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Original Research Article

Evaluation of the predictive value of uterine artery doppler in second trimester of pregnancy as a screening tool for preeclampsia

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ABSTRACT

Background and Objective: This study was carried out to determine the validity and reliability of Uterine Artery (UtA) Doppler imaging as a screening tool for predicting preeclampsia among pregnant women attending a tertiary care hospital of the Armed Forces in second trimester.

Methods: Our study was a prospective diagnostic study carried out in 680 pregnant women (age group of 19 to 30 years) in second trimester. Maternal BP was recorded using automated BP apparatus on three occasions (15 minutes apart) in supine posture. This was followed by uterine artery Doppler with measurement of Resistivity index (RI) and Pulsatility index (PI). Patients were followed up every month till 12 weeks post-partum. Statistical analysis was done using SPSS version 21.

Results: The mean uterine artery PI was 1.21 ± 0.296 and the mean uterine artery RI value was observed to be 0.58 ± 0.18 . The incidence of preeclampsia among the study participants was observed to be 9.9%. The mean uterine artery PI and RI among patient with preeclampsia was found to be significantly higher than those without preeclampsia (p value < 0.001). The uterine artery PI values of ≥ 1.3 when defined as a diagnostic cut off, the sensitivity and specificity was found to be 79.1% and 70.8% respectively. The accuracy was observed to be 71.62%. The uterine artery RI values of ≥ 0.7 when defined as a diagnostic cut off, the sensitivity and specificity was found to be 44.78% and 89.72% respectively. The accuracy was observed to be 85.29%.

Interpretations and Conclusion: Uterine artery PI parameter is found to have better sensitivity than RI in predicting preeclampsia. Consideration of both PI and RI parameters for prediction of preeclampsia significantly increased the specificity of Uterine Artery Doppler Imaging. Uterine Artery Doppler is a useful tool in predicting the risk of preeclampsia among women in second trimester of pregnancy.

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1. Introduction

Preeclampsia is considered to be a multi-system disorder characterized by new onset hypertension (Systolic Blood Pressure ≥ 140 mmHg and Diastolic Blood Pressure ≥ 90 mm Hg) and proteinuria (≥ 300 mg/24 hours) occurring after 20 weeks of gestation in a previously normotensive

woman.¹

The incidence of preeclampsia is 2 to 8% of the pregnancies worldwide.¹ Variations in incidence reflect differences in the maternal age distribution and proportion of primiparous women among populations.² Globally, 10 to 15% of direct maternal deaths (i.e., resulting from obstetric complications of pregnancy) are found to be associated with preeclampsia/eclampsia.³ Preeclampsia/eclampsia is

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one among four leading causes of maternal death, along with hemorrhage, cardiovascular conditions, and thromboembolism.⁴

Preeclampsia leads to increased risk of maternal and/or fetal mortality or serious morbidity.⁵ Serious maternal effects include life-threatening events such as placental abruption, acute renal failure, cerebral hemorrhage, hepatic failure, pulmonary edema, disseminated intravascular coagulation, and progression to eclampsia. Fetal effects include greater risk of restricted fetal growth and preterm birth.

Mild preeclampsia present with mild hypertension ($\geq 140/90$ & $<160/110$ mmHg) and proteinuria ≥ 300 mg/24 hours, or significant increase from baseline. Severe pre-eclampsia has been characterized by one or more of the following criteria: sustained systolic BP ≥ 160 mmHg or diastolic BP ≥ 110 mmHg while on bed rest, nephrotic-range proteinuria (≥ 3 g/24 hours or 3+ on urine dipstick), sudden oliguria, central nervous system disturbances, pulmonary edema or cyanosis, epigastric or right upper quadrant pain, liver dysfunction, thrombocytopenia, and fetal growth restriction.⁶

The onset of clinical manifestations of preeclampsia can be varied. Majority are “late onset preeclampsia, that present after 34 weeks of gestation especially in the peripartum period.”⁷ Around 10% present before 34 weeks of gestation as “early onset preeclampsia”. Few cases present as “Postpartum preeclampsia” that occurs more than 48 hours of delivery but less than four weeks after delivery.^{8,9}

Abnormal cytotrophoblastic invasion and abnormal remodeling of maternal uterine spiral arteries lead to pathological resistance to placental blood flow and hence, placental ischemia, resulting in various maternal and fetal effects.

The pathological changes of preeclampsia begin to appear as early as in first trimester. These changes can be easily detected by Doppler studies of the maternal uterine vessels and therefore help in detecting women at risk not only of preeclampsia, but also of intra-uterine growth restriction. Abnormal Doppler studies in both the first and second trimesters have been reported to be associated with preeclampsia.¹⁰

Our study was conducted in a tertiary care hospital of the armed forces and was undertaken to determine the validity and reliability of Uterine Artery (UtA) Doppler imaging as a screening tool for predicting preeclampsia during second trimester.

2. Materials and Methods

Our study was conducted in 680 patients as a prospective diagnostic study from July 2016 to April 2018 in a tertiary care hospital of the Armed Forces at Delhi. Antenatal women in second trimester in the age group of 19 to

30 years attending antenatal care outpatient department were included in the study population. Exclusion criteria were: established cases of preeclampsia, co-morbidities such as hypertension, diabetes, asthma, anemia, etc., known risk factors of preeclampsia like obesity (BMI >30 kg/m²), multiple gestation, history of smoking/alcohol/any drug intake and history of preeclampsia in previous pregnancies.

The minimum required sample size was calculated to be 664 using the formula, “ $A = [\text{Sensitivity} * (1 - \text{Sensitivity})] / (\text{Acceptable Deviation})^2$ ” & $N = \frac{A}{\text{Prevalence}}$

Deviation = 5%. According to Barati M et al., Sensitivity of uterine artery Doppler is 79% and specificity of uterine artery Doppler is 95.5%.¹¹ According to National Health Portal 2016, prevalence of preeclampsia in India is 10%.¹²

The study was carried out with strict adherence to Pre-Conception and Pre-Natal Diagnostic Techniques Act, 1994 (amended in 2014). Duly filled form ‘F’ was obtained for each patient. The eligible patients were explained about the procedure in detail, informed written consent was obtained subsequently. Maternal history was collected through pre-formatted questionnaire in patient’s own language. Maternal BP was recorded using automated BP apparatus (Omron Digital Arm Bp Monitor HEM-8712) on three occasions (15 minutes apart) in supine posture. Blood pressure was recorded again four hours later in those who present with SBP >140 mmHg and DBP >90 mmHg. This was followed by uterine artery Doppler using M/S Wipro GE Medical Systems, Logiq P5 for measurement of Resistivity index (RI) and Pulsatility index (PI).

Patients were followed up every month till four weeks post-partum to look for symptoms associated with preeclampsia, increased blood pressure and presence of proteinuria, elevated AST & ALT, low platelet counts and elevated serum creatinine.

Data entry was done by using MS Excel 2010 and analysis was done by using the software SPSS version 21. The reliability and validity of the screening methods were assessed by measuring sensitivity, specificity and predictive values. ROC curve was made to determine cut off values and AUC calculations. Differences in proportions and means between groups were tested by chi square test and independent sample t test respectively. A p value <0.05 was considered statistically significant.

Institute Ethical Committee approval and certification were sought and obtained before starting the study. Study participants were explained in detail about the implications of participating in the study in their own language and informed written consent was obtained before interview and examination.

3. Results

Majority of the study participants were in the age group of 18-25 years (63.1%), followed by 26-30 years who represented 29.9% of the study population. The mean age

of the study participants was observed to be 24.9 ± 3.5 years. (Table 1)

Table 1: Distribution of study participants based on age (n=680)

Age (in years)	Frequency	Percent
18-25	429	63.1
26-30	203	29.9
31-37	48	7.1
Total	680	100.0

Majority of the study participants were primigravida (70%), while 30% were multigravida.

The mean uterine artery PI was 1.21 ± 0.296 and the mean uterine artery RI value was observed to be 0.58 ± 0.18 . (Table 3)

Table 2: Distribution of study participants based on gravidity score (n=680)

Gravidity score	Frequency	Percent
1	476	70.0
2	149	21.9
3	50	7.4
4	5	0.7
Total	680	100.0

Table 3: Distribution of study participants based on uterine artery PI and RI parameters (n=680)

Parameters	Uterine artery PI	Uterine artery RI
Mean	1.21	0.58
Standard Deviation	0.296	0.18

Table 4: Distribution of study participants based on incidence of preeclampsia (n=680)

Preeclampsia	Frequency	Percent
Developed	67	9.9
Not developed	613	90.1
Total	680	100.0

The incidence of preeclampsia among the study participants was observed to be 9.9%. Presence of proteinuria was observed in 9.9% of all the study participants. Higher proportions of mothers in younger age group are found to have preeclampsia than those who are in 26-30 years of age. Also, this association was found to be statistically significant (p value – 0.029). The mean uterine artery PI among patient with preeclampsia was found to be significantly higher than those without preeclampsia. (p value <0.001). The mean uterine artery RI among patient with preeclampsia was found to be significantly higher than those without preeclampsia. (p value <0.001)

The uterine artery PI values of ≥ 1.3 when defined as a diagnostic cut off, the sensitivity and specificity was found

to be 79.1% and 70.8% respectively. The accuracy was observed to be 71.62%. The cut off was decided based on the ROC analysis showing maximum AUC.

The uterine artery RI values of ≥ 0.7 when defined as a diagnostic cut off, the sensitivity and specificity was found to be 44.78% and 89.72% respectively. The accuracy was observed to be 85.29%. The cut off was decided based on the ROC analysis showing maximum AUC. The sensitivity and specificity of uterine artery indices of PI ≥ 1.3 and RI ≥ 0.7 was 37.31% and 96.57% respectively.

The predicted risk ratio of preeclampsia was observed to be 16.78 times when both PI ≥ 1.3 and RI ≥ 0.7 were observed on USG evaluation. The sensitivity and specificity of uterine artery indices of PI ≥ 1.3 or RI ≥ 0.7 was 86.57% and 63.95% respectively. The predicted risk ratio of preeclampsia was observed to be 11.43 times when either PI ≥ 1.3 or RI ≥ 0.7 was observed on USG evaluation.

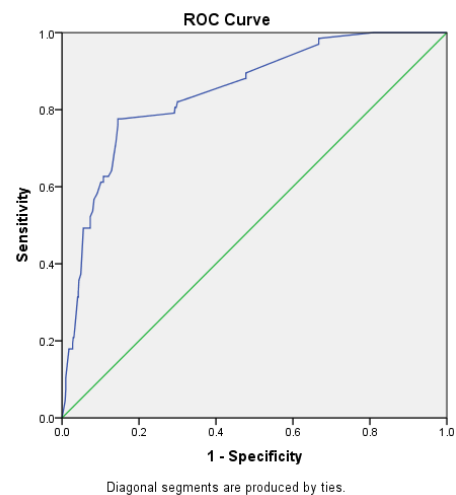


Fig. 1: ROC analysis uterine artery PI values in predicting preeclampsia (n=680)

4. Discussion

Majority of the study participants were in the age group of 18-25 years (63.1%), the mean age of the study participants was observed to be 24.9 ± 3.5 years. The mean uterine artery PI was 1.21 ± 0.296 and the mean uterine artery RI value was observed to be 0.58 ± 0.18 . The incidence of preeclampsia among the study participants was observed to be 9.9%.

The mean uterine artery PI and RI among patient with preeclampsia was found to be significantly higher than those without preeclampsia (p value <0.001). The uterine artery PI values of ≥ 1.3 when defined as a diagnostic cut off, the sensitivity and specificity was found to be 79.1% and 70.8% respectively. The accuracy was observed to be 71.62%. The uterine artery RI values of ≥ 0.7 when defined as a diagnostic cut off, the sensitivity and specificity was found

Table 5: Association between age and occurrence of preeclampsia (n = 680)

Age (in years)	Preeclampsia		Total n (%)	p value*
	Present n (%)	Absent n (%)		
18-25	52(12.1)	377(87.9)	429(100.0)	0.029
26-30	11(5.4)	192(94.6)	203(100.0)	
>30	4(8.3)	44(91.7)	48(100.0)	
Total	67(9.9)	613(90.1)	680(100.0)	

* Chi Square test was applied to test statistical difference in proportions

Table 6: Distribution of study participants based on uterine artery PI (n=680)

Uterine artery PI	Preeclampsia	
	Present (n=67)	Absent (n=613)
Mean	1.59	1.17
Standard Deviation	0.29	0.26
Difference in mean (95% CI)	0.425 (0.35 - 0.49)	
p value*	<0.001	

*Independent sample t test was applied

Table 7: Distribution of study participants based on uterine artery RI (n=680)

Uterine artery RI	Preeclampsia	
	Present (n=67)	Absent (n=613)
Mean	0.732	0.57
Standard Deviation	0.2	0.17
Difference in mean (95% CI)	0.16 (0.12 - 0.21)	
p value	<0.001	

*Independent sample t test was applied

Table 8: Diagnostic accuracy of uterine artery PI

Uterine artery PI	Preeclampsia		Total
	Present	Absent	
Present (≥ 1.3)	53	179	232
Absent (< 1.3)	14	434	448
Total	67	613	680
Sensitivity	79.1%(67.43-88.08)		
Specificity	70.8%(67.04-74.37)		
Positive predictive value	22.84%(19.92-26.06)		
Negative predictive value	96.88%(95.1-98.02)		
Cohen's kappa value of agreement	0.238		
LR Positive	2.71 (2.28-3.22)		
LR Negative	0.30 (0.18-0.47)		
Accuracy	71.62 (68.07-74.98)		

Table 9: Diagnostic accuracy of uterine artery RI

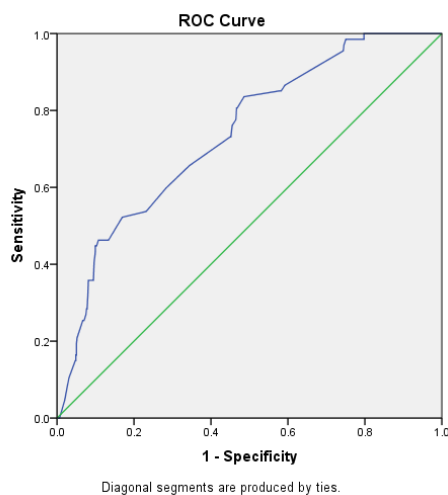
Uterine artery RI	Preeclampsia		Total
	Present	Absent	
Present(≥ 0.7)	30	63	93
Absent (< 0.7)	37	550	587
Total	67	613	680
Sensitivity	44.78%(32.6-57.42)		
Specificity	89.72%(87.04-92.01)		
Positive predictive value	32.26%(25.05-40.43)		
Negative predictive value	93.7%(92.29-94.86)		
Cohen's kappa value of agreement	0.294		
LR Positive	4.36 (3.06-6.21)		
LR Negative	0.62 (0.5-0.76)		
Accuracy	85.29 (82.41-87.87)		

Table 10: Diagnostic accuracy of both uterine artery indices

Uterine artery indices	Preeclampsia		Total
	Present	Absent	
Present (PI \geq 1.3 and RI \geq 0.7)	25	21	46
Absent	42	592	634
Total	67	613	680
Sensitivity		37.31%(25.8-49.99)	
Specificity		96.57%(94.81-97.87)	
Positive predictive value		54.35%(41.38-66.75)	
Negative predictive value		93.38%(92.13-94.43)	
Cohen's kappa value of agreement		0.394	
LR Positive		10.89 (6.46-18.37)	
LR Negative		0.65 (0.54-0.78)	
Accuracy		90.74 (88.3-92.81)	
OR		16.78(8.68-32.44)	

Table 11: Diagnostic accuracy of either one of uterine artery indices

Uterine artery indices	Preeclampsia		Total
	Present	Absent	
Present (PI \geq 1.3 or RI \geq 0.7)	58	221	279
Absent	9	392	401
Total	67	613	680
Sensitivity		86.57%(76.03-93.67)	
Specificity		63.95%(60.01-67.76)	
Positive predictive value		20.79%(18.56-23.21)	
Negative predictive value		97.76%(95.94-98.77)	
Cohen's kappa value of agreement		0.21	
LR Positive		2.4 (2.08-2.77)	
LR Negative		0.21 (0.11-0.39)	
Accuracy		66.18(62.48-69.73)	
OR		11.43(5.56-23.51)	

**Fig. 2:** ROC analysis uterine artery RI values in predicting preeclampsia (n=680)

to be 44.78% and 89.72% respectively. The accuracy was observed to be 85.29%.

The sensitivity and specificity of uterine artery indices of PI \geq 1.3 and RI \geq 0.7 was 37.31% and 96.57% respectively. The predicted risk ratio of preeclampsia was observed to be 16.78 times when both PI \geq 1.3 and RI \geq 0.7 were observed.

High sensitivity is more preferable than high specificity because minimizing false negatives over false positives is advantageous considering the benefits and harms due to unnecessary treatment or intervention. Studies of uterine artery Doppler velocimetry for prediction of preeclampsia are difficult to compare because investigators have used different Doppler sampling techniques, definitions of abnormal flow velocity waveform, populations, gestational age at examination, and criteria for the diagnosis of preeclampsia.

Chakraborty S et al.¹³ in their study among 100 antenatal women in India stated that specificity and sensitivity of PI Index, and RI Index as 91.67% and 87.5%; 85.71% and 71.43% respectively along with PI PPV 80%, NPV 94.29% and accuracy of 90%, whereas RI Index PPV 68.97%, NPV 88.73% and accuracy of 83% showing PI Index is having higher specificity and sensitivity along with other

parameters. The sensitivity of the indices was higher than the present study evaluation, though the specificity values were comparable. Also, the accuracy of PI and RI values in both the studies were similar.

Verma D et al¹⁴ performed uterine artery Doppler at 22–24 weeks of gestation in 165 pregnant women with singleton pregnancies. A pulsatility index (PI) more than 1.45 or bilateral uterine notching was labelled as abnormal Doppler. In the presence of abnormal Doppler, the risk of preeclampsia [OR=10.7, 95% confidence interval (CI): (3.91–29.1); $p < 0.001$] is increased. The positive predictive value of abnormal uterine artery Doppler was highest for preeclampsia (36.84%). These results were similar and comparable to that of the present study results though different operational definitions were used in these studies for Doppler indices and abnormalities.

Albaiges et al¹⁵ reported similar findings, with a higher detection rate for preeclampsia and the risk of preeclampsia as 40%. In a separate study by Harrington et al¹⁶ 81.2% of patients with abnormal uterine artery Doppler developed preeclampsia when followed up until delivery. Fonseca et al¹⁷ in 2006 demonstrated a significant association of mean bilateral increased uterine artery PI at 22–24 weeks and spontaneous early delivery among mothers with preeclampsia. However, the study also concluded that uterine artery Doppler does not provide a significant improvement in the prediction of spontaneous early delivery provided by maternal characteristics and previous obstetric history developed preeclampsia. The findings of the above study with respect to the uterine artery Doppler indices were identical to that of the observations of our study.

5. Strengths and Limitations

5.1. Strengths

1. Appropriate sample size calculation was done and adequate numbers of samples were studied.
2. The study explored the role of both UtA indices combined and individually in predicting preeclampsia.
3. The study population included a wide range of ethnicity from all over the country.

6. Limitations

1. The study did not include the role of uterine artery Doppler in 1st trimester of pregnancy considering the feasibility and availability of resources.
2. No differentiation of early onset and late onset preeclampsia was done (to compare the predictive accuracy in each).

7. Conclusion

The incidence of preeclampsia among the study participants was found to be 9.9%. The mean values of uterine artery

PI and RI were found to be significantly high among women who developed preeclampsia as compared to those who did not. Uterine artery PI parameter is found to have better sensitivity than RI in predicting preeclampsia. Consideration of both PI and RI parameters for prediction of preeclampsia significantly increased the specificity of uterine Doppler imaging. Uterine artery Doppler is a useful tool in predicting the risk of preeclampsia among women in second trimester of pregnancy.

8. Source of Funding

Nil.

9. Conflict of Interest

The authors have none to declare.

10. Ethical Approval


Institutional ethical committee approval obtained prior to the study.

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