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First Trimester Uterine Artery Doppler in Early prediction of Preeclampsia

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Abstract

Research on the second trimester's use of ultrasound to detect preeclampsia and growth restriction in the baby has been going on since at least the 1970s. Recently, there has been an increase in the usage of Doppler interrogation throughout the first trimester of pregnancy. The relationship between uterine artery Doppler velocimetry and adverse pregnancy outcomes has been evaluated using various measurement techniques and impedance indices, Aim and objectives; to determine the clinical value of first trimester uterine artery Doppler indices in the prediction of early preeclampsia, Subjects and methods of determining A cross-sectional study of 60 pregnant women from Banha University's Obstetrics & Gynecology Department or inpatient Banha University Hospital was performed. In terms of previous pre-eclampsia, there was a statistically significant difference between individuals who were preterm, at term, and without it. Conclusion: First-trimester uterine artery Doppler had higher predictive accuracy than late-onset illness in the identification of early-onset preeclampsia and FGR. Using uterine artery Doppler indexes to predict preeclampsia in women at low risk, the sensitivity ranges from 34% to 76% and the specificity ranges from 83% to 93% This test's poor sensitivity makes it ineffective as a sole disease marker. Preeclampsia and other poor pregnancy outcomes may be better detected using multiparametric models in the first trimester, according to increasing data.

Keywords: preeclampsia, Fetal growth restriction, first trimester; uterine artery Doppler.

1. Introduction

Preeclampsia is a major cause of maternal and perinatal death all across the globe, and it's no surprise why. A worldwide prevalence of between 2 and 8 percent [1] of pregnancies are complicated by preeclampsia.

When a woman has previously normal blood pressure, she may develop preeclampsia, which is characterised by new-onset hypertension (140 mm Hg or higher systolic blood pressure or 90 mm Hg or higher diastolic blood pressure or more on two occasions at least four hours apart after 20 weeks of pregnancy) and new-onset proteinuria (300 mg or higher diastolic blood pressure or 110mm Hg or higher diastolic blood pressure) (used only if other quantitative methods not available) [2].

Preeclampsia is more likely in women who have a number of risk factors for pregnancy complications. Nulliparity, multiple pregnancy, preeclampsia in a previous pregnancy, chronic hypertension, pregestational diabetes, gestational diabetes mellitus thrombophilia sysemia, prepregnancy BMI greater than 30, antiphospholipid antibody syndrome, maternal age 35 years or older, kidney disease, assisted reproductive technology, obstructive sleep apnea are all risk factors for preeclampsia [3].

However, it's crucial to keep in mind that the majority of preeclampsia instances involve young, healthy, nulliparous women with no known health risks.

No one knows for sure how genetic-environmental interactions influence preeclampsia risk and incidence, but new research suggests that the propensity to develop preeclampsia may have some genetic component [4].

Noninvasive Uterine Artery Doppler may be used to evaluate trophoblast development and perfusion of the uterus in the womb. First-trimester observations show that preeclampsia is caused by a relative failure of trophoblast invasion, which warrants monitoring uterine artery Doppler results throughout the first trimester of pregnancy [5].

This research favoured the resistance index (RI) over the pulsatility index (PI) because the ultrasound operator using it had superior intraobserver and interobserver variability [6].

The study's goal is to see whether uterine artery Doppler indices from the first trimester may help detect preeclampsia early on.

2. Patients and methods

This prospective study included 60 pregnant females from outpatient clinic or inpatient department of Obstetrics and Gynecology department at Banha University Hospital.

2.1. Inclusion criteria

- Pregnant women with gestational age from 10 to 16 weeks.

2.2. Exclusion criteria

- cases with fetal chromosomal or structural abnormalities
- concurrent maternal disease(e.g. chronic hypertension , renal disease , connective tissue disease)

Explanation of the procedure to all women participating in the study and full informed consent was taken from all patients before starting the study with counseling about risk and benefit of study.

All Patients were subjected to full history and clinical examination and lab investigation and Doppler.

2.3. Laboratory Investigations

- A complete blood count was performed via BECKMAN COULTER DxH520-2019 device for the estimation of platelet indices (platelet count,

mean platelet volume, platelet distribution width) using kits from BIO RAD\DiaMed.
- Urine analysis had be also done to detect proteinuria.
- Routine laboratory investigations (Blood group, Rhesus factor, random blood sugar, liver and kidney function tests) were conducted

2.4. Doppler
- Once a viable intrauterine pregnancy confirmed, the uterine artery Doppler assessment was performed on a (GE.VOLUSON 730 PRO_V) ultrasound unit using a trans-abdominal approach.
- To ensure consistency of results, the researcher were the only person performing the scans and the ultrasound unit was serviced and calibrated regularly.
- The probe was placed lateral to the uterus and the transducer gently tilted medially until the uterine artery identified where it crossed over the external iliac artery.
- The sample gate was placed over the entire diameter of the artery and pulsed wave Doppler was used to obtain three consecutive uterine artery measurements.
- Wave forms and the pulsatility index (PI) were measured bilaterally, the resistance index (RI) is measured and the mean calculated.
- The presence of the uterine artery notching and a PI > 1.5 during the first trimester was considered indicative of increased vascular resistance in the placental bed.
- The Doppler assessment of the uterine artery was repeated at monthly intervals.

2.5. Ethical Consideration

Study protocol had been submitted for approval by Institution Research Board (IRB) of faculty of medicine Banha University. Informed verbal consent had been obtained from each participant sharing in the study. Confidentiality and personal privacy had been respected in all levels of the study**.**

2.6. Statistical Analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures were coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) **(**Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative result were represented as number and percentage , quantitative continues group were represented by mean ± SD , the following tests were used to test differences for significance;., correlation by Pearson's correlation or Spearman's . P value was set at <0.05 for significant results & <0.001 for high significant result.

3. Results

This study is cross section study that included (60) pregnant females with gestational age from 10 to 16 weeks to determine the clinical value of first trimester uterine artery Doppler indices in the prediction of early preeclampsia. the mean age of studied group was 28.28 (±4.09 SD) with range (22-35) years, among the studied group there were 32 (53.3%) primiparity, 3 (5%) with party equal 1, 15 (25%) with parity equal 2 and 10 (16.7%) with parity more than 2, there were 2 (3.3%) with previous pre-eclampsia, the mean gestational age was 13.23 (±2.01 SD) with range (10-16) weeks, the mean BMI was 29.22 (±2.89 SD) with range (25.4-33.9) kg/m^2, the mean systolic blood pressure was 120.17 (±7.92 SD) with range (110-130) mmHg and the mean Diastolic blood pressure was 71.67 (±8.06 SD) with range (60-80) mmHg. table (1)

Table (1) Descriptive demographic data of studied patients

	Demographic data	Cases	
	Range.	22.0 – 35.0	
	Mean ± SD.	28.28 ± 4.09	
Age (years)	**Parity**	No.	%
	Primiparity	32	53.3
	1	3	5.0
	2	15	25.0
	>2	10	16.7
	Previous pre-eclampsia	No.	%
	No	58	96.7
	Yes	2	3.3
Gestational age (weeks)	**Range.**	10.0 – 16.0	
	Mean ± SD.	13.23 ± 2.01	
	BMI		
	Range.	25.4 – 33.9	
	Mean ± SD.	29.22 ± 2.89	
Systolic BP	**Range.**	110.0 – 130.0	
	Mean ± SD.	120.17 ± 7.92	
Diastolic BP	**Range.**	60.0 – 80.0	
	Mean ± SD.	71.67 ± 8.06	

The mean RI of studied group was 0.70 (±0.1 SD) with range (0.54-0.93), among the studied group there were 22 cases (36.7%) with bilateral notches. table (2)

There was statistically significant difference between patients with preterm, at term and without groups as RI. table (3)

There was statistically significant difference between patients with preterm, at term and without groups as Birth week and Apgar 5. table (4)

Using SAA it was shown that above 0.695, it can discriminate between cases and control with AUC of 857, level of sensitivity 100%, specificity 60.4%, PPV 25% and NPV 60.4%. Using IL 17 it was shown that above 138.935, it can discriminate between cases and control with AUC of 1.00, level of sensitivity 100%, specificity 100%, PPV 100% and NPV 100%. figure (1)

Table (2) First term uterine artery indices among studied cases.

uterine artery indices	**Cases**	
RI		
Range.	0.54 – 0.93	
Mean ± SD.	0.70 ± 0.10	
Bilateral notches	No.	%
Present	22	36.7
Absent	38	63.3

Table (3) Comparison patients with preterm, at term and without groups as regard first term uterine artery indices.

uterine artery indices	**Pre-eclampsia**						**Test**	**p**
	No		**Pre-term**		**At term**			
RI								
Range.	0.54 – 0.86		0.70 – 0.93		0.74 – 0.93		F=3.602	0.002*
Mean ± SD.	0.69 ± 0.10		0.83 ± 0.12		0.83 ± 0.08			
			P_1=0.040*, P_2=0.018*					
Bilateral notches	No.	%	No.	%	No.	%		
Present	17	32.1	2	66.7	3	75.0	χ^2=4.175	0.128
Absent	36	67.9	1	33.3	1	25.0		

F: **F for ANOVA test**, Pairwise comparison bet. each 2 groups was done using **Post Hoc Test (Tukey)**

χ^2: **Chi square test**

p: p value for comparing between the studied groups

p1: p value for comparing between patients without pre-eclampsia and preterm pre-eclampsia

p2: p value for comparing between patients without pre-eclampsia and at term pre-eclampsia

*: Statistically significant at $p \leq 0.05$

Table (4) S Comparison patients with preterm, at term and without groups as regard secondary outcome

	Mean ± SD	**Range**	**F**	**p**
Birth week				
No	37.17 ± 1.64	35.0 – 40.0	9.375	<0.001
Pre-term	33.67 ± 0.58	33.0 – 34.0		
At term	39.0 ± 2.0	36.0 – 40.0		
Birth weight (kg)				
No	3.31 ± 0.74	2.0 – 4.4	1.749	0.183
Pre-term	2.53 ± 0.38	2.10 – 2.80		
At term	3.1 ± 0.66	2.20 – 3.80		
Apgar 1				
No	6.34 ± 1.83	4.0 – 9.0	2.108	0.131
Pre-term	4.33 ± 1.15	3.0 – 5.0		
At term	5.50 ± 1.29	4.0 – 7.0		
Apgar 5				
No	8.55 ± 1.20	6.0 – 10.0	4.180	0.020
Pre-term	7.0 ± 1.73	5.0 – 8.0		
At term	7.25 ± 0.96	6.0 – 8.0		

F: F for ANOVA test, Pairwise comparison bet. each 2 groups was done using **Post Hoc Test (Tukey)**

p: p value for comparing between the studied groups

p1: p value for comparing between patients without pre-eclampsia and preterm pre-eclampsia

p2: p value for comparing between patients without pre-eclampsia and at term pre-eclampsia

*: Statistically significant at $p \leq 0.05$

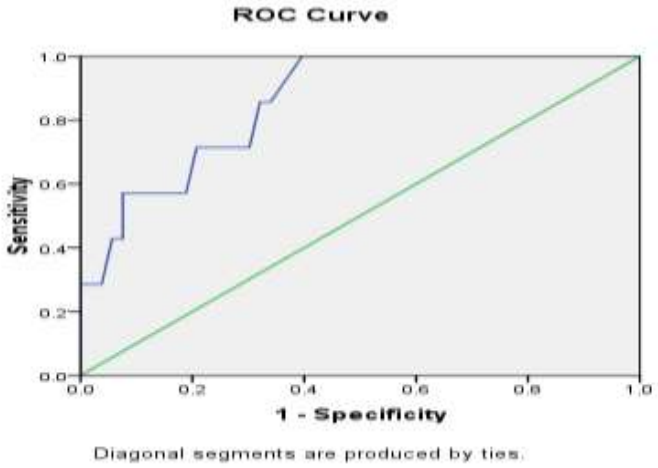

Fig. (1) Roc curve analysis for the use of RI to predict Pre-eclampsia.

4. Discussion

This study's findings revealed a statistically significant difference (p= 0.002) between patients with preterm birth and those who were born at term and those who did not. In accordance with these findings, the uterine artery Pulsatility Index (PI) was shown to be substantially linked to preterm birth. One additional unit of maternal-fetal index (PI) in high-risk pregnancies doubles (95 percent confidence interval, odds ratio = 6.09, 241.9, P 0.001) the likelihood of PE, while researchers at the University of Kansas School of Medicine have found a link between an abnormal maternal-fetal index (2 = 16.29, P = 0.00), an abnormal S/D ratio, and the combined result (2 = 11.5, P = 0.007) with PE. The combined result of 86.6 percent specificity, 95.8 percent NPV, and 25 percent positive predictive value (PPV) had the greatest sensitivity (53.8 percent), with an area under the curve (AUC) of 0.71. (95 percent confidence interval [CI]: 0.534-0.871). The NPV of a normal outcome was very high across the board. All indicators had higher accuracy in predicting severe PE, with the greatest AUC of 0.830 (95 percent CI: 0.624-1.000; P = 0.01) for the combined result.

While Melchiorre et al. [9] reported that the first-trimester uterine artery RI was significantly higher in women who later developed preterm pre-eclampsia (mean RI, 0.79) than in those with a normal outcome (mean RI, 0.70; P=0.0001) or those who developed pre-eclampsia at term (mean RI, 0.72; P=0.002). Preterm pre-eclampsia (75.8%) had a greater incidence of bilateral first-trimester uterine artery notches than pregnancies with a normal result (44.7 percent, P=0.0001) or pregnancies with pre-eclampsia at term (50.9 percent, P=0.036). Between women who had a normal pregnancy outcome and those who had pre-eclampsia at term, there were no significant changes in first-trimester mean uterine artery RI (P=0.136) or prevalence of bilateral notches (P=0.459).

There was a significant increase in the mean PI in women who later developed pre-eclampsia, according to the findings of Gomez et al. [10], who also found that complicated pregnancies had a higher prevalence of bilateral notching (58 percent vs. 41 percent; P = 0.04) and a higher mean PI (2.04 vs. 1.75; P = 0.05, t-test). Elwakel et al. [11]

The difference between patients who were preterm, full-term, and not pregnant was statistically significant in our sample.

Women with preeclampsia had significantly shorter gestations than their controls (p 0.01), and their babies were smaller and shorter when they were born, according to Jasovic Siveska and Jasovic [12].

Preterm birth rates were higher in the severe group than in the mild group, according to Kamel et al. [13], and this was linked with a higher than average incidence of foetal growth restriction. When comparing the two groups, the SHP had significantly poorer neonatal outcomes (FGR, preterm birth, and low birth weight) than the MHP did.

Also, according to Khader et al. [14], preeclampsia patients had substantially higher rates of low birth weight (LBW) delivery (32.5 percent vs. 8.3 percent), preterm (30.8 percent vs. 7 percent), and newborn death (81 percent vs. 12 percent per 1000 live births).

AUC of 857, sensitivity of 100%, specificity of 60%, PPV of 25%, and NPV of 60% were found in the present research using SAA. It was shown that this method can distinguish between cases and controls with an AUC over 0.695. In studies using IL 17, it was found that AUC of 1.00, 100 percent sensitivity, 100 percent specificity, 100% PPV, and 100% NPV could be used to distinguish between cases and controls above 138.935. In other studies, it was found that AUC of 0.857, 100 percent sensitivity, and 60.4% specificity could be used to predict pre-eclampsia above 0.695 using RI. In yet another study, it was found that AUC of 0.839

According to Erdodu et al. [15], the ROC curve had a 95% confidence interval of 0.70-0.88 and the standard error was 0.046 (p0.001). On average, UtA PI was shown to be 45.5% sensitive, 50% positive predictive value, and 94.44% negative when used at the

2.56 threshold value for 5% false positives in predicting preeclampsia. It was discovered that 63.6 percent sensitivity, 93.3 percent specificity, 23.3 percent and 98.8 percent negative predictive value of the 2.56threshold value of preeclampsia uterine artery pulsatility index were used to identify preeclampsia at an early stage. With early-onset PE we discovered that when we evaluated the UtA PI value using the ROC curve, the area under the curve was 0.83 (95% CI 0.71-0.95) and the standard error was 0.062 (p0.001). For early-onset preeclampsia, the sensitivity was found to be 45.5%, while the positive predictive value was 23.8%, and the negative predictive value was found to be 98.2% when using UtA PI at the 2.72 threshold value. There was a 33.3% sensitivity, 96.9% specificity, a 52.4% positive predictive value, and a 93.4 percent negative predictive value at the 2.72 threshold value of the uterine artery pulsatility index in the prediction of preeclampsia. The assessment of UtA PI was shown to be more important for early-onset PE screening than previously thought.

5. Conclusion

First-trimester uterine artery Doppler's predictive accuracy is greater than late-onset disease in the identification of early-onset preeclampsia and FGR. They range from 34% to 76% for the sensitivity and from 83% to 93% for the specificity of using ultrasound to predict the presence of pre-existing pre-eclampsia in low-risk women. This test's poor sensitivity makes it ineffective as a sole disease marker. Preeclampsia and other poor pregnancy outcomes may be better detected using multiparametric models in the first trimester, according to increasing data.

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