43 (28.67%) had abnormal uterine artery doppler and 17 (11.33%) had abnormal umbilical artery doppler. 12 women had both uterine artery and umbilical artery doppler abnormalities, out of these 9 developed IUGR. 7 patients had uterine artery persistent early diastolic notch between 24-25 weeks, 2 had unilateral notch and 5 had bilateral notches. Out of these 5 women who had bilateral notches 3 delivered IUGR baby. The uterine artery PI above 1.45 was observed in 4 fetuses, out of these one developed growth restriction later on. Only one woman had absent diastolic flow in umbilical artery in third trimester which subsequently gave birth to 1.5 kg IUGR baby.

For predicting IUGR in second trimester, the right uterine artery RI was most sensitive with highest Negative Predictive Value (NPV) and right uterine PI was most specific. The positive predictive value (PPV) of PI of right uterine and umbilical artery was highest. (Chart 1)

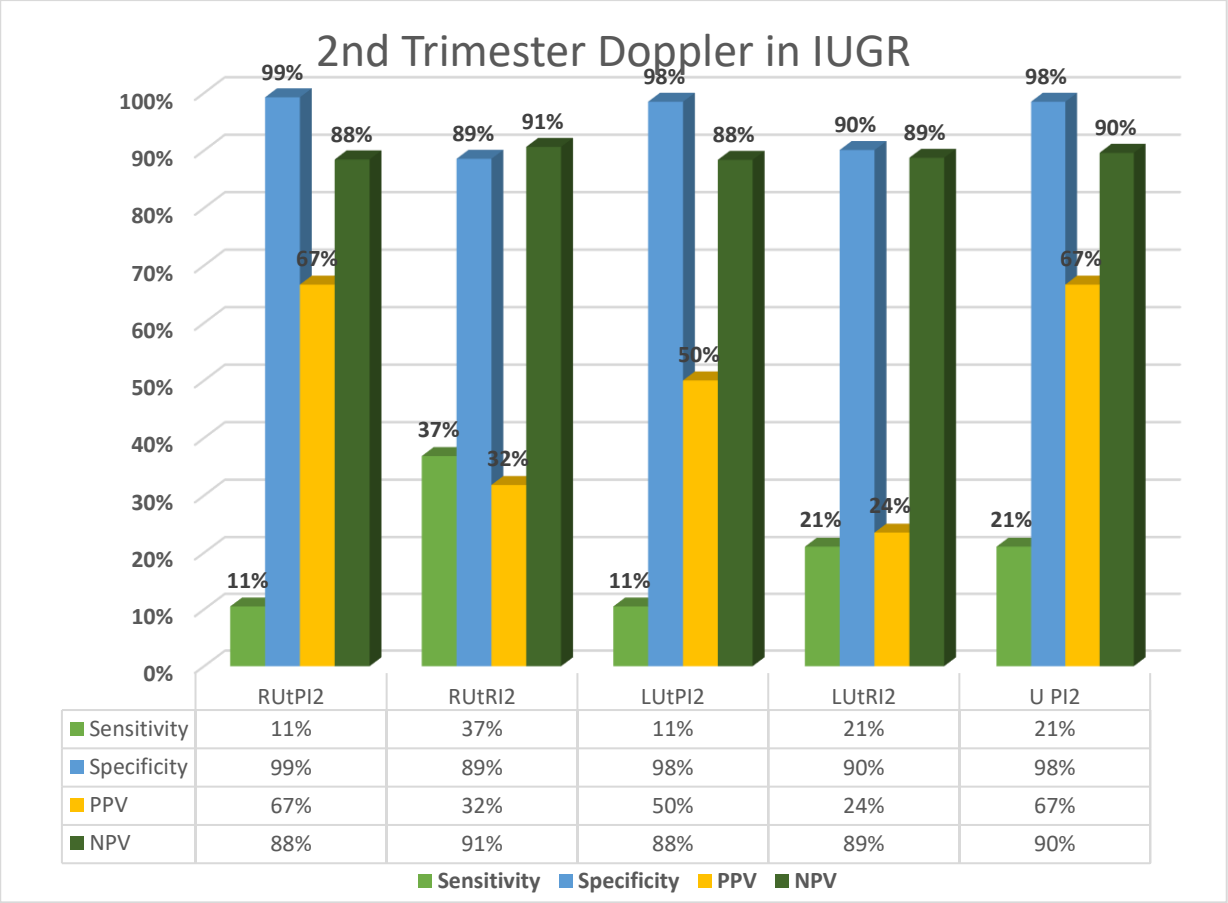

Fig 1: Comparative statistical analysis of 2nd Trimester Doppler parameters for Prediction of IUGR

Positive predictive value of uterine artery notch is 50%, so as a single predictor notch can be a better predictor of IUGR.

For IUGR prediction in third trimester, all doppler parameters were highly specific and had good NPV. The sensitivity of all the parameters was low, the highest being 37% for left uterine RI and S/D. The PPV of umbilical artery RI (83%) was significantly higher than others (Chart 2).

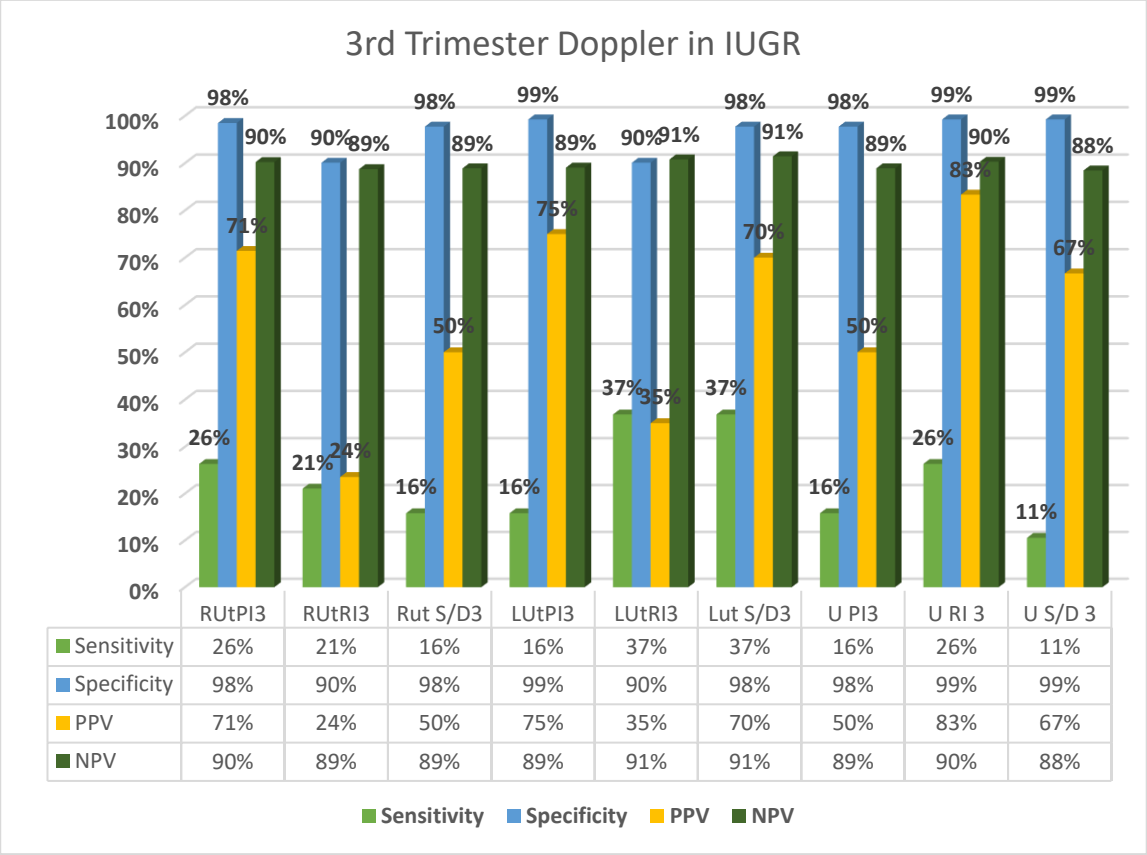

Fig 2:Comparative statistical analysis of 3rdTrimester Doppler parameters for Prediction of IUGR

In both the trimesters the sensitivity, specificity and NPV of all the Doppler parameters was similar, therefore it is advisable to perform second trimester Doppler for early prediction and timely intervention especially in high-risk pregnancy.

The statistical analysis of combined abnormal uterine and umbilical artery doppler reveals a higher sensitivity (47.37%), NPV (92.81%) and PPV (75%). The specificity (97.72%) was not much affected. It indicates that combined uterine artery and umbilical artery doppler is a better predictor.

Discussion

In this study most of the participants are between 20 to 29 years of age which is similar to the study population of T Nagar et al [3] where 55% patients were in age group of 21-25 years and 33% were between age group of 26-30 years. Whereas in J Adekanmi [25] study who evaluated Doppler indices in normal pregnancy, most (40%) were in the 30-40 years age range.

We have done second trimester doppler scan between 21-25 weeks and repeated again at 31-35 weeks. Mean gestational age was approximately 23rd week for second trimester scan and 32-33rd week for third trimester scan. The gap between two trimester scans was 9-10 weeks. Asthis much minimum time gap is required for change in impedance of the blood flow. In study of J Adekanmi [25] second trimester doppler scan was done between 21-25 weeks and repeated again at 31-35 weeks. P R Desai did two study on 50 patients having IUGR and 50 patients excluding PIH, polyhydramanios, gestational diabetes, heart disease, severe anaemia etc between 20-24 weeks and repeated 26-36 weeks for uterine artery Doppler [26]and umbilical artery Doppler[27].

In our study incidence of IUGR was 12.67% which is similar to study of Bewley et al (12.9%) [28].

The mean S/D, RI, and PI values of uterine artery in our study were almost similar to the findings of Lakhkar and Ahamed [15] of India, and mean PI values of Bahlmann et al [29]of Germany. The PSV, RI values of Right and left uterine are lower and PI values is almost similar to 2nd trimester findings of J Adekanmi et al [25]. S/D values in Right uterine artery was similar to this Adekanmi study [25] but left uterine artery S/D was higher in our study.

3rd trimester Uterine artery PI, S/D in high-risk pregnancy (n=50) were higher and PSV, RI values were lower in in our study in comparison to Adekanmi study [25]. Higher values of PI are seen in Brazilian study of Peixoto et al. [30] and Spanish study of Gσmez et al [14] compared to our study, whereas higher PI, RI, S/D values were seen in study of Oloyede and Iketubosin [31] in Lagos, Nigeria. These differences may be due to Socio- demographic factors of these countries or differences in study methodology.

The Umbilical artery Doppler indices in our study (PI, RI, S/D) are lower than Chanprapaph et al [13] of Thailand and Lakhkar and Ahamed [15] of India and lower RI than the Acharya et al [17].

The Uterine artery PI, RI, S/D ratio values reduced from second trimester to third trimester which is more statistically significant in normal pregnancy than in IUGR pregnancy which was similar to study done by P R Desai et al [26]. This physiological phenomenon is described by Sieroszewski P [32].The Umbilical artery Doppler PI, RI; S/D values too decrease from second trimester to third trimester as seen in our study as well as in P R Desai [27] importance of which is explained by Olofsson et al [33].

In our study mean uterine artery PI were higher in IUGR than normal pregnancy in both trimesters which explains the failure of physiological changes in uteroplacental flow leading to high risk of obstetrical complication (Schulman [34], Papageorghiou[35]). In our study mean Umbilical artery PI, RI, S/D is slightly higher in IUGR

than normal pregnancy in both trimesters which indicates failure to increase diastolic flow, also explained by Gudmundsson S and Marshal K[36]. Mean PSV of Uterine artery and Umbilical artery was lower in both trimesters in IUGR than normal pregnancy indicating failure to physiological changes.

Our study had higher specificity and higher positive predictive value in terms of IUGR (Table 2 and 3). These differences may be due to difference in the characteristics of the study population and study methodology. Also, our study was a time restricted study need larger study population to evaluate further.

Table 2. Comparison of Uterine artery Doppler screening studies to predict IUGR

Studies	Uterine artery Doppler Abnormal results	Gestational Age (weeks)	Sensitivity to predict IUGR (%)
Torres C and Raynor B et al37	PI>1.0,RI>.57,S/D>2.6,notch	2nd Trimester	16.70
Bewley et al. 199128	Mean RI > 95th centile	16–24	15
North et al. 38	RI > 0.57	19–24	50
Irion et al. 39	Mean RI > 0.57	26	29
Kurdi et al.40	RI >0.55 & bilateral notches	19–21	45
	Bilateral notches & RI > 0.55		
	or unilateral notch & RI > 0.65		
	or mean RI > 0.7		
Frusca et al.41	Mean RI > 0.58	20 & 24	43
Dhar et al.42	PI>95 th percentile	23-24	50
Albaiges et al.43	Mean PI > 95th	23	21
Harrington et al.44	RI > 95th or notches	20 & 24	32
T Nagar et al3	RI	26- 30	25
	S/D ratio		37.5
	Notch		50
current study	PI>95th percentile of ref value	21-25	11(RtUt)
			11(Lt ut)
	RI> 95thpercentile of ref value		37(Rtut)
			21(Rt Ut)
	Notch		16(Rtut)
			16(LtUt)

#trimester *IUGR in Previous studies was EFW

The statistical analysis of combined uterine and umbilical artery to predict IUGR reveals sensitivity of 47.37% and specificity of 97.73% which is concurrence with observation by T Nagar [3] study.

Table 3: Comparison of Umbilical artery Doppler screening studies to predict IUGR

Studies	Abnormal results	GA weeks	Sensitivity	Specificity	PPV	NPV
Beattie et al[45]	PI	34	32%	89%	12%	97%
	Resistance parameters		33%	88%	12%	97%
	S/D ratio		40%	84%	11%	97%
Gramellini et al[46]	PI	30-41	64%	90.70%	72.70%	86.70%
Goyal et al[47]	PI	>28weeks	41.30%	50	83.33%	41.37%
	S/D ratio		65.21%	57.40%	83.33%	41.37%
	RI		45.65%	78.57%	87.50%	23.91%
Lakhar et al[15]	PI	20, 28 & 34	58%	56.50%	35%	86.80%
	RI		58%	71.70%	35%	86.80%
	S/D ratio		75%	41.30%	25%	86.30%
T Nagar et al[3]	RI	26-30	42.86%	94.62%	37.50%	95.65%
	S/D ratio		25%	96.59%	40%	93.41%
Current study	PI	31-35	16%	98%	50%	89%
	RI		26%	99%	83%	90%
	S/D ratio		11%	99%	67%	88%

The positive predictive value of uterine artery diastolic notch was 50% which is greater than the other indices. Thus Notch probably is a better predictor of IUGR which is similar to opinion of T. Nagar et al [3].

Conclusion

In this prospective study we found that the uterine artery and umbilical artery doppler velocimetry is a potential tool for uteroplacental and fetoplacental surveillance especially in high-risk pregnancies. In high risk pregnancies the decline in value doppler indices in both arteries in the two trimesters should be monitored as there is less reduction in these women as compared to normal pregnancy. In both the trimesters the sensitivity, specificity and NPV of all the Doppler parameters was similar, therefore it is advisable to perform second trimester Doppler's for early prediction and timely intervention especially in high-risk pregnancy. The combination of uterine artery and umbilical artery Doppler is a better predictor for IUGR. The second trimester uterine RI and persistent uterine artery diastolic notch have good predictive value for growth restriction. The absent diastolic flow in umbilical artery in third trimester is useful for timely intervention and better perinatal outcome.

Author's Contribution:

SM- data collection, Interpreted the results **MB**-Interpreted the results, review of literature and manuscript preparation, **RS**-data collection, prepared first draft of manuscript; Critical revision of the

manuscript. **DM**-Concept of the study, Data collection, review of literature, Critical revision of the manuscript

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