



# Early Uterine and Umbilical Artery Doppler Indices as Predictor for Preeclampsia and Intrauterine Growth Restriction

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**Background:** Preeclampsia (PE) is a disorder that causes hypertension and proteinuria after week 20 of pregnancy. Several Uterine Artery (UtAs) Doppler characteristics have been investigated for their ability to predict PE. The purpose of this research is to look into the uterine and umbilical arterial Doppler indices in the early second trimester for the prediction of late preeclampsia or intrauterine growth restriction.

**Methods:** This is a prospective cohort clinical study and was done at Obstetrics and Gynecology department, faculty of medicine Tanta university hospital from January 2020 till April 2021. 150 pregnant women aged from 18 to 30 years old with gestational age from 13 to 16 weeks of pregnancy. Study was done by the same observer by machine MINDRAY DC60 Measurement of fetal biometry (BPD, FL, AC, HC) Gestational age was confirmed with Detection of congenital malformation.

**Results:** There is a significant difference between the groups regarding uterine and umbilical artery doppler Indices. Uterine RI only yielded significance for predicting IUGR with sensitivity of 62% and specificity of 88%, with Positive predictive value (PPV) 37% and Negative predictive value (NPV)

92%. Umbilical resistance index achieved sensitivity of 56% and specificity of 82%, with PPV 31% and NPV 30% with on statistical significance.

**Conclusions:** Combination of uterine and umbilical artery Doppler study in early pregnancy is one of the best indicator for prediction of preeclampsia and IUGR. Therefore, Doppler study may be used for the prediction of preeclampsia and IUGR to reduce the maternal and perinatal morbidity and mortality.

*Keywords: Uterine; umbilical artery; doppler; preeclampsia; intrauterine growth restriction.*

## 1. INTRODUCTION

Preeclampsia (PE) is a disease defined by hypertension and proteinuria after gestational week 20; it is estimated to impact 5% to 7.5 % of all pregnancies and is a leading cause of maternal, fetal, and neonatal morbidity and death worldwide [1,2]. The origins of PE are unknown, but evidence is mounting to support the hypothesis of aberrant placentation [3,4]. The underlying pathological anomaly is most likely present from the first trimester, although symptoms of the disease usually appear in the late second to third trimester.

Changes in the levels of specific biomarkers in the maternal blood and urine have been documented to occur many weeks to months before the start of clinical PE; these changes correlate with disease severity and normalize after birth [5,6].

However, assessing the amounts of these biomarkers in the blood and urine has little clinical value in predicting PE illness [7,8]. The use of ultrasonic evaluation of the UtA Doppler in predicting PE is another topic of significant study in this discipline [9,10].

Several UtA Doppler characteristics have been tested for their ability to predict PE [11,12]. Although the pulsatility index (PI) has typically been assessed in both UtAs and the mean of the two readings is used to predict PE, the lowest UtA PI has been proven to have the greatest predictive value performance [13]. Nonetheless, research on the use of UtA Doppler velocimetry in the prediction of PE has shown varying degrees of sensitivity.

The flow impedance in the UtA on the side of implantation is lower than the flow impedance on the contralateral side [14]. The purpose of this research is to look at the uterine and umbilical arterial Doppler indices in the early second trimester for the prediction of late preeclampsia or intrauterine growth restriction.

## 2. PATIENTS AND METHODS

This is a prospective cohort clinical research that was conducted at Tanta University Hospital's Obstetrics and Gynecology Department from January 2020 to April 2021.

150 pregnant ladies ranging in age from 18 to 30 years old, with gestational ages ranging from 13 to 16 weeks. The research design is a cross-sectional study.

Age group 18-30 years old is the inclusion criterion. Primigravida. The gestational age ranges from 13 to 16 weeks. Pregnancy with a singleton.

**Exclusion Criteria:** Medical problems in the patient.

In this research, each patient was exposed to the following:

- i. Complete medical history is obtained.
- ii. A general and obstetric exam.
- iii. Routine prenatal testing, including as CBC, random blood sugar, liver and kidney function tests, and coagulation profiling.

**Ultrasound Examination:** The examination was performed by the same observer using the MINDRAY DC60 machine:

The gestational age was determined.

Fetal biometry measurement (BPD, FL, AC, HC).

Congenital malformation detection.

Color Doppler detected the uterine artery [10] as it began its climb to the uterine body. At this moment, Doppler indices were measured.

The signal was refreshed until it produced a clear, consistent waveform. Resistance index, pulsatility index, and the presence or absence of

a protodiastolic notch were all measured. After that, the operation was performed on the other uterine artery.

In the absence of fetal movement, the umbilical artery Doppler waveform was acquired from a free loop of cord, and measurements were made when a clear waveform was achieved. Resistance index, pulstility index, and the presence or absence of a protodiastolic notch were all measured using Doppler indices.

The patients were followed throughout the pregnancy till delivery for the development of preeclampsia or IUGR. Preeclampsia is defined as hypertension (systolic blood pressure more than 140 mm Hg or diastolic blood pressure greater than 90 mm Hg) along with proteinuria greater than 300mg in 24 hours. IUGR was diagnosed as (tenth centile) for a pregnant woman of the same gestational age.

At birth, the fetal weight, APGAR score at 1 and 5 minutes, and gestational age were all recorded.

### 2.1 Statistical Analysis

The sample size was calculated using Epi-Info software statistical package created by World Health organization and center for Disease Control and Prevention, Atlanta, Georgia, USA version 2002. The criteria used for sample size calculation ( $n > 33$ ) were 95% confidence limit, 80% power of the study, expected outcome in in treatment group 90% compared to 60% for control groups.

Analysis of data were performed by SPSS v25 (SPSS Inc., Chicago, IL, USA). Quantitative parametric variables (e.g. age) were presented as mean and standard deviation (SD). They were compared between the two groups by unpaired student's t- test and within the same group by paired T test. Quantitative non-parametric variables (e.g. VAS) were presented as median and range and compared between the two groups by Mann Whitney (U) test and within the same group by Wilcoxon test. P value  $< 0.05$  was considered significant.

### 3. RESULTS

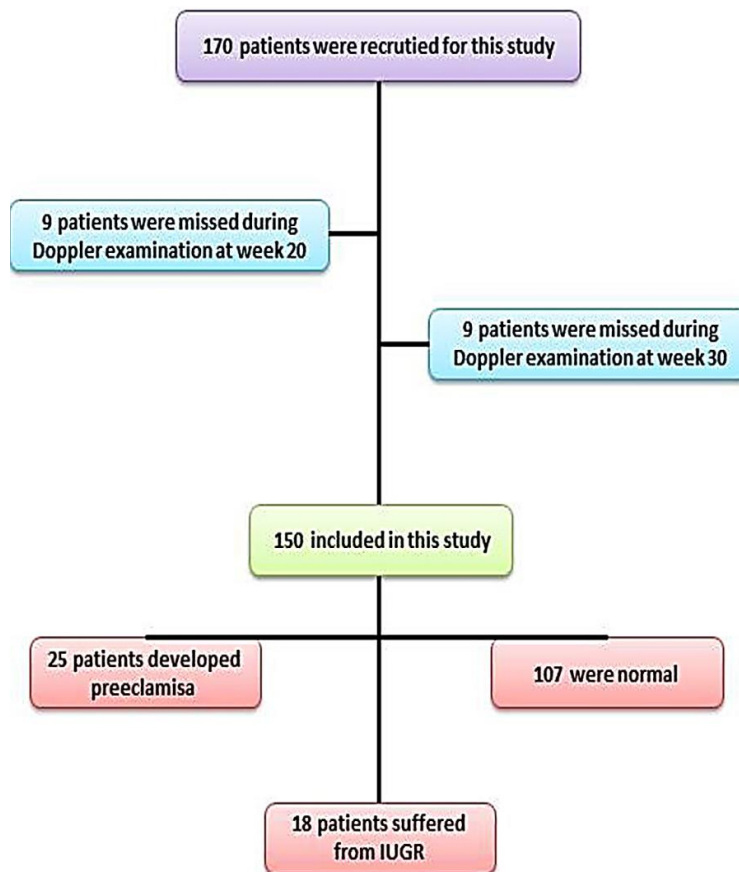


Fig. 1. Pregnancy outcome distribution among the studied patients

**Table 1. Pregnancy outcome distribution among the studied patients**

	Patients (n=150)	
	N	%
Normal	107	71.3
Pre- eclampsia	25	16.6
IUGR	18	12

Most of the patients were normal (71.3%) followed by pre-eclampsia (16.6%), and IUGR (12%)

**Table 2. Demographic data of the three studied groups**

	Pre-eclampsia (N=25)	IUGR (N=18)	Normal (N=107)	F	P	LSD
<b>Age (years)</b> Mean ± SD	25.29 ± 2.42	24.37 ± 3.71	25.31 ± 2.27	1.08	.343	P1=0.347 P2=0.969 P3=0.152
<b>BMI (kg/m<sup>2</sup>)</b> Mean ± SD	26.32 ± 2.69	24.62 ± 3.39	25.44 ± 2.38	2.36	.098	P1=0.074 P2=0.107 P3=0.208

P1: Comparison between Pre-eclampsia group & IUGR group

P2: Comparison between Pre-eclampsia group & Normal group

P3: Comparison between IUGR group & Normal group

**This table shows:** There is no significant difference between the three studied groups or within the groups regarding age and BMI.

**Table 3. Uterine artery (UtA) and umbilical artery (UmA) doppler indices (resistant index RI, pulstility index PI) in early pregnancy of the studied patients among different groups**

	Pre-eclampsia (N=25)	IUGR (N=18)	Normal (N=107)	F	P	LSD
<b>UmA RI</b> Mean ± SD	0.742 ± 0.138	0.682 ± 0.124	0.629 ± 0.121	<b>8.67</b>	<b>.001*</b>	P1=0.150 <b>P2=0.001*</b> P3=0.089
<b>UmA PI</b> Mean ± SD	1.029 ± 0.281	0.941 ± 0.181	0.875 ± 0.143	<b>7.99</b>	<b>.001*</b>	P1=0.251 <b>P2=0.001*</b> P3=0.084
<b>UtA RI</b> Mean ± SD	0.651 ± 0.137	0.616 ± 0.129	0.584 ± 0.115	<b>3.33</b>	<b>.038*</b>	P1=0.402 <b>P2=0.013*</b> P3=0.285
<b>UtA PI</b> Mean ± SD	1.38 ± 0.539	1.12 ± 0.375	0.935 ± 0.167	<b>12</b>	<b>.000*</b>	P1=0.086 <b>P2=0.001*</b> <b>P3=0.001*</b>

\* significant p value < 0.05

P1: Comparison between Pre-eclampsia group & IUGR group

P2: Comparison between Pre-eclampsia group & Normal group

P3: Comparison between IUGR group & Normal group

There is a significant difference between the three studied groups regarding uterine and umbilical artery doppler Indices by doppler. Moreover, they were significantly higher in preeclampsia patients compared to normal, also uterine artery PI was significantly higher in IUGR group compared to normal (Table 3).

There is a significant difference between the three studied groups regarding GA, birth weight and Apgar at 5 min (Table 4).

Uterine RI only yielded significance for predicting IUGR with sensitivity of 62% and specificity of 88%, with Positive predictive value (PPV) 37% and Negative predictive value (NPV) 92%.

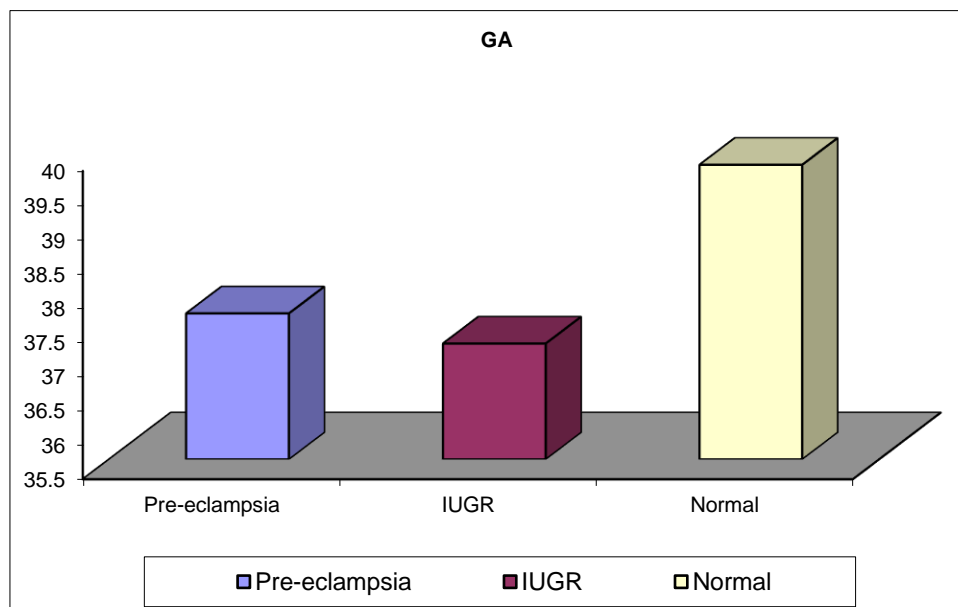
Umbilical RI achieved sensitivity of 56% and specificity of 82%, with PPV 31% and NPV 30% with on statistical significance (Fig. 2).

**Table 4. Gestational age at delivery & neonatal outcomes distribution among different groups**

	Pre-eclampsia (N=25)	IUGR (N=18)	Normal (N=107)	F	p	LSD
<b>GA (weeks) Mean ± SD</b>	37.63 ± 0.927	37.19 ± 1.08	39.8 ± 0.629	<b>5.24</b>	<b>.006*</b>	P1=0.159 <b>P2=0.001*</b> <b>P3=0.001*</b>
<b>Birth weight (kg) Mean ± SD</b>	2.86 ± 0.438	2.67 ± 0.565	3.08 ± 0.413	<b>9.31</b>	<b>.000*</b>	P1=0.456 <b>P2=0.001*</b> <b>P3=0.007*</b>
<b>Apgar at 1 min Mean ± SD</b>	7 ± 1.54	6.49 ± 2.26	7.32 ± 1.27	2.67	.072	P1=0.383 P2=0.279 <b>P3=0.026*</b>
<b>Apgar at 5 min Mean ± SD</b>	9.7 ± 1.09	8.81 ± 2.92	9.75 ± 0.499	<b>5.06</b>	<b>.007*</b>	P1=0.169 P2=0.729 <b>P3=0.002*</b>

\* significant p value < 0.05

P1: Comparison between Pre-eclampsia group & IUGR group  
 P2: Comparison between Pre-eclampsia group & Normal group  
 P3: Comparison between IUGR group & Normal group



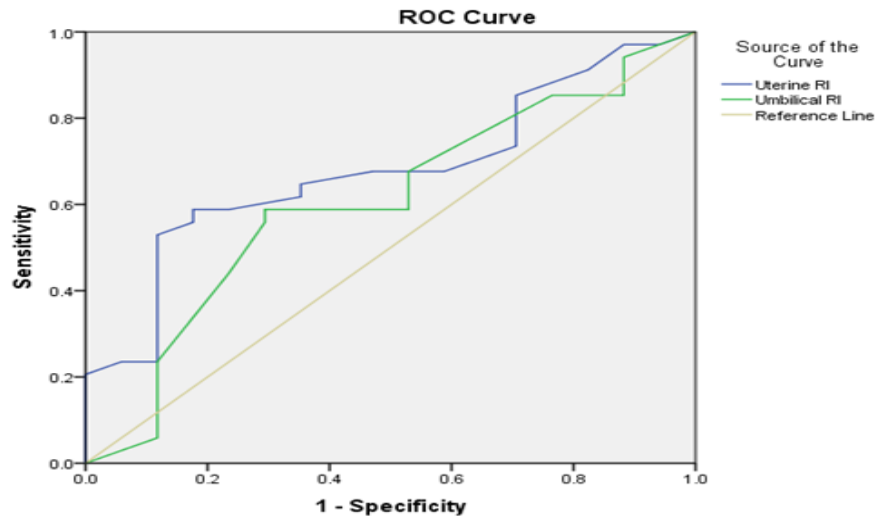
**Fig. 2. Gestational age among different groups**

**Table 5. Comparison between uterine artery and umbilical artery Doppler to predict IUGR**

Variables	AUC	S.E.	Sig.	95% Confidence Interval
Uterine RI	.679	.076	<b>.039*</b>	0.529 - 0.829
Umbilical RI	.606	.085	.223	0.439 - 0.772

Variables	Sensitivity	Specificity	PPV	NPV
Uterine RI	61.8%	88.2%	37%	92%
Umbilical RI	55.9%	82.4%	31%	90%



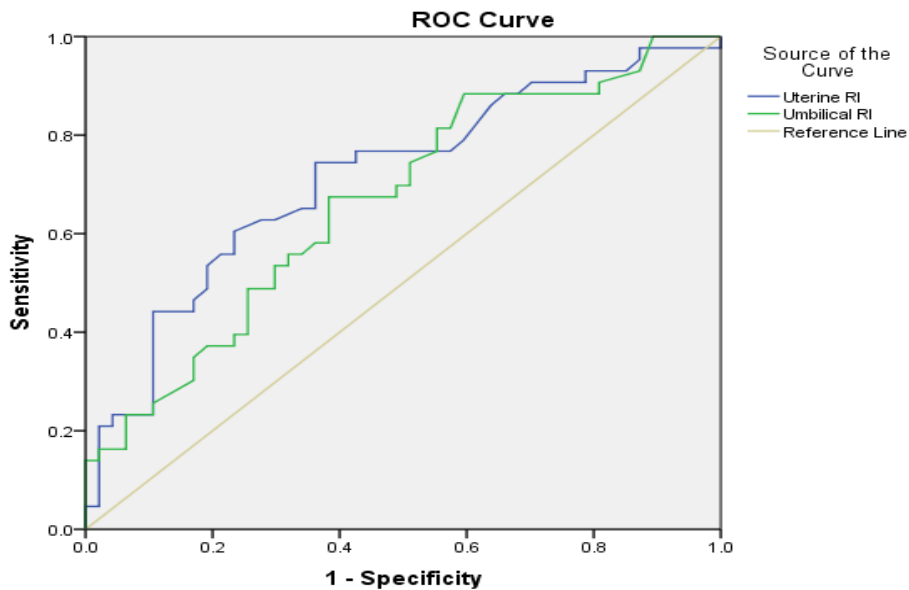
**Fig. 3. ROC curve of uterine and umbilical Doppler to predict IUGR**

Uterine and Umbilical RI achieved significance for predicting pre-eclampsia with sensitivity of (63%, 58%) and specificity of (92%, 87%), with PPV (43%, 33%) and NPV (92%, 89%), respectively.

**Table 6. Comparison between uterine artery and umbilical artery Doppler to predict PE**

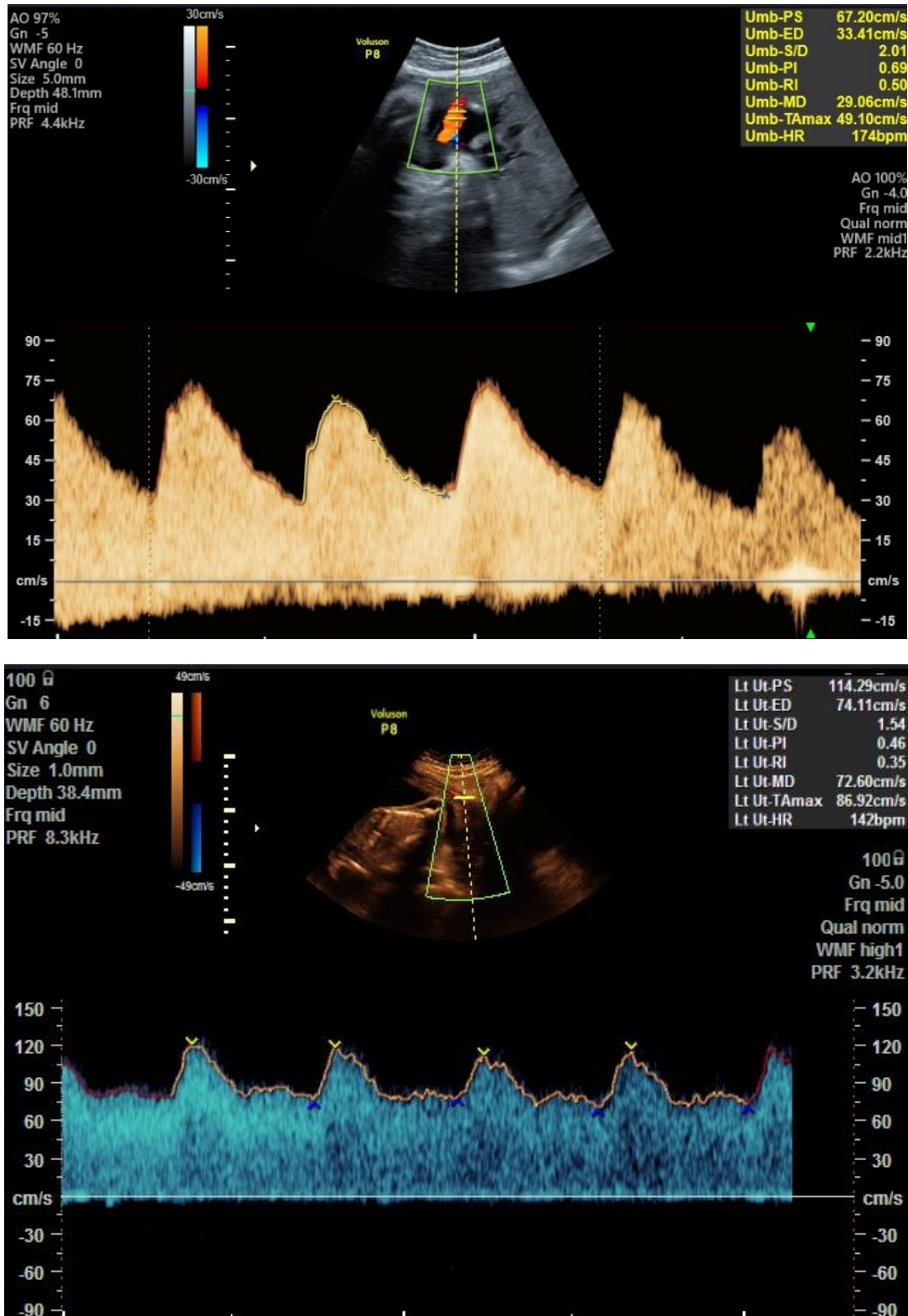
Variables	AUC	S.E.	Sig.	95% Confidence Interval
Uterine RI	.714	.055	.000*	0.607 - 0.821
Umbilical RI	.676	.057	.007*	0.554 - 0.777

Variables	Sensitivity	Specificity	PPV	NPV
Uterine RI	62.8%	91.6%	43%	92%
Umbilical RI	58.1%	87.2%	33%	89%



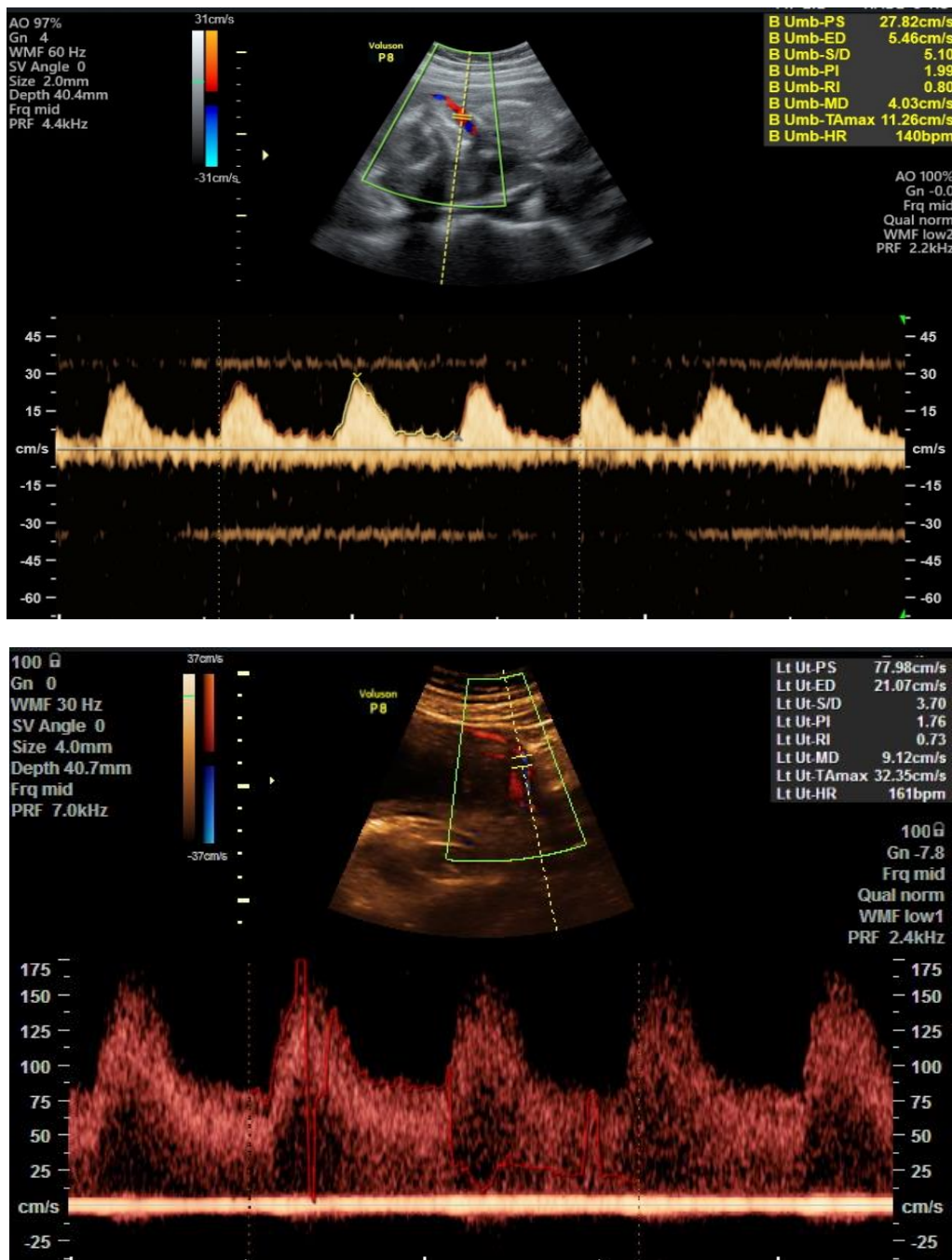
**Fig. 4. ROC curve of uterine and umbilical doppler to predict PE**

Cases Presentations



**Fig. 5. Show normal umbilical and uterine artery doppler indices**  
*This case continued normally till the end of pregnancy*





**Fig. 6. Show high umbilical and uterine artery doppler indices**  
*This case suffered from IUGR after that*

#### 4. DISCUSSION

Pre-eclampsia is a disease with a wide range of maternal and fetal symptoms. Pre-eclampsia complicates 3–8% of pregnancies globally, and it is responsible for 10- 15% of maternal fatalities [15].

Our findings were confirmed by the findings of Nagar et al. (16), who found that 16 of the 110

patients had preeclampsia, with a sensitivity of 60%, 40%, and 60% for uterine artery S/D ratio, RI, and notch, respectively. For all indices, the specificity ranged from 93% to 94%. This is comparable to the findings of Kurdi et al., [16] and Bhattacharya et al., [17] in a sample of 179 women. This suggests that notch is a more accurate predictor of preeclampsia. This is



consistent with the views of Bower et al. [18] and Antsaklis et al. [19].

Out of 50 patients with abnormal umbilical arteries, 10 developed preeclampsia, with sensitivity of 40%, 40%, and 100% for S/D ratio, RI, and absent end diastolic flow, respectively, and specificity of 96.84 percent, 93.68 percent, and 100% for S/D ratio, RI, and absent end diastolic flow, respectively. Mirza et al., [20] studied 268 women and found 57 instances of abnormal Doppler. Preeclampsia was identified in 14% of these patients. Positive predictive values for S/D ratio, RI, and absence end diastolic flow were 40%, 25%, and 100%, respectively. This suggests that umbilical artery Doppler is more accurate than uterine artery Doppler.

In the present research, 40 patients had IUGR infants, which were predicted by aberrant uterine artery Doppler in 25 instances, with sensitivity of 37.5 percent, 25%, and 50% for S/D ratio, RI, and notch, respectively. It is comparable to the views of Irion et al., [21], North et al., [22], and Bower et al. [23] For S/D, RI, and notch, the specificity was 93.48 percent, 94.56 percent, and 95.65 percent, respectively. Velauthar et al., [24], conducted a meta-analysis of 18 studies involving 55,974 women and discovered that the sensitivities of abnormal uterine artery Doppler for predicting preeclampsia and fetal growth restriction were 26.4 percent and 15.4 percent, respectively, with specificities of 93.4 percent and 93.3 percent. Notch's positive predictive value was 50%, which was the highest. Again, notch outperformed all other indicators as a predictor.

In the research by Nagar et al. [25], 15 of 50 individuals with aberrant umbilical artery Doppler had IUGR deliveries, with a sensitivity of 25% and 42.86 percent for S/D ratio and RI, respectively. It is consistent with the views of Antsaklis et al., [26] and Beattie et al., [27], as well as Romero et al. [28] They discovered that aberrant umbilical Doppler is linked to a lower birth weight, a poorer Apgar score, and substantial newborn morbidity. The sensitivity of missing end diastolic flow was 100%. Doppler scans of the uterine and umbilical arteries were abnormal in ten individuals. With a sensitivity and specificity of 100 percent, all patients developed preeclampsia and IUGR.

In Rashid et al. [29] 's research, the PPV and NPV for pulsatility index expressed 66 percent

and Notch were reported as (36 percent, 99 percent ) and (30 percent, 99 percent ), respectively. Similarly, both parameters express to be similarly sensitive in determining IUGR, with a sensitivity of 95%, while. As a result, Notch determination is much more specific and sensitive for determining intrauterine growth limitation (IUGR).

In the research of Llurba et al., [30], uterine artery mPI (mean Pulsatility Index) was compared with maternal history factors in women who later had PE and those who did not. Furthermore, by constructing ROC curves to compare the two ways of screening for early-onset PE and late-onset PE, they were able to distinguish between the two. By comparing the areas under the curves, it was discovered that uterine Doppler mPI (AUC = 0.90, 95 percent CI (0.85–0.96) P =.001) performed better than maternal history alone (AUC = 0.75, 95 percent CI (0.63–0.87) P =.001) in detecting early-onset PE, despite the fact that there was no statistical difference when both AUCs were compared (P =.076).

It may jeopardize the ability to detect several aberrant diseases associated with pregnancy, such as preeclampsia and IUGR [31].

## 5. CONCLUSION

Uterine and umbilical artery fusion Doppler ultrasound in early pregnancy is one of the strongest predictors of preeclampsia and IUGR. As a result, a Doppler scan may be utilized to predict preeclampsia and IUGR in order to decrease maternal and neonatal morbidity and death..

## CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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