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ORIGINAL ARTICLE

First Trimester Uterine Artery Doppler Indices in Prediction of Small Gestational Age Pregnancy and Intrauterine Growth Restriction in Low-risk Population

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Abstract

Background: **Pregnancy complications including growth restriction are linked to serious morbidities such foetal death and long-term neurodevelopmental impairments for gestational age, small (SGA), which can have a variety of reasons, is frequently associated with placental insufficiency.**

Aim: **To examine the relationship between the first-trimester uterine artery Doppler indices and the intrauterine growth retardation (IUGR) in postpartum SGA new born (IUGR).**

Patients and methods: **A prospective observational research involving 120 patients was carried out. The study was conducted at Al-Azhar University Hospitals. The duration of the study ranged from 6 to 12 months.**

Result: **When it comes to uterine artery Indices by Doppler and notching, there is a substantial difference between the three groups that were analysed. Thus, RI and PI were significantly highest in IUGR group and lowest in normal group.**

Conclusion: **By measuring uterine artery pulsatility index (UtA-PI) and SGA and IUGR can be predicted using first-trimester uterine artery Doppler (IUGR).**

Keywords: Intrauterine growth retardation, IUGR, Small-for-gestational-age, UA Doppler

1. Introduction

The placenta develops into an organ for delivering nourishment and oxygen to the foetus through implantation and trophoblastic invasion. Two stages of placental remodelling take place. During the first stage, trophoblastic cells enter the individual area of the spiral arteries between 8 and 12 weeks of gestation. From 14 weeks of gestation forward, the spiral arteries' myometrial parts have a more intense trophoblastic invasion.[1]

By 16–18 weeks of gestation, the placenta has finished remodelling. Oxidative stress, hypoxia reperfusion injury, and hypoperfusion injury are all effects of improper placental implantation. Pre-eclampsia, foetal growth limitation, and gestational hypertension are thought to be caused by abnormalities in trophoblastic differentiation Fetal growth restriction (FGR). Preterm labour, placental abruption, and second-trimester losses may also be caused by defective implantation.[2]

The primary goal of prenatal care is to concentrate on early risk identification, allowing for the early implementation of treatment techniques to reduce the likelihood of unfavourable pregnancy outcomes.[3]

Oblique artery the gravid uterus's uteroplacental hemodynamics are assessed sonographically during the early stages of pregnancy has benefited from the use of Doppler. Practitioners have been analysing or separating pregnancies that are at-risk for negative outcomes using it as a predictive tool over time. In

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order to evaluate blood flow, a number of characteristics can be determined, Common quantitative values include the resistive index (RI), systolic/diastolic ratio, and pulsatility index (PI).[4] With increasing gestational age, uterine artery pulsatility index (UtA-PI) and RI values decline. This change is assumed to be due to a decrease in uterine vascular impedance following trophoblastic invasion.[5]

FGR that arises without preeclampsia may also have its roots in a problem with the placenta.[6] Because the phrases 'short for gestational age (SGA)', 'FGR', and 'intrauterine growth restriction (IUGR)' have sometimes been used interchangeably, The concept of SGA has significant impacts even if it covers a spectrum from truly small, healthy children to those whose genetic growth potential was not met, necessitating premature birth.[5]

In this study, the association between uterine artery Doppler indices in the first trimester and subsequent birth of infants with IUGR or SGA was investigated(IUGR.

2. Patients and methods

This was a Prospective observational study conducted on 120 cases at Al-Azhar University Hospitals for 12 months. All included women were singleton in the first trimester. All women with second and third trimester pregnancy, Multiple pregnancies, Exclusion criteria for the study included concomitant maternal diseases such as renal diseases, along with foetal chromosomal or anatomical abnormalities, intrauterine infections, malnutrition, heart conditions, and diabetes mellitus, toxic insults, medications (aspirin, heparin, antioxidants, or steroids), and concomitant toxic insults.

Prior to include pregnant women with singleton pregnancies (11–14 weeks gestation) in the study, the usual first trimester nuchal translucency ultrasound examination received approval from the ethical committee. All pregnant women with singletons who were getting a first-trimester ultrasound as part of standard care were given the choice to take part in the trial. All patients had a thorough medical history obtained, excluding any acute or chronic medical conditions, and taking into account things like age, parity, gravidity, past abortions, stillbirths, and neonatal deaths.

At the 10th to 12th week of pregnancy, during the first trimester visit, Colour Doppler was utilised to find the paracervical vascular plexus and then to find the uterine artery and collect uterine artery waveforms. Three waveforms with similar characteristics were obtained, and a proto-diastolic notch was identified. Then, the RI was established. In this study, the RI was favoured above the PI.

All women in this study attended twice before delivery, first time was in the first trimester at 10th to 12th week of pregnancy, and second time was in second trimester at 22nd to 26th week of pregnancy. In the two times uterine artery Doppler indices were recorded.

The weight of the newborn at time of delivery was measured, the relation between results was evaluated.

Using SPSS 22.0 for Windows, all data were gathered, tabulated, and statistically examined (SPSS Inc., Chicago, IL, USA).

3. Results

Table 1.

The patients aged between 20 and 33 years with mean 27.1 years and mean BMI 26.34 kg/m^2 40% of the patients were primigravida and 60% of the patients were multiparous Table 2.

Most of the patients were normal (65%) followed by SGA (14.2%), and IUGR (11.7%).

Mean uterine artery RI was 0.788 ± 0.193 while mean uterine artery PI was 2.11 ± 0.359. Notching prevalence is 19.2% of the studied patients Table 4.

There was a significant difference between the three studied groups regarding uterine artery Indices by doppler and notching. Thus, RI and PI were significantly highest in IUGR group and lowest in normal group Table 5.

In terms of gestational age (GA), birth weight, and Apgar at 5 min, there was a substantial difference between the three groups under investigation Table 6.

Fetal biometry did not significantly differ between any of the three study groups Table 7.

Uterine RI only yielded significance for predicting SGA with sensitivity of 62.5% and specificity of 87.6%, with positive predictive value (PPV) 34% and negative predictive value (NPV) 90% Table 8.

Uterine RI and PI achieved significance for predicting IUGR with sensitivity of (65%, 58%) and specificity of (92%, 89%), with PPV (37%, 33%) and NPV (95%, 92%), respectively.

Table 1. Demographic data of the studied patients.

	Studied patients (N = 120)
Age (years)	
Mean ± SD	27.11 ± 5.62
Range	20–33
BMI (kg/m^2)	
Mean ± SD	26.34 ± 2.84
Gravida and parity	
Primigravida	48 (40%)
Multiparous	72 (60%)

Table 2. Pregnancy outcome distribution among the studied patients.

	Patients ($N = 120$) N (%)
Normal	80 (66.7%)
Spontaneous preterm delivery	8 (6.7%)
SGA	17 (14.2%)
IUGR	13 (10.8%)
Preterm IUGR	2 (1.7%)

Table 3. Uterine artery Indices by Doppler of the studied patients.

	Studied patients ($N = 120$)
Uterine artery resistance index	
Mean ± SD	0.788 ± 0.193
Uterine artery pulsatility index	
Mean ± SD	2.11 ± 0.359
Notching	23 (19.2%)

4. Discussion

Pregnancy complications including growth restriction are linked to serious morbidities such foetal death and long-term neurodevelopmental impairments. The severity of the condition is defined differently in the scientific literature, Despite the fact that the phrase is frequently used to describe birth weights or estimated foetal weights that are below the 10th, fifth, or third percentile for gestational age (GA) for the SGA, which can have a number of reasons, is typically associated with placental insufficiency. According to current studies, high-risk pregnant women may be able to significantly reduce their chance of SGA by starting to take daily aspirin before 16 weeks of pregnancy Levine and colleagues.[7]

Since many years ago, unfavourable outcomes caused by the placenta have been detected and predicted using the Ut A-PI evaluated with Doppler ultrasound. Increased Ut A-PI is linked to inadequate uterine spiral artery transformation, pre-eclampsia risk, and SGA risk Velauthar and colleagues.[8]

This study's main goal was to examine any associations between first-trimester uterine artery Doppler indices and late delivery of SGA babies or IUGR.

This Prospective observational study was conducted on 120 cases. The study was conducted at Al-Azhar University Hospitals. The duration of the study ranged from 6 to 12 months.

In our study, the patients aged between 20 and 33 years with mean 27.1 years and mean BMI 26.34 kg/m2. 40% of the patients were primigravida and 60% of the patients were multiparous.

While, in the study of Elwakel and colleagues[9] Their examined cases were primigravida and ranged in age from 22 to 34 years, with a mean age of 24.78 2.51. The average maternal age was 31.4 5.1 years, and the average BMI was 23.9 8, according to Melchiorre and colleagues[10] research. Most of them had never had children. According to the current study, the majority of patients (65%) were normal, followed by SGA (14.2%) and IUGR (11.7%).

Study by Familiari and colleagues[11] which stated that there were 1615 (6.8%) preterm births, confirmed our findings and 2943 (12%) SGA births, which were characterised as births below the 10th centile.

In contrast, in the study by Drouin and colleagues,[12] SGA was detected at birth in 486 patients (10.5%), of whom 15 (0.3%) had premature deliveries. 391 (83%) of the cases of SGA were mild, 80 (or 17%) cases were severe. Four (27%) of the preterm SGA were severe, compared with 11 (73%) that were mild. In the study by He and colleagues, 76 (4.2%) mothers had a foetus with FGR out of 1796 pregnant women between the ages of 18 and 42. Furthermore, Gupta and Agrawal,[13] revealed that among their studied group; 25.86% developed IUGR.

The current study showed that mean uterine artery RI was 0.788 ± 0.193 while mean uterine artery PI was 2.11 ± 0.359. Notching prevalence is 19.2% of the studied patients.

In contrast, the mean RI of the uterine artery in the study by Dugoff and colleagues[14] was the same for the entire cohort on both the right and left sides (0.59 0.14). Of the 1067 females, 34.2% showed diastolic notches, while 23.8% had just one, and 10.4% had both unilateral and bilateral notches.

Moreover, Melchiorre and colleagues[10] found that the population under research had uterine artery RI 90th and 95th centiles of 0.82 and 0.85, respectively, at 11–14 weeks of gestation. In 270/3010 (9.0%)

Table 4. Uterine artery Indices by Doppler of the studied patients among different groups.

	SGA ($N = 17$)	IUGR ($N = 15$)	Normal ($N = 88$)	F	*P*
RI					
Mean ± SD	0.724 ± 0.138	0.795 ± 0.131	0.684 ± 0.118	**5.54**	**0.006**
PI					
Mean ± SD	1.24 ± 0.539	1.53 ± 0.425	1.06 ± 0.267	**14**	**0.000**
Notching	8 (47.1%)	7 (46.7%)	8 (9.1%)	**22**	**0.000**

Table 5. Neonatal outcomes distribution among different groups.

	SGA ($N = 17$)	IUGR ($N = 15$)	Normal ($N = 88$)	F	*P*
GA (weeks)					
Mean ± SD	37.63 ± 0.927	37.19 ± 1.1	37.8 ± 0.629	**4.4**	**0.015**
Birth weight (kg)					
Mean ± SD	2.57 ± 0.573	2.73 ± 0.438	2.98 ± 0.314	**10**	**0.000**
Apgar at 1 min					
Mean ± SD	7 ± 1.54	6.84 ± 1.76	7.32 ± 1.27	1.02	0.364
Apgar at 5 min					
Mean ± SD	9.56 ± 1.09	9.18 ± 1.32	9.75 ± 0.499	**3.9**	**0.023**

Table 6. Fetal biometry of the studied patients according to groups.

	SGA ($N = 17$)	IUGR ($N = 15$)	Normal ($N = 88$)	F	*P*
Biparietal diameter					
Mean ± SD	77.15 ± 3.86	75.42 ± 4.53	75.77 ± 5.36	0.608	0.546
Abdominal circum.					
Mean ± SD	25.25 ± 3.68	24.11 ± 3.92	25.23 ± 4.11	0.443	0.643
Femur length					
Mean ± SD	54.88 ± 3.49	55.18 ± 3.98	56.9 ± 4.06	2.64	0.075

Table 7. Correlation between uterine doppler indices and SGA.

Variables	AUC	S.E.	Significance.	95% Confidence Interval
RI	0.679	0.076	**0.035***	0.529–0.829
PI	0.606	0.085	0.182	0.439–0.772
Variables	Sensitivity	Specificity	PPV	NPV
RI	62.5%	87.6%	34%	90.3%
PI	54.1%	82%	28%	89.1%

instances, in 136/3010 (4.5%) cases, the mean uterine artery RI was above the 90th percentile and above the 95th percentile. Of the cases, 1356 (45.0%) involved bilateral notches.

In the current investigation, there was a significant difference in the uterine artery Indices by Doppler and notching between the three analysed groups. As a result, the RI and PI were significantly higher in the IUGR group and lower in the normal group. Drouin and colleagues study provided evidence to corroborate our findings.[12]

They found that all SGA categories had significantly higher mean log UtA-PI values, including the SGA in advance (1.14 0.62 MoM; mild term: 1.11 0.62; severe term: 1.29 0.61; *P* 0.0001). (1.85 0.39 MoM; *P* 0.0001; mild preterm: 1.90 0.40; *P* 0.0001; severe preterm: 1.71 0). Whether or not pre-eclampsia developed, women with SGA prior to term had higher first-trimester mean UtA-PIs. According to He and colleagues study's,[15] notching was 40% higher (*P* 0.0001) and the mean UtA-PI and RI were higher in FGR foetuses than in non-FGR foetuses, is in agreement with our findings. Additionally, Abdel Moety and colleagues[16] found that patients who experienced problems had considerably higher UtA-PI and RI than individuals who did not.

Table 8. Correlation between uterine doppler indices and IUGR.

Variables	AUC	S.E.	Sig.	95% Confidence Interval
RI	0.714	0.055	**0.000***	0.607–0.821
PI	0.676	0.057	**0.009***	0.554–0.777
Variables	Sensitivity	Specificity	PPV	NPV
RI	65.3%	91.6%	37%	94.7%
PI	58.4%	89.2%	33.5%	92.1%

Fratelli and colleagues[17] discovered that 46 (61%) of the 76 high-risk mothers had normal Doppler waveform shape and RI, while 30 (39%) of these mothers had aberrant UAD at 11–14 weeks. In this study, women with aberrant 11–14-week UAD, Preeclampsia (17% vs. 0%; $P = 0.0041$), FGR (27% vs. 0%; $P = 0.0002$), intrauterine foetal mortality (13% vs. 0%; $P = 0.0109$), and iatrogenic preterm birth (20% vs. 2%; $P = 0.0086$) had statistically significantly higher rates.

In addition, Familiari and colleagues,[11] said that the likelihood of SGA below the fifth centile was strongly correlated with foetal biometry and uterine artery Doppler indices (*P* 0.01).

Additionally, Melchiorre and colleagues[10] noted that women who later gave birth to an SGA infant had first-trimester uterine artery RI values that were considerably greater women who received a normal result than those of other women (median RI = 0.74; *P* 0.001) (Table 3). In addition, compared with pregnancies that ended normally, there was a statistically significant increase in the frequency of bilateral uterine artery notches in the first trimester (56%).

While Dugoff and colleagues[14] found that women with uterine artery mean RIs above the 75th percentile had a 5.5-fold higher chance of developing IUGR (95% CI: 1.6–18.7). Notching and IUGR had no meaningful association at all. The current study revealed a significant difference in GA, birth weight, and Apgar at 5 min across the three groups. Fetal biometry did not significantly differ between any of the three study groups.

The results showed that as regard ROC curve of uterine Doppler indices to predict SGA; uterine RI only yielded significance for predicting SGA with sensitivity of 62.5% and specificity of 87.6%, with PPV 34% and NPV 90%. As regard ROC curve of uterine doppler indices to predict IUGR; Uterine RI and PI achieved significance for predicting IUGR with sensitivity of (65%, 58%) and specificity of (92%, 89%), with PPV (37%, 33%) and NPV (95%, 92%), respectively. According to a study by Drouin and colleagues,[12] which validates our findings, first-trimester UtA-PI is a very good predictor of SGA in all of its manifestations (term, preterm, moderate, and severe), but particularly successful at predicting SGA delivered preterm.

UtA-PI exhibited a sensitivity of 39% for preterm SGA and 15% for all SGA in the first trimester, according to Velauthar and colleagues meta-findings.[8] Those slightly lower sensitivities in comparison to the current results would have been bigger if GA had been taken into account at the time of UtA-PI measurement in all trials and with the combination of maternal characteristics. SGA and preeclampsia frequently coexist. They found that first-trimester UtA-PI is predictive of preterm SGA whether or not PE is present. In the study by Abdel Moety and colleagues, UtA-PI demonstrated the highest sensitivity (100%) but the lowest specificity (56% and 45%) in predicting preeclampsia and IUGR, respectively.[16] The area under the curve for the combination of UtA-PI and pregnancy-associated plasma protein-A (PAPP-A) was, respectively, 0.788 (95% CI: 0.735, 0.842), 0.816, and 0.758 in a study by He and colleagues[15] on the sensitivity and specificity of early FGR diagnosis. PAPP-A and uterine artery Doppler analyses performed better together than they did separately for predicting FGR (all *P* values.05), and serum PAPP-A significantly improved specificity.

Furthermore, Mohammed and colleagues[18] showed that compared with serum -hCG level (74.5%), Mean UtA-PI (75%) and RI (79.6%) had a higher sensitivity to IUGR prediction. The combined instruments' sensitivity (90%) was higher than the sum of the sensitivity of the individual diagnostic tests.

4.1. Conclusion

In the first trimester, measuring UtA-PI and employing uterine artery Doppler can be used to predict SGA and IUGR (IUGR).

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

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Conflict of interest

The authors declared that there were NO conflicts of Interest.

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