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Uses of the Color Doppler of the Uterine Arteries in the Early Second Trimester for Prediction of the Intrauterine Growth Restriction

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ABSTRACT

Background: The introduction of sonography altered obstetrics practice by offering a window through which the fetus's anatomic structure could be assessed. Many investigations have found a link between second trimester uterine artery Doppler pulsatility and resistance indices (PI and RI) and the development of intrauterine growth restriction. There is an indication; however, that trophoblast invasion is greatest during the first trimester, when uterine artery blood flow can also be evaluated with a Doppler.

Aim of the work: To investigate the role of uterine artery Doppler in the prediction of intrauterine growth restriction during the early second trimester.

Patients and methods: A cross-sectional observational study on 100 pregnant women attending the Obstetric and Gynecology Outpatient clinic at Al-Azhar University Hospitals was done. A Doppler analysis of uterine artery flow velocimetry waveforms utilizing a continuous wave type was done. The results of the PI and the RI were registered and standard deviations were estimated.

Results: Uterine PI achieved significance for predicting IUGR at cutoff point ≥1.63 with sensitivity of 83% and specificity of 91.6% with PPV 54% and NPV 88%. While, uterine RI achieved significance for predicting IUGR at cutoff point ≥0.67 with sensitivity of 71.8% and specificity of 87.2% with PPV 47% and NPV 82%.

Conclusion: Abnormal UtA Doppler ultrasonography (elevated PI) in second trimester can predict IUGR among women with high risk factors which can be enhanced by biochemical tests.

Keywords: *Color Doppler; Uterine arteries; IUGR; Early second trimester.*

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INTRODUCTION

The uterine artery can be studied with Doppler ultrasonography to learn more about utero-placental blood flow. Because of trophoblastic invasion, the uterine artery creates a low-impedance flow during normal pregnancy. Hypoxemia and necrosis in the placental bed originate from the failure of normal trophoblastic invasion of spiral arteries, resulting in unfavorable maternal and newborn outcomes like IUGR, preeclampsia, placental abruption, and stillbirth.[1]

According to the data, insufficient trophoblast invasion has been connected to the continuation of resistive flow or abnormal uterine artery Doppler velocimetry in the late 2nd or 3rd trimester. The PI and RI of the uterine artery were described as effective tests for identifying women who are at risk

of preeclampsia, IUGR, or stillbirth in the 2nd trimester.[2]

The efficacy of Doppler velocimetry in predicting negative pregnancy results, on the other hand, is still being debated. While numerous researchers have found that uterine artery Doppler velocimetry is a beneficial noninvasive intrauterine method for identifying pregnancies that are prone to being complicated by IUGR or preeclampsia, others have found that it has a high false positive rate in an unselected group. In addition, there is no agreement on the optimum indicators or the optimal gestational age for screening.[3]

Prenatal care's overall purpose is to enhance pregnancy results. The discovery of effective prenatal monitoring methods, which could reduce the risk of unfavorable obstetric results, would have significant advantages for both the obstetrician and the obstetric patient in terms of informing resource allocation and administering preventative measures that would result in the birth of a healthy newborn. The Doppler examination's noninvasive nature could render it an effective screening tool for the prediction

of negative pregnancy results in otherwise low- risk patients.[4]

Doppler ultrasound is an extremely useful technique for managing high-risk pregnancies. By contrasting diastolic and systolic waveforms, direct evaluation of trophoblast invasion allows noninvasive assessment of the uteroplacental circulation.[5]

Sonographic estimated fetal weight below the 10th percentile for gestation age is classified as IUGR. IUGR is "one of the most common and difficult disorders in modern obstetrics," as per the American College of Obstetricians and Gynecologists. This classification is comprehensible given the diverse published criteria, low detection rates, few preventive or therapeutic choices, several related morbidities, and a higher risk of perinatal death linked to IUGR.[6]

In adulthood, suboptimal growth is connected to reduced intellectual performance and diseases like high blood pressure and obesity. Current clinical challenges in the therapy of IUGR involve accurately diagnosing the genuinely growth-restricted fetus, selecting suitable fetal monitoring, and optimizing birth time.[7]

The goal of this research was to see if uterine artery Doppler could predict intrauterine growth restriction in the early second trimester.

PATIENTS AND METHODS

A cross-sectional observational study on 100 pregnant women attending the Obstetric and Gynecology Outpatient clinic at Al-Azhar University Hospitals was done, divided into 3 groups (normal, SGA, and IUGR).

Inclusion criteria: Women in their early second trimester of pregnancy (from 16–22 weeks) and pregnant women with a history of hypertensive disorders in pregnancy, IUGR, or preterm labour.

Exclusion criteria: (a) Any pregnant woman who has a history of: diabetes mellitus, renal Diseases, connective tissue diseases, history of maternal consumption of smoking and alcohol, and heart diseases. (b) Multifetal pregnancy.

Al- Azhar University's academic and ethical committee gave their approval to the research. Each participant completed an informed written consent form acknowledging their willingness to undergo the surgery.

All Patients were subjected to:

Complete history taking involving: personal history, obstetric history, menstrual history, current history of any chronic diseases or medications, previous history of any medical condition, family history of any similar condition, history of allergy to any medication, and any surgical history

Examination: (a) General examination: Evaluation of vital signs, and measurement weight, height to calculate BMI. (b) Abdominal clinical examination: To evaluate the fundal level and gestational age, as well as any prior surgery scars, mass, discomfort, or rigidity, and any clinically visible pathology in the abdomen or pelvis.

Transvaginal ultrasound examination: All the patients had undergone a first trimesteric ultrasonographic measurement of the crown-rump length to ensure the gestation age and estimate a more specific due date as Hadlock et al 1984 stated that the crown-rump length in the 1st trimester of pregnancy is the most sensitive measurement.

Transabdomial uterine Doppler ultrasound approach

A curvilinear transabdominal transducer was placed about 2-3 cm within the iliac crests and guided to the uterus's lateral side. After that, every uterine artery was identified using color flow Doppler. The uterine artery was then crossed over the external iliac artery about 1 cm from the point where the pulsed wave Doppler was applied. As a result, Doppler velocities have been collected from the major uterine artery trunk as a result of this. A 2 mm Doppler sample gate was used. The smallest angle of insonation (<30∘) was used with caution.

At the very least, three comparable waves should be obtained, and the maximum systolic velocity should be greater than 60 cm/s after adjusting the insonation angle, confirming that the insonated vessel was the uterine arteries in their proximal section. The mean PI measurements of both the right and left arteries have been used to compute the average uterine artery PI. Measurements taken at the distal portions of the vessel show a low PI, but the cervical branches have higher PI values, which overestimate the chance of pregnancy problems.

Uterine artery Doppler has been conducted between 16 and 22 weeks gestation.
A PI of > 1.58 or the appearance of any diastolic notch was considered abnormal.
The results of the PI, the RI have been registered and standard deviations estimated.

PI = Peak systolic velocity – End diastolic velocity
Mean velocity

RI = Peak systolic velocity – End diastolic velocity

Peak systolic velocity

Follow-up:

The pregnant women had been followed up using the ordinary antenatal care program.

The three-transabdominal images required to measure the fetal biometry are: (1) HC and biparietal diameter: Transverse view of the head at the level of the septum cavum pellucidum. (2) AC: Transverse abdominal view at the stomach and umbilical vein level. (3) FL: Longitudinal view of the femur.

The EFW has been computed according to the Hadlock formula.

Serial measurement of fetal size four weeks apart starting from the 26th week gestation had been determined. The fetal size had been assessed by measurement of the AC and EFW. The resulted measurement and the exact gestational age (GA) had been put on the Customized Growth chart. A lower cut off of 10th centile and an upper cut off of 90th centile had been taken as limits for a normal fetal growth. The IUGR fetuses had been determined

when the measured (AC) and the EFW are less than the 10th centile on the Customized Growth chart.

The results of the PI and the RI of the uterine artery Dopplerin the 16th to 22nd week of gestational age have been plotted against the measured (AC) and the (EFW) after processing in the centile calculator.

Statistical Analysis:

SPSS 22.0 for Windows has been employed to collect, tabulate, and statistically analyze all of the data (SPSS Inc., Chicago, IL, USA). The Shapiro Walk test has been performed to determine if the data had a normal distribution. Frequencies and relative percentages have been employed to depict qualitative data. The difference between qualitative variables has been calculated using the Chi-square test ($\chi 2$) and Fisher exact as specified. For parametric data, mean ± SD (standard deviation) has been employed, and for non-parametric data, median and range have been used. For parametric and non-parametric parameters, the independent samples T test and the Mann-Whitney test have been employed to calculate the difference between quantitative variables in two groups. More than two dependent groups of normally distributed variables were compared using the one-way ANOVA test. The ROC curve was created to allow for the choice of test result threshold values and the comparison of various testing strategies. The Cantor technique was used to calculate areas under ROC curves and standard errors, which were then compared by employing the normal distribution, with correlations of data from the same instances corrected. Value of area under a ROC curve (AUC) indicates: 0.90 – 1 = excellent, 0.80-0.90 = good, 0.70-0.80 = fair; 0.60-0.70 = poor; and 0.50-0.60 = fail. At the point of maximal precision, the best cutoff point has been determined. P values of < 0.05 have been deemed significant.

RESULTS

		Studied patients (N=100)
Age (years)		
Mean ± SD		**24.1 ± 5.12**
Range		**18 - 30**
BMI (kg/m^2)		
Mean ± SD		**25.61 ± 2.84**
Gravida & parity	Primigravida	**40 (40%)**
	Multiparous	**60 (60%)**
Pregnancy outcome:	Normal	**61 (61%)**
	SGA	**23 (23%)**
	IUGR	**16 (16%)**

Table 1: Patient demographic data and pregnancy outcomes:

The patients aged between 18 – 30 years with mean 24.1 years and mean BMI 25.61 kg/m2. 40% of the patients were primigravida and 60% of the patients were multiparous. Most of the patients were normal (61%) followed by SGA (23%) and IUGR (16%) (Table 1).

	IUGR (N=16)	SGA (N=23)	Normal (N=61)	P
RI Mean ± SD	0.671 ± 0.138	0.611 ± 0.131	0.584 ± 0.115	**.075**
PI Mean ± SD	**1.63 ± 0.539**	**1.12 ± 0.285**	**0.935 ± 0.167**	**.000**

Table 2: Uterine artery Indices by Doppler of the studied patients among different groups

There have been significant differences between the three studied groups concerning uterine artery PI. Moreover, uterine artery RI was significantly greater in the IUGR group than in the normal group (Table 2).

	IUGR (N=16)	SGA (N=23)	Normal (N=61)	P
Biparietal diameter Mean ± SD	74.42 ± 4.53	75.77 ± 5.36	77.15 ± 3.86	**.105**
Abdominal circum. Mean ± SD	22.11 ± 3.92	23.23 ± 4.11	26.11 ± 3.68	**.002**
Femur length Mean ± SD	**54.88 ± 4.06**	**55.18 ± 3.98**	**56.9 ± 3.49**	**.058**

Table 3: Fetal biometry of the studied patients according to groups:

There have been significant differences between the three studied groups concerning abdominal circumference (Table 3).

	IUGR (N=16)	SGA (N=23)	Normal (N=61)	P
GA (weeks) Mean ± SD	37.33 ± 1.09	37.19 ± 1.11	37.8 ± 0.629	**.006**
Birth weight (kg) Mean ± SD	2.67 ± 0.565	2.98 ± 0.314	2.79 ± 0.438	**.039**
Apgar at 1 min Mean ± SD	6.49 ± 2.26	7 ± 1.54	7.32 ± 1.27	**.192**
Apgar at 5 min Mean ± SD	**8.81 ± 2.92**	**9.34 ± 1.09**	**9.75 ± 0.499**	**.043**

Table (4): Neonatal outcomes distribution among different groups:

There have been significant differences between the three studied groups concerning GA and Apgar at 5 min (Table 4).

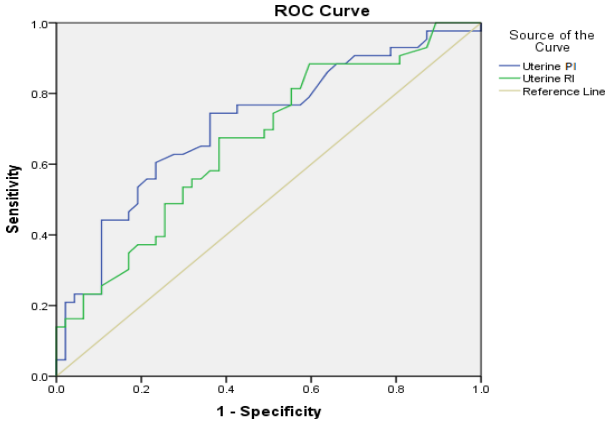

Fig. 1: ROC curve of uterine doppler indices for predicting IUGR.

Variables	AUC	S.E.	Cut off	Sig.	95% Confidence Interval
Uterine PI	.714	.055	1.63	.002*	**0.607 - 0.821**
Uterine RI	.679	.057	0.67	.017*	**0.554 - 0.777**
	Sensitivity	Specificity	PPV	NPV	
Uterine PI	83.2%	91.6%	54%	**88%**	
Uterine RI	**71.8%**	**87.2%**	**47%**	**82%**	

Table 5: Uterine doppler indices for predicting IUGR.

Uterine PI achieved significance for predicting IUGR at cutoff point ≥1.63 with sensitivity of 83.2% and specificity of 91.6% with PPV 54% and NPV 88%. While, uterine RI achieved significance for predicting IUGR at cutoff point ≥0.67 with sensitivity of 71.8% and specificity of 87.2% with PPV 47% and NPV 82% (Figure 1 and Table 5).

DISCUSSION

Analysis of our findings revealed that patients aged between 18 – 30 years with mean 24.1 years and mean BMI 25.61 kg/m^2. 40% of the patients were primigravida and 60% of the patients were multiparous.

In a study on the prognostication of preeclampsia or IUGR by 2nd trimester serum screening and uterine Doppler velocimetry, Audibert et al.[8] found that the existence of a uterine notch has been linked to a considerably greater danger of both preeclampsia and IUGR, and a PPV for IUGR of 50 and 43%, respectively, was seen when a bilateral uterine artery notch was combined with a reduced hCG level or a

greater AFP level. According to the study, combining serum indicators with abnormal uterine Doppler ultrasonography enhances the detection of pregnant women at risk for problems, including IUGR.

Diastolic notching seems to be a prevalent characteristic of UtA Doppler waveforms in the research of Elwakel et al.[9]. [10] Notching, comparable to UtA PI, diminishes with advancing gestation age till 25 gestational weeks and then stays steady. Early diastolic notching in the UtA displays lower diastolic velocities relative to those in later diastole and demonstrates vascular flexibility.[11]

Generally, notching has a poor PPV for pre-eclampsia and FGR, despite having a 97 % NPV for both conditions in a high-risk research population. Because of the low reproducibility of UtA notching, it has been excluded from contemporary studies in this field, with a tendency toward including more objective measurements of vascular resistance, favoring PI.[9]

Adefisan et al.[4] concluded that Doppler velocimetry of the uterine artery in the late 2nd trimester has limited potential to anticipate unfavorable pregnancy results in a low-risk cohort.

On the other hand, we further divided studied cases according to the occurrence of IUGR or not into three groups: the IUGR group, other outcomes group, and the normal group, and we found that there were significant differences among the three tested groups concerning uterine artery PI. Moreover, uterine artery RI was significantly greater in the IUGR group than in the normal group. Furthermore, we found that there were significant differences among the three tested groups concerning Apgar score at 5 min. There have also been significant differences between the three studied groups concerning abdominal circumference, which decreased among the IUGR group.

Axt-Fliedner et al.[12] found the usefulness of uterine artery Doppler in anticipating serious pregnancy problems in a high-risk cohort. In that research, 56 pregnant women have been assessed, with singleton "risk" pregnancies occurring between 19 and 26 weeks of pregnancy. They indicated that using Doppler ultrasonography of the uterine artery in the 2nd trimester of pregnancy to anticipate abnormal results in high-risk pregnancies is a beneficial approach.

Sankaran and Kyle[13] looked at the link between uterine artery Doppler measurement and birth weight between 19 and 23 weeks. They looked at 2035 pregnancies that had been scanned between the 19th and 23rd pregnancy weeks. They found that uterine artery Doppler screening for FGR was less sensitive than preeclampsia.

Konje et al.[14] examined alterations in uterine artery flow volume in IUGR pregnancies and compared them to pregnancies of AGA. At 20 and 24 weeks' pregnancy, they examined uterine artery Doppler velocimetry in 32 women who were pregnant with IUGR risk factors and 25 women who were pregnant without IUGR risk factors. The researchers hypothesized that the diameter and volume of the proximal uterine artery change during pregnancy and discovered significant differences between AGA and IUGR pregnancies. Such alterations began early in pregnancy and became more pronounced as the pregnancy progressed.

Interestingly, we demonstrated that uterine PI achieved significance for predicting IUGR at cutoff point ≥1.63 with sensitivity of 83% and specificity of 91.6% with PPV 54% and NPV 88%. While, uterine RI achieved significance for predicting IUGR at cutoff point ≥0.67 with sensitivity of 71.8% and specificity of 87.2% with PPV 47% and NPV 82%.

We disagree with the results of Adefisan et al.4, who discovered a low sensitivity for prediction of IUGR utilizing RI and PI of 23.1% and 0%, respectively. In a low-risk pregnancy, it was also discovered that PI in the 2nd trimester had no link to the risk of eventual IUGR. The observed RI sensitivity (23%) is in the range of 11–53% observed by Schwarze et al.15 in a similar low-risk cohort utilizing similar RI cutoffs. Such results are consistent with a meta-analysis by Chien et al.16, who reported that uterine artery Doppler ultrasonography is a poor indicator of IUGR and perinatal mortality in low- risk women.

According to Adefisan et al.[4], RI and PI have a sensitivity of 60.0% and 20.0%, respectively, for predicting low neonatal birth weight. In an unselected sample, the sensitivity of PI for the prediction of poor birth weight (20.0%) was equal to the value of 21% published by Lopez-Mendez et al.[17], but less than the value of 45.4% published by Verma and Gupta[18]. In a huge prospective group study examining the role of 2nd trimester uterine artery Doppler tests in the prediction of SGA newborns, low-risk women were found to have poor sensitivity to RI and PI when applying comparable cutoffs. They came to the conclusion that uterine artery Doppler investigations were ineffective in identifying SGA in pregnant women.

Velauthar et al.[20] conducted a recent meta-analysis to assess the efficacy of UtA Doppler analysis in the 1st trimester in predicting FGR and pre-eclampsia. Eighteen studies with a total of 55 974 women have been assessed, 15 of which included women with low-risk pregnancies. To determine abnormal flow velocity waveforms, UtA RI or PI of at least 90th centile and the existence of notching (unilateral or bilateral) have been utilized. Because there have been just two investigations examining the role of UtA notching, pooling values for pre-eclampsia prediction was not possible for this factor. With a sensitivity of 26.4 and 47.8%, an abnormal UtA PI in the 1st trimester was indicative of pre-eclampsia and early-onset pre-eclampsia, respectively. Early-onset FGR was linked to a 39.2% higher sensitivity, whereas FGR was expected to be 15.4%. For placental abruption, the sensitivity was 44.4%. This meta-

analysis found that detection of unfavorable pregnancy outcomes using UtA Doppler analysis in the 1st trimester was similar to detection based solely on maternal risk variables. The authors found no considerable alteration in the estimations for secondary results with notching or any negative results with waveform anomalies after including investigations in high-risk ladies, despite the fact that the studies assessing early-onset illness had been conducted in ladies who were thought to be at low risk during pregnancy.

Cnossen et al.[21] discovered that in low-risk females in the second trimester, an elevated pI with notching was the strongest predictor of IUGR (positive probability ratio of 9.1, 95% CI 5.0–16.7; negative probability ratio of 0.89, 95% CI 0.85–0.93). In low-risk females in the second trimester, elevated pI (positive probability ratio 13.7, 95 % CI 10.3–16.9; negative probability ratio 0.34, 95% CI 0.23–0.48) or elevated pI with notching (positive probability ratio 14.6, 95% CI 7.8–26.3; negative probability ratio 0.78, 95% CI 0.68–0.87) were the best predictors of serious IUGR. The diagnostic features of Doppler evaluation to predict IUGR in high-risk women were low. In high-risk women, an elevated RI in the second trimester (> 0.58 or > 90th centile) best predicted serious IUGR (positive probability ratio 10.9, 95% CI 10.4–11.4; negative probability ratio 0.20, 95% CI 0.14–0.26).

CONCLUSION

The findings of this research concluded that Doppler ultrasonography is a reliable, noninvasive method of examining uteroplacental perfusion. Abnormal UtA Doppler ultrasonography (elevated PI) in second trimester can predict IUGR among women with high risk factors, which can be enhanced by biochemical tests.

Conflict of interest : none

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