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Uterine arterial Doppler ultrasound in prediction for preeclampsia in 2nd trimester of pregnancy

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Abstract
Background: Pre-eclampsia (PE) is a significant contributor to maternal and perinatal mortality and morbidity. The uterine arteries' blood flow velocity waveforms can be recorded non-invasively with a Doppler examination. This study set out to assess the importance of the uterine artery. The potential predictive value of Doppler screening for pre-eclampsia during the second trimester of pregnancy.
Methods: This study involved the enrolment of 100 pregnant women during the second trimester. Among them, 50 had low-risk pregnancies while the other 50 had high-risk pregnancies. The procedure involved the utilization of a uterine artery Doppler ultrasound machine equipped with B-mode, pulsed Doppler, and colour flow imaging capabilities.
Results: Doppler data were compared to pregnancy outcomes, such as hypertension or IUGR. The study assessed uterine artery parameters' sensitivity, specificity, PPV, NPV, and accuracy for preeclampsia prediction. Sensitivity, specificity, PPV, NPV, and accuracy were 91.7%, 95.3%, and 94%. Additionally, the study examined the bilateral notch and notch for preeclampsia, with respective values of 50%, 96.9%, 90%, 77.5%, and 80%. The risk factors associated with the highest rate of pulmonary embolism (PE) were history (80%), hypertension (75%), abortion (66.7%), renal disease (66.7%), and obesity (60%). Regarding the risk factors associated with the highest rate of intrauterine growth restriction (IUGR), the past medical history ranked first with a prevalence of 60%, followed by a history of abortion and hypertension, both with a prevalence of 50%.
Conclusions: Women who exhibit abnormal uterine arteries Doppler examination results are at a heightened risk of experiencing subsequent complications, especially those that necessitate premature delivery. The University of Texas at Austin the Doppler technique is an advantageous and promising non-invasive method for detecting obstetric outcomes.

Keywords: Uterine arterial doppler ultrasound, preeclampsia, pregnancy

Introduction
Specifically, the occurrence of preeclampsia or intrauterine growth restriction (IUGR) was taken into consideration while analyzing the findings of the Doppler examination in connection to the outcomes. Uterine artery characteristics were assessed for their ability to accurately predict preeclampsia, as well as their sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The sensitivity, specificity, PPV, NPV, and accuracy were determined to be 91.7%, 95.3%, 91.7%, 95.3%, and 94% respectively [1].
Maternal mortality rates in developing countries are partly caused by preeclampsia and its consequences, which are estimated to claim the lives of over a million women annually worldwide by the World Health Organization. The rate in developing countries is 5-10%, while in developed countries it exceeds 18% [2].
Furthermore, preeclampsia is classified as one of the pregnancy-specific diseases, exhibiting symptoms of hypertension and proteinuria occurring after the 20th week of gestation [3].
There is still a lack of clarity regarding the actual etiology of the disorder; however, evidence suggests that preeclampsia is associated with an imbalance in the synthesis of prostacyclin, thromboxane A2, and vascular spasm [4].
The development of haemolysis, higher levels of liver enzymes, and a reduced platelet count (HELLP) syndrome is a significant set of complications. This is because the occurrence of end-organ involvement, which includes heart failure, pulmonary edema, liver engagement, and abnormalities in the coagulation system, is followed by the development of these complications. Furthermore, preeclampsia is marked by a reduction in renal function, brain

involvement, seizures, and possibly catastrophic effects for the mother. Each of these symptoms appears simultaneously. In contrast, it is important to point out that there is a possibility of intrauterine growth restriction (IUGR) and intrauterine fetal death due to reduced placental perfusion. Both outcomes are possible [5].

The evaluation of blood flow within the placenta is made possible by the application of Doppler ultrasonography, which is a technique that does not involve any intervention. The trophoblastic invasion of the musculo-elastic membrane of uterine spiral arteries causes the resistance of uterine artery flow to gradually decrease during the first and second trimesters of a typical pregnancy. This occurs due of the maturation of the uterine arteries [6].

In addition, placental pathology in preeclamptic pregnancies indicates that the normal flow of the mother's placental arteries to vessels with low resistance has been interrupted [7].

Studies suggests that patients at elevated risks for preeclampsia can be identified with an abnormal Doppler examination performed during the second trimester of pregnancy [8].

The objective of this study was to evaluate the efficacy of uterine artery Doppler screening as an indicative tool for preeclampsia during the 2nd trimester of pregnancy.

Patients and Methods

This study is a prospective cohort study conducted on a sample of 100 pregnant women between the ages of 18 and 40. The participants had singleton pregnancies and were in their second trimester (16-22 weeks) with a body mass index (BMI) ranging from 24 to 33. The study was conducted at the Radio-diagnosis and Medical Imaging Department and the Obstetrics and Gynecology Department in Tanta University. The data collection period for this study was from February 2019 to February 2022.

The study was conducted following approval from the Ethical Committee of Tanta University Hospitals and registration with clinicaltrials.gov. A duly informed written consent has been acquired from the patient or their close relatives.

The exclusion criteria encompassed pregnant women aged over 40 years or under 18 years, pregnancies with twins, and pregnant females in their first or third trimester.

The patients were further split into 2 groups: Group I consisted of 50 pregnant women who served as a control group and had low-risk pregnancies. The study sample for Group II included 50 pregnant women who were identified as having a high-risk pregnancy. In this group, there were women who were first-time mothers who were elderly, women who were first-time mothers who had a history of hypertension or diabetes mellitus, and women who were multigravida who had a history of hypertension, diabetes mellitus, pre-eclamptic toxaemia, or intrauterine growth restriction.

The study involved the evaluation of all patients through a comprehensive clinical assessment, which included a thorough history taking, clinical examination, laboratory investigation, and radiological assessment. The radiological assessment consisted of ordinary obstetric ultrasound sonography and Doppler ultrasound on the uterine artery. The uterine artery Doppler ultrasound machine used for this purpose was the Toshiba aplio 500, equipped with B-mode, pulsed Doppler, and color flow imaging system.

Uterine artery Doppler

Obtained a sagittal section of the uterus and the cervical canal, which was then followed using color flow imaging to generate a color map of the flow throughout the region. Wave with pulsations There was an application of the Doppler gate in order to obtain the flow wave shape, and the image was frozen once there were at least three consecutive waveforms formed. The Pulsatility index (PI), Resistance index (RI), and peak systolic/diastolic ratio were the doppler indices that were automatically created by the system. After that, the Mean Pulsatility Index (MPI) was computed. PIH was diagnosed when there was an increase in systolic pressure of at least 30mm of Hg or an increase in diastolic pressure of at least 15mm of Hg over the previously known blood pressure; an absolute rise in the blood pressure of at least 140/90mm of Hg; and a diastolic blood pressure that was greater than 90mmHg measured on at least two occasions after 20 weeks of gestation in a woman who had previously been considered to have normal blood pressure.

Statistical analysis

For the purpose of this investigation, the Statistical Package for Social Sciences (SPSS) version 26 intended for Windows was applied. A test known as the Shapiro-Wilk test was utilized in order to determine whether or not the distribution of continuous numerical data was normal. In order to summarize the variables that were assumed to have a normal distribution, the mean values plus or minus the standard deviation were utilized. For the purpose of making comparisons between two groups, the independent samples T-test methodology was applied. In order to provide a concise summary of the categorical variables, the frequencies (count and percentage) were utilized. The Chi-square test for independence developed by Pearson and Fisher's exact test were the statistical tests that were utilized in order to analyze the link between the categorical variables and the groups, depending on what was judged to be suitable. For the purpose of determining whether or not Doppler ultrasound measures of uterine arteries are capable of discriminating between cases of preeclampsia (PE), the research performed a Receiver Operating Characteristic (ROC) curve analysis. When interpreting the statistical tests, a level of significance of $p<0.05$ was utilized for interpretation.

Results

There was no significant difference between the studied groups regarding the distribution of age (p=0.542), gravidity (p= 0.568), or gestational age (p = 0.678). Table 1

Table 1: The age distribution, gravidity, and gestational age of the included pregnant women

		Group I N (%)	Group II N (%)	P value
Age (years)	18-24	15 (30.0%)	20 (40.0%)	0.542
	25-34	27 (54.0%)	22 (44.0%)	
	35-42	8 (16.0%)	8 (16.0%)	
Gravidity	I	29(40.0%)	14 (28.0%)	0.568
	II	11 (22.0%)	16 (32.0%)	
	III	13 (26.0%)	14 (28.0%)	
	IV	6 (12.0%)	6 (12.0%)	
Gestational age at enrolment (Weeks)	16-18	2 (4.0%)	4 (8.0%)	0.678
	19-22	48 (96.0%)	46 (92.0%)	

Data was presented as frequency and percentage.

The most common risk factor in group II was obesity which was encountered in 40%, followed by abortion (24%), past history (20%), then family history and hypertension (16%). Renal disease and diabetes mellitus were found in 12%. Table 2

Table 2: The maternal risk factors in group II

Risk Factor	N (%)
Obesity	20 (40%)
Abortion	12 (24%)
Past-History	10 (20%)
Family History	8 (16%)
Hypertension	8 (16%)
Renal Disease	6 (12%)
D.M	6 (12%)

Data was presented as frequency and percentage, DM: diabetes mellitus

Group II had significantly higher mean systolic and blood pressure and RI and PI of the right and left uterine artery and percentage of pregnant women having delivery during the gestational weeks 34 – 36 and live births. The rate of pre-eclampsia in group I higher than II. Table 3

Table 3: Systolic and diastolic blood pressure, uterine artery flow indices, Pre-eclampsia and Gestational age, neonatal weight at birth and Pregnancy outcome in groups I and II

	Group I	Group II	P-value
Blood Pressure (mmHg) (Mean ± SD)			
Systolic	105.66 ± 16.82	140.08 ± 27.87	<0.001*
Diastolic	74.60 ± 10.17	94.52 ± 17.61	<0.001*
Right uterine artery (Mean ± SD)			
RI	0.57 ± 0.14	0.71 ± 0.14	<0.001*
S/D Ratio	2.70 ± 0.88	3.57 ± 1.03	<0.001*
PI	1.05 ± 0.40	1.56 ± 0.48	<0.001*
Left uterine artery (Mean ± SD)			
RI	0.55 ± 0.12	0.69 ± 0.13	<0.001*
S/D Ratio	2.82 ± 1.03	3.78 ± 1.20	<0.001*
PI	0.98 ± 0.33	1.56 ± 0.52	<0.001*
Mean PI of left & right uterine arteries (Mean ± SD)			
PI	1.02 ± 0.31	1.56 ± 0.46	<0.001*
Pre-eclampsia (N %)			
Yes	4 (8.00%)	32 (64.00%)	<0.001*
No	46 (92.00%)	18 (36.00%)	
Gestational age at birth (weeks) (N %)			
34-36	2 (4.0%)	30 (60.0%)	<0.001*
37-39	40 (80.0%)	12 (24.0%)	
40-41	7 (14.0%)	6 (12.0%)	
Stillbirth/IUFD **	1 (2.0%)	2 (4.0%)	-
Birth weight (kg) (N %)			
1.5-2.5	2 (4.0%)	30 (60.0%)	<0.001*
2.6-3.5	28 (56.0%)	8 (16.0%)	
≥3.6	19 (38.0%)	10 (20.0%)	
Stillbirth/IUFD **	1 (2.0%)	2 (4.0%)	-
Pregnancy outcomes (N %)			
Normal	47 (94.00%)	18 (36.00%)	<0.001*
Abnormal **	3 (6.00%)	32 (64.00%)	
Fetal outcome (N %)			
Live birth	49 (98.00%)	48 (96.00%)	1.000

IUFD/still birth	1 (2.00%)	2 (4.00%)	
IUGR (N %)			
Yes	2 (4.00%)	16 (32.00%)	<0.001*
No	47 (94.00%)	32 (64.00%)	

PI: pulsatility index; RI: resistive index; IUGR: Intra uterine growth restriction; IUFD: Intra Uterine Fetal Death;

SD: standard deviation; * significant at $p<0.05$, ** weight for stillbirths and IUFD were not available and these cases were not included in the statistical test; ** abnormal outcome refers to birth weight <2.5, prematurity, stillbirth and IUFD.

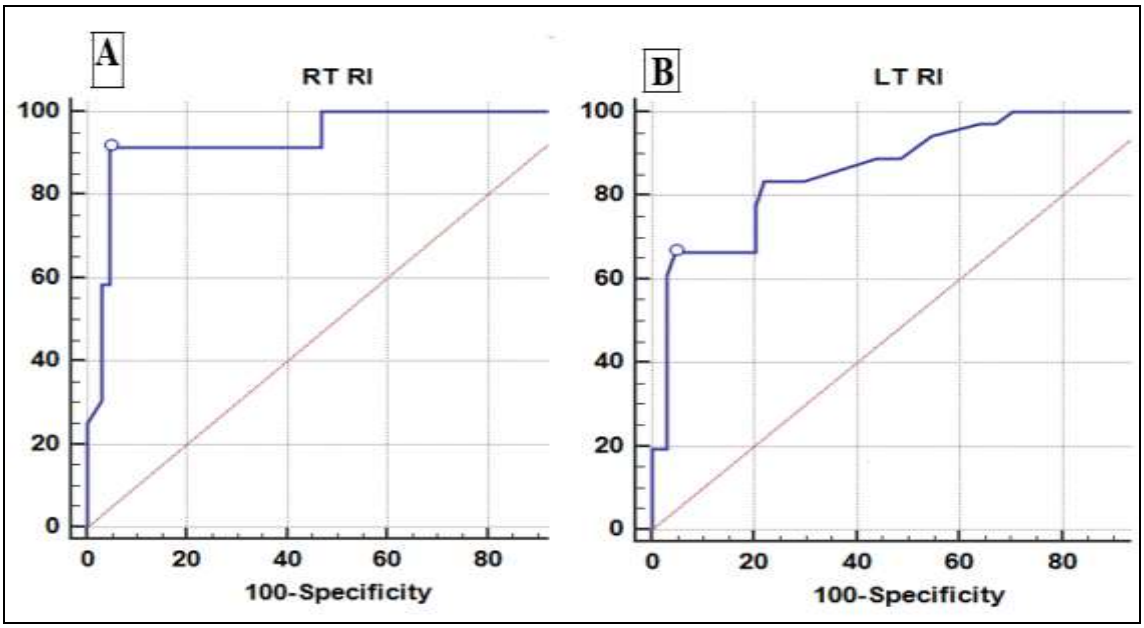
Preeclampsia was significantly associated with RI >0.7 of the right and left uterine arteries and with a mean PI >1.45 ($p<0.001$). Table 4

Table 4: Relation between RI, PI, and preeclampsia in the right and left uterine arteries

Uterine artery flow indices		Preeclampsia		P-value
		Yes (N = 36)	No (N = 64)	
Right uterine artery N (%)				
Resistive index > 0.7	Yes	33 (91.7%)	3 (4.7%)	<0.001*
	No	3 (8.3%)	61 (95.3%)	
Left uterine artery N (%)				
Resistive index > 0.7	Yes	24 (66.7%)	3 (4.7%)	<0.001*
	No	12 (33.3%)	61 (95.3%)	
Mean PI of left & right uterine arteries N (%)				
Mean PI > 1.45	Yes	33 (91.7%)	3 (4.7%)	<0.001*
	No	3 (8.3%)	61(95.3%)	

PI: Pulsatility index, *Significant at $p<0.05$

The AUCs of mean PI of both arteries and right uterine artery RI were above 0.9 (AUC=0.949 and 0.936, respectively), indicating excellent diagnostic power. The AUc of the left uterine RI index was slightly lower than that of the right artery or mean PI of both arteries (AUC= 0.866). The highest accuracy was seen with the RI of the right artery and the mean PI of both arteries (94%), followed by the RI of the left artery (accuracy = 85%). Figure 1



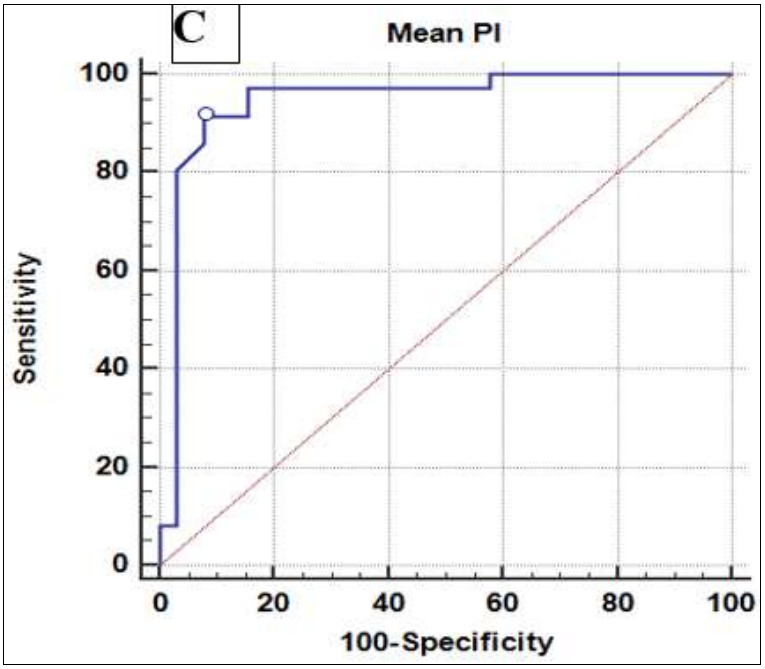


Fig 1: ROC curve for predictor of pre-eclampsia, A: ROC curve for Rt RI, B: ROC curve for Lt RI, C: ROC curve for mean PI.

The presence of bilateral notch demonstrated sensitivity, specificity, PPV, NPV, and overall accuracy of 50, 96.9, 90, 77.5, and 80%. Table 5

Table 5: Diagnostic performance of uterine artery in discrimination of preeclampsia and non-preeclampsia (Notch)

	TP	FP	TN	FN	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Bilateral Notch	18	2	62	18	50.0	96.9	90.0	77.5	80.0

TP: true positive; FP: false positive; TN: true negative; FN: false negative.

In group I, four cases had preeclampsia, three of them had high uterine flow indices. In addition, IUGR was recorded in two cases with PE who had elevated uterine artery flow parameters. In group II, 32 cases had preeclampsia and all of them had elevated flow indices while 18 had bilateral notching. IUGR was diagnosed in 16 group II patients who had elevated flow indices while bilateral notching was recorded in eight of them. Table 6

Table 6: The diagnosed cases of preeclampsia and IUGR in groups I, II

Pregnancy outcome	Group I			Group II		
	No.	Uterine artery parameters		No.	Uterine artery parameters	
		Indices (PI, RI, S/D ratio)	Notch		Indices (PI, RI, S/D ratio)	Notch
Preeclampsia	4	↑ 3 cases	0	32	↑ 32	18
IUGR	2	↑ 2 cases	0	16	↑ 16	8
Preeclampsia with IUGR	2	↑ 2 cases	0	16	↑ 16	8

PI: pulsatility index; RI: resistive index, IUGR: intrauterine growth retardation.

The risk factors that were associated with the highest rate of PE in group II patients included past history (80%), followed by hypertension (75%), then abortion (66.7%), renal disease (66.7%), and obesity (60%). As regards the risk factors associated with the highest rate of the IUGR, past history ranked the first (60%), followed by abortion (50%) and hypertension (50%). Table 7

Table 7: The maternal risk factors included in group II and related development of preeclampsia and IUGR

Risk Factor	No (%)	Preeclampsia		IUGR	
		% within group II	% within risk factor	% within group II	% within risk factor
Obesity	20 (40.0%	12 (24.0%)	60.0	4 (8%)	20.0
Abortion	12 (24.0%)	8 (16.0%)	66.7	6 (12%)	50.0
Past History	10 (20.0%)	8 (16.0%)	80.0	6 (12%)	60.0
Family History	8 (16.0%)	4 (8%)	50.0	0 (0.0%)	0.0
Hypertension	8 (16.0%)	12 (24.0%)	75.0	4 (8%)	50.0
Renal Disease	6 (12.0%)	4 (8%)	66.7	0 (0.0%)	0.0
D.M	6 1(2.0%)	2 (4%)	33.3	0 (0.0%)	0.0

DM: diabetes mellitus. HTN: hypertension. IUGR: intrauterine growth retardation

Discussion

Preeclampsia is a pathological condition characterized by abnormal blood pressure during pregnancy, which leads to decreased perfusion of organs due to severe constriction of blood vessels [9].

The WHO has estimated that more than one million women worldwide perish annually because of preeclampsia and its associated complications. It is observed that maternal mortality in developing nations can be attributed to this circumstance [2].

Furthermore, preeclampsia typically manifests in young women who have not yet given birth, and its occurrence is significantly impacted by factors such as race, ethnicity, and genetic predisposition [10].

In addition, preeclampsia typically manifests in young women who have not previously given birth, and its occurrence is significantly impacted by factors such as race, ethnicity, and genetic predisposition [11].

The assessment of the uterine artery was performed utilizing doppler ultrasound within the gestational timeframe of 16-22 weeks in our investigation, similar to the study conducted by Barati *et al*. [12] who evaluated uterine artery doppler at 16-22 weeks. The mean age of cases in our study was 25.60±6.52 like Afrakhteh *et al*. [13] study where the mean age of cases was 26.4±5.11.

Costa *et al*. [14] found that The historical record of prior preeclampsia is a widely recognized risk factor for the likelihood of a new occurrence in a subsequent pregnancy, with recurrence rates varying from less than 10% to 65% and Thekkedathu *et al*. [15] found that previous preeclampsia and history of IUGR contributed significantly to preeclampsia and IUGR in agreement with our study as we examined 10 cases having history of previous preeclampsia and IUGR, two cases developed preeclampsia and six cases developed preeclampsia and IUGR with recurrence rate 10 to 55%.

Hauth *et al*. [16] discovered that Pre-existing diabetes was identified as a significant risk factor for the development of preeclampsia. When comparing the occurrence of preeclampsia in non-diabetic women, it is observed that the incidence is relatively low.

In agreement with Lin *et al*. [17] who revealed that high pre-pregnancy BMI was associated with an increased risk of preeclampsia agreeing with our study where obesity in our study is the most common risk factor encountered in twenty cases twelve of them developed preeclampsia only and four cases developed preeclampsia and IUGR.

In our study we examined 100 pregnant women at second trimester of pregnancy 62 cases had normal uterine doppler study, no case developed complications of uteroplacental insufficiency, while 38 cases had abnormal uterine doppler study, 35 case developed complication of uteroplacental insufficiency.

In the study of Barati *et al*. [12] A total of 379 cases were analyzed to investigate the use of doppler interrogation on the uterine arteries during the gestational period of 16-22 weeks. A total of 17 cases of abnormal uterine artery doppler results were observed, with 15 of these cases subsequently developing preeclampsia. Additionally, four cases were identified where neonates were classified as small for gestational age. To predict the occurrence of preeclampsia, it was necessary for the mean uterine artery PI to exceed the threshold of 1.45. This prediction method exhibited a specificity of 95.5% and a sensitivity of 79%.

Whereas, in the study of Cnossen *et al*. [18] A total of 108 cases were analyzed to investigate the use of doppler interrogation in assessing the uterine arteries during the gestational period of 18-22 weeks. A total of 28 cases were identified with abnormal uterine artery doppler results, out of which 27 cases subsequently developed preeclampsia. It was observed that the mean uterine artery PI had to be greater than 1.5 in these cases.

In our study, 100 women were involved 36 cases had preeclampsia, right uterine artery in 33 women was >0.7(91.7%) and only 3 cases were <.07(8.3%). And 64 cases had normal pregnancy, the right uterine artery was >0.7 in 3 cases only (4.7%) and less than 0.7 in 61 cases (95.3%). The right uterine artery sensitivity, specificity was 91.7, 95.3 respectively.

Whereas, the 36 cases who had preeclampsia their left uterine artery doppler showing 24 cases with RI >0.7(66.7%) and 12 cases with RI<.07(33.3%). And the 64 cases, 3 cases were >0.7(4.7%) and 61 cases were <0.7(95.3%). The left uterine artery sensitivity, specificity was 66.7, 95.3 respectively.

Comparable to Pereira PM *et al*. [19] found that the risk index (RI) for predicting preeclampsia is equal to or greater than 0.58. The results for sensitivity, specificity, positive predictive value, and negative predictive value were 50%, 93.9%, 33.3%, and 96.9%, respectively. Studies of Paretti *et al*. [20], Melchiorre *et al*. [21] utilized the Resistance Index (RI) as the primary index in their investigation to assess the negative results of pregnancy. Conversely, a combination of multiple Doppler parameters demonstrated greater effectiveness compared to a single parameter, despite the strong correlation between these parameters.

Pereira PM *et al*. [19] descibed the abnormal uterine artery Doppler can be characterized by Doppler indices with a mean PI greater than 1.45, a RI greater than 0.7, and the presence of a persistent diastolic notch.

Within the scope of our investigation, it can be concluded that Doppler indices with a mean PI greater than 1.45 and a RI greater than 0.7 can be classified as abnormal uterine artery Doppler. Additionally, the identification of early diastolic notches in either of the uterine arteries can be utilized as a predictor for preeclampsia, with a sensitivity rate of 50%.

In research that was done by Becker and Vonk [22], the evaluation centred on examining the relationship between uterine artery Doppler outcomes during the gestational period of 20-23 weeks and adverse obstetric outcomes. The study provided evidence of the occurrence of preeclampsia, intrauterine growth restriction (IUGR), intrauterine or neonatal mortality, and preterm birth. The study conducted by the authors revealed a significant association between impedance evaluation and the occurrence of adverse pregnancy outcomes, with complication rates varying from 3.2% to 38.4%. The mean principal investigator (PI) value in this study was found to be 2. The researchers have arrived at the conclusion that Doppler sonography of the uterine arteries conducted during the gestational period of 20-23 weeks possesses the capability to forecast specific unfavourable outcomes.

The present study involved the implementation of Doppler screening during the gestational period ranging from 16 to 22 weeks. A cohort of 50 low-risk women underwent examination, revealing that 4 of them exhibited elevated impedance. Among these cases, one woman developed

preeclampsia exclusively, while two women experienced both preeclampsia and intrauterine growth restriction (IUGR). The mean principal investigator (PI) value in our study was calculated to be 1.45. The application of Doppler sonography on the uterine arteries has shown the potential to predict a subset of adverse pregnancy outcomes, in line with the results reported in a previous study.

Concurring with Garcia *et al.* [23] who stated the optimization of predicting preeclampsia and intrauterine growth restriction (IUGR) is accomplished by employing a combination of maternal risk factors, the average PI of the uterine artery, and the concentration of placental growth factor. The results of our study suggest that the correlation between maternal risk factors and uterine artery parameters significantly influences the ability to predict preeclampsia.

In agreement with Mysaa chyad *et al.* [24] who discovered that the uterine artery The Doppler technique has the potential to serve as an important tool for predicting the occurrence of preeclampsia during the second trimester of pregnancy. Specifically, the mean PI of the uterine artery was found to be 1.34±0.58. The resistive index of right and left uterine artery were0.71±0.06, 0.70±0.16 respectively. In our study the mean PI of uterine artery is 1.56±0.46. The resistive index of right and left uterine artery are0.34±1.00, 0.39±0.96 respectively.

Sufriyana *et al*. [25] found that the optimization of predicting preeclampsia and IUGR is achieved through the utilization of a combination of maternal risk factors, the average PI of the uterine artery, and the concentration of placental growth factor. The findings of our study indicate that the interaction between maternal risk factors and uterine artery parameters has a substantial impact on the prediction of preeclampsia.

Conclusions

Women who exhibit abnormal uterine arteries Doppler examination are at a heightened risk of experiencing subsequent complications, particularly those that necessitate preterm delivery. UT A Doppler is a valuable, promising, and non–invasive technique for the detection of obstetric outcome. The identification of patients who are exposed to develope pre-eclampsia is beneficial for implementing vigilant and personalized antenatal surveillance, as well as initiating prophylactic therapy at an early stage. This approach aims to minimize the negative maternal and fetal outcomes associated with pre-eclampsia.

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Conflict of Interest: Nil.

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