



PREDICTION OF PREECLAMPSIA BY UTERINE ARTERY DOPPLER

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ABSTRACT **Objective:** To evaluate the role of mean pulsatility index by first trimester uterine artery doppler in prediction of preeclampsia. **Methodology:** A prospective observational study was conducted in a tertiary care center. Of 200 women screened, 136 women met eligible criteria and 130 consented for participation in the study. In addition to nuchal translucency and crown-rump length, mean uterine artery pulsatility index (PI) was measured at 11–13+6 weeks, and women were followed up till delivery to observe the development of gestational hypertension, preeclampsia and fetal growth restriction (FGR). Categorical variables were analyzed using ROC curve, and $P \leq 0.05$ (5%) was used to calculate significance. **Results:** Among 130 women followed till delivery, 9 (6.92%) had mean PI $>95\%$ and 121 (93.08%) had normal Doppler. A significantly higher number of women with PI $\geq 95\%$ had preeclampsia (55.55%) ($p < 0.001$), and the sensitivity of PI in prediction of preeclampsia was 55.55% with specificity of 98.80%. No association was found between PI and FGR ($p = 0.228$). **Conclusion:** This study showed a positive association with the development of preeclampsia. The predictive accuracy of first trimester uterine artery Doppler using PI with cutoff of $>95\%$ has low sensitivity in prediction of preeclampsia (55.55%) but it has high specificity (98.80%) for prediction of PE (Preeclampsia).

KEYWORDS : Preeclampsia, Pulsatility index, Fetal growth restriction

INTRODUCTION

Most pregnancies, labours, and deliveries are normal biological processes that result in a healthy outcome for mothers and babies. Those that are not normal, however, can result in maternal and/or perinatal mortality or substantial morbidity. Modern antenatal care provision is focused on a risk-based approach to monitoring for adverse pregnancy outcomes such as preeclampsia, fetal growth restriction, placental abruption, and stillbirth. Preeclampsia (PE) is a major cause of maternal and perinatal morbidity and mortality¹⁻³ and is thought to be predominantly as the consequence of impaired placentation. Evidence suggests that PE can be subdivided into early onset PE, requiring delivery before 34 weeks gestation and late onset PE, with delivery at or after 34 weeks, because the former is associated with a higher incidence of adverse outcome⁴⁻⁷. A major challenge in modern obstetrics is early identification of pregnancies at high-risk of early onset PE and undertaking the necessary measures to improve placentation there by allowing early commencement of management strategies to minimise the risk of adverse outcome, including facilitation of an appropriate level of pregnancy monitoring.

Uterine artery Doppler wave form analysis has been extensively studied in the second trimester of pregnancy as a predictive marker for the later development of preeclampsia. The use of Doppler interrogation in the first trimester has gained momentum in recent years. Various measurement techniques and impedance indices have been used to evaluate the relationship between uterine artery Doppler velocimetry and adverse pregnancy outcomes. Overall, first-trimester Doppler interrogation of the uterine artery performs better in the prediction of early-onset than late-onset preeclampsia. As an isolated marker of future disease, its sensitivity in predicting preeclampsia and fetal growth restriction in low risk pregnant women is moderate, at 40–70%. Multiparametric predictive models, combining first-trimester uterine artery pulsatility index with maternal characteristics and biochemical markers, can achieve a detection rate for early-onset preeclampsia of over 90%. The ideal combination of these tests and validation of them in various patient populations will be the focus of future research.

AIMS AND OBJECTIVES OF STUDY

The aim of this work is to evaluate the role of mean pulsatility index by first trimester uterine artery doppler in prediction of preeclampsia.

MATERIALS

This is a prospective observational study for the detection of PE held at tertiary care center. A written and informed consent was obtained from

all women willing to participate in the study. After the enrollment demographic data, obstetric history and current pregnancy details were obtained through an interview. Women attending antenatal clinic at 11–13+6 weeks of gestation underwent an ultrasound scan for confirmation of gestational age from measurement of crown-rump length, fetal nuchal translucency and to diagnose uterine artery Doppler imaging by transabdominal ultrasound examination. These women were subjected to clinical examination. The data obtained were recorded on the predesigned and pretested pro forma. Of 200 women screened, 136 women met inclusion criteria and 130 consented for participation in the study.

INCLUSION CRITERIA

Singleton, normotensive pregnancies irrespective of age and parity.

EXCLUSION CRITERIA

Pregnant women with missed abortion, chronic hypertension, multiple gestation, major fetal anomalies incompatible with life, and not willing to participate in the study.

METHODOLOGY

A transabdominal ultrasound was used for Doppler assessment of uterine circulation for uterine artery indices using a 5 or 3.5-MHz curvilinear transabdominal transducer. For this procedure, the probe was placed on lower quadrants of abdomen, angled medially, and color Doppler imaging was used to localize the uterine artery at its crossing over the external iliac artery. A minor movement of probe toward flanks, along with medial rotation, shows common iliac artery and its division. As soon as internal iliac artery was identified, the measurement was made at right and left angles. When three similar consecutive waveforms were seen, bilateral uterine artery PI and resistivity index were calculated, and mean PI was obtained. The values were then compared with published charts within normal limits or increased (>95 percentile for the gestational age).

The pregnant women were then followed up to delivery to analyze whether there is development of PE and gestational hypertension and fetal growth restriction (FGR). The neonatal outcomes such as gestational age at delivery and birth weight at delivery were recorded. Data of 130 women successfully followed up till term were included in the analysis. The data obtained were coded and entered into Microsoft Excel Worksheet. The predictive performance was also evaluated by the receiver operating (ROC) curve, with calculation of area under the curve. The rejection level for the null hypothesis was set as $P \leq 0.05$ (5%).

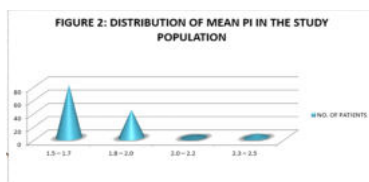
RESULTS

- Of 200 women screened, 136 women met inclusion criteria and 130 consented for participation in the study.
- Out of 130 women in the study population, 9 (6.92%) had mean PI $>95\%$ and 121 (93.08%) had normal Doppler. Among women who had increased PI, 5 (55.55%) developed PE as shown in figure 1.
- 61.53% of the study population had a mean PI between 1.5 and 1.7 followed by 32.30% who had it between 1.8 and 2.0 as shown in figure 2. The mean PI in those with pre eclampsia was 2.17 ± 0.33 when compared to 1.70 ± 0.17 in healthy women suggesting that the PI in those with PE was much higher than healthy women. This difference was also found to be statistically significant with p value <0.05 as shown in figure 3.
- Maternal age ranged between 21 to 40 years. The maximum number (44.34%) of study participants were in the age group between 21 and 25 years followed by 35.38% in the 26-30 years, followed by 19.52% in the 31-35 years category. Only 0.76% belonged to 36-40 years age group. The mean age was 26.42 ± 3.97 years, suggesting that most of the women in this study were young.
- With regard to obstetric history, most of the women were gravida 2 (66.15%) followed by gravida 1 (26.15%), gravida 3 (7.69%).
- Majority of the women (96.42%) had body mass index (BMI) between 19.06 and 27.20 kg/m². The mean BMI was 22.70 ± 1.4 kg/m², and median BMI was noted as 21 kg/m².
- In this study, gestational age at delivery ranged between 26.23 weeks and 39.06 weeks. However, a majority of the women (78.46%) delivered between 37 weeks and 39+6 weeks. The mean gestational age at delivery was 37.42 ± 2.55 weeks. These findings suggest that most of the women had term delivery. There were six preterm deliveries of them, one had intrauterine death (IUD), one had severe FGR, and 4 preterm delivery (PTD).
- In this study, of 130 women, 22 (16.92%) women had comorbidities, and the most common comorbidity was FGR noted in 7 (5.38%) women. The other uncommon comorbidities noted were, hypothyroid (4.14%), Rh negative pregnancy (3.98%), gestational diabetes mellitus (GDM) (3.42%). In this study, not many women were identified to have a high proportion of severe complications.
- This study showed a positive association between PE and PI as significantly higher number of women with PI of $\geq 95\%$ had preeclampsia (55.55%) compared with only 0.82% of the women with PI $<95\%$. This difference was statistically significant ($p < 0.001$). Furthermore, the sensitivity of PI with a cutoff value of 95% in prediction of PE was 82.30% with specificity of 98.80%, positive predictive value of 89%, and negative predictive value of 98.60% as shown in figure 4.

Fig 1: ASSOCIATION OF PRE-ECLAMPSIA WITH PULSATILITY INDEX

PULSATILITY INDEX	PREECLAMPSIA	NO PREECLAMPSIA	CHI SQUARE VALUE	P VALUE
$\geq 95\%$	5	4	56.9948	$<0.0001^*$
$<95\%$	1	120		

Fig 2 : DISTRIBUTION OF MEAN PI IN THE STUDY POPULATION



61.53% of the study population had a mean PI between 1.5 and 1.7 followed by 32.30% who had it between 1.8 and 2.0.

Figure 3: DIFFERENCE IN MEAN PI BETWEEN THE TWO GROUPS

SNO	GROUPS	MEAN PI	T VALUE	P VALUE	95% CONFIDENCE INTERVAL
		(Mean \pm SD)	6.283	$<0.0001^*$	0.3220 – 0.6180
1	Pre-eclampsia	2.17 ± 0.33			
2	Healthy Women	1.70 ± 0.17			

The mean PI in those with pre eclampsia was 2.17 ± 0.33 when compared to 1.70 ± 0.17 in healthy women suggesting that the PI in those with PE was much higher than healthy women. This difference was also found to be statistically significant with p value <0.05 .

FIGURE 4: VALIDITY OF PULSATILITY INDEX IN PREDICTION OF PRE-ECLAMPSIA

PARAMETERS	PERCENTAGE
Sensitivity	82.30%
Specificity	98.80%
Positive Predictive Value	89%
Negative Predictive Value	98.60%

DISCUSSION

- In this study, the mean calculated PI was 2.17. The pregnancies complicated by PE were 4.61% with sensitivity of 82.30% and specificity of 98.80% among patients with increased PI. The low sensitivity of this test limits its utility as a disease marker in isolation. However, these findings need further validation due to certain limitations of this study, that is, smaller sample size and single-center design, which limit the observations from study in generalizing to the entire population. Further research is required to evaluate the generalizability of multiparametric models in different resource settings, in addition to assessing the impact of screening on clinical outcomes.
- In a proposed new approach to prenatal care the potential value of an integrated clinic at 11-13 weeks' gestation in which maternal characteristics and history are combined with the results of a series of biophysical and biochemical markers to assess the risk for a wide range of pregnancy with low-dose aspirin is the subject of an ongoing randomized multicenter European study. The prophylactic use of low-dose aspirin for prevention of PE has been an important research question in obstetrics for the last three decades. In 1979, Crandon and Isherwood observed that nulliparous women who had taken aspirin regularly during pregnancy were less likely to have PE than women who did not. Subsequently, more than 50 trials have been carried out throughout the world and a meta-analysis of these studies reported that the administration of low dose aspirin in high-risk pregnancies is associated with a decrease in the rate of PE by approximately 10%⁹. It is likely that a similar integrated clinic at 30-33 weeks will emerge for effective prediction of pregnancy complications that develop during the third-trimester. The potential value of such a clinic is to improve perinatal outcome by rationalizing and individualizing the timing and content of subsequent visits for selection of the best time for delivery.
- In a study by Martin et al., the pregnancies complicated by PE were 2.1% and FGR 9.5%.¹⁰ The high rate of PE could be due to small numbers in population with high PI.
- Another study by Harrington et al. showed sensitivity of 93% and specificity of 85% for prediction of PE.¹¹
- The sensitivity of predicting PI was 55.56% and for FGR 18.75% whereas in contrast to a study by Gomez et al. reported a sensitivity 24%.¹²

CONCLUSION

- This study showed a positive association with the development of PE of Pregnancies with an increased risk of preeclampsia have an abnormally increased UTA-PI in early pregnancy.
- However, the use of a single uterine Doppler measurement for screening purposes in unselected early pregnancy populations has limited clinical value. The use of UTA-PI combined with high risk factors and other maternal serum biomarkers like maternal Serum pregnancy-associated plasma protein-A (PAPP-A), placental growth factor (PlGF), soluble fms-like tyrosine kinase-1 (sFlt-1), soluble endoglin (sEng), activin-A, and inhibin-A needs to be determined.
- The identification of patients who will develop early PE (before 34 weeks) is of great interest for further research since these cases have a greater disease severity.

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