First Trimester Screening For Pre-Eclampsia Using Uterine Artery Pulsatility Index: A Prospective Observational Study at Tertiary Centre in Jaipur, India

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Abstract

Objective: As it is well known that early detection and timely intervention can prevent severity of pre-eclampsia and thus reduce the associated maternal and perinatal mortality and morbidity. Our objective is to assess if raised uterine artery Doppler Pulsatility Index at 11 to 13+6 weeks can predict pre-eclampsia.

Material and Method: A prospective study was conducted at a tertiary centre in Jaipur from September 2022 to March 2024. Total of 160 patients reporting to OPD showing raised uterine artery pulsatility index in NT/NB scan were selected and started on Tab Ecosprin. Their detailed history and socioeconomic parameters were recorded.

These patients were then followed until term and studied for the development of pre-eclampsia and obstetric management was done according to maternal and fetal condition.

Results: Sensitivity (95% CI), Specificity (95% CI), Positive predictive value (95% CI) and Negative predictive value (95% CI) of our study is 84.51%(74.0 - 92.0%), 65.17%(54.3 - 75.0%), 65.9%(55.3 - 75.5%) and 84.1%(73.3 - 91.8%) respectively. The diagnostic accuracy of this test is 73.75% and the p- value is <0.0001.

Conclusion: Pre-eclampsia screening is a crucial factor to reduce preeclampsia associated morbidity and mortality. Uterine artery pulsatility index is a non-invasive method for predicting the chance of developing pre-eclampsia. Such patients can be started on Tab ecosprin for the prevention of pre-eclampsia and decreasing the morbidity and mortality and improving both maternal and fetal outcome.

Keywords: First trimester screening, Uterine artery pulsatility index, Pre-eclampsia screening, Pregnancy induced hypertension, Prevention of Pre-eclampsia

Introduction

Background/rationale

Pregnancy induced hypertension presents significant health problem, pre-eclampsia being the most common among them[1]. It is a multisystem disorder and presents a major risk to the mother and foetus[2].

Between 8th to 13th week cytotrophoblast cells penetrate the decidual part of spiral arteries. This invasion is essential for widening and remodelling of these arteries, reducing their resistance and increasing blood flow to the placenta. Between 14th to 18th week Trophoblast invades myometrial part of spiral arteries. This further enhances the transformation of these vessels, ensuring adequate blood supply to the developing placenta.[3]

In a significant number of women who develop pre-eclampsia, this transformation process is incomplete or delayed. Consequently, the spiral arteries preserve their muscular structure and poses high impedence to blood flow. This condition is often referred to as impaired spiral artery remodelling or shallow trophoblast invasion.[8] Since direct assessment of uterine artery is not possible, hence uterine artery doppler provides an accurate method to assess the penetration of cytotrophoblast of uterine artery.[4,5]

For analysing the resistance to flow in uterine artery, several research studies have advocated for the use of the Pulsatility Index as the most reliable Doppler index. This index has been shown to correlate with adverse obstetric outcomes such as foetal growth restriction, pre-eclampsia and preterm birth when abnormal raised values are detected.[6]

Objectives

Various studies have shown that an increased uterine artery PI in early pregnancy is linked to an elevated likelihood of developing pre-eclampsia. As the only definitive treatment of pre-eclampsia is termination of pregnancy, early identification of high-risk women remains the mainstay of management. Early detection allows for interventions aimed at preventing or reducing the severity of pre-eclampsia. Our objectives are:

1. To evaluate sensitivity and specificity of uterine artery Doppler index (Pulsatility index) in prediction of pre-eclampsia.

2. To evaluate usefulness of maternal characteristics like height, weight, previous pregnancy outcomes to predict the risk for pre-eclampsia.

Materials and methods

Ethics statement: An approval from Institutional research ethical committee was obtained- MGMC&H/IEC/JPR/2022/1033.

Study design and setting: This was a prospective analytical study conducted at a tertiary centre at Jaipur in September 2022 to March 2024.

Participants: All pregnant women attending antenatal OPD, having raised pulsatility index in 11-13+6 weeks scan were included and followed up till term. A written and informed consent was taken for participation in the study.

Variables and data measurements: A detailed history was taken including any presenting complaints, obstetric history, past medical and surgical history were recorded. History of pre-eclampsia in previous pregnancy and past history of any convulsions were taken down. Maternal characteristics like age, BMI, parity, socioeconomic status, family history of hypertension, conception using ART were noted. Meticulous general physical, systemic and abdominal examination performed. Routine investigations sent.

160 pregnant women attending antenatal OPD, having raised pulsatility index in 11-13+6 weeks scan were followed up till term and studied. They were started on Tab Ecosprin 150mg once daily and called up for regular ANC visits. At each antenatal visits, vitals were recorded and relevant investigation were sent and noted. Regular iron and calcium supplementation were prescribed. All patients having raised blood pressure with proteinuria or in absence of proteinuria having features of organ damage were duly noted. Investigations like complete haemogram, platelet count, kidney function tests, liver function tests, serum prothrombin time, bleeding time and clotting time,

fundoscopy, 24 hours urine for protein were performed in patients presenting with features of pre-eclampsia. Complaints suggestive of severity of pre-eclampsia like headache, vomiting, epigastric pain and blurring of vision were noted at each antenatal visit.

A thorough clinical fetal well-being assessment and obstetric sonography along with doppler study performed after careful assessment and stabilization of the maternal status.

On the basis of above examination and investigations, patients diagnosed with severe pre-eclampsia were treated and followed up further to study the maternal and fetal outcome.

Corticosteroids for fetal lung maturity was administered in patients standing in need for termination of pregnancy with gestational age less than 34 weeks. Antihypertensive drugs labetalol and if needed, nifedipine were used to control blood pressure.

MgSO4 was given to patients during the management for better maternal and fetal outcome as per obstetrical indications.

Patients with uncontrolled hypertension were managed in accordance with multidisciplinary teams of physician and anaesthetist as per standard protocols.

Obstetric management was done according to the maternal and fetal condition. The decision to deliver the patient vaginally (either spontaneous or induced) or by caesarean section was individualized and decided as per the standard hospital protocol.

At the end of the study, the data was collected, complied and analysed.

Statistical analysis

The presentation of the categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data were presented as the means

± SD and as median with 25th and 75th percentiles (interquartile range). The data normality was checked by using Shapiro-Wilk test. The cases in which the data was not normal, we used non parametric tests. The following statistical tests were applied for the results:

1. The association of the variables which were quantitative and not normally distributed in nature were analysed using Mann-Whitney Test and variables which were quantitative and normally distributed in nature were analysed using Independent t test.

2. The association of the variables which were qualitative in nature were analysed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.

3. Multivariate logistic regression was used to find out independent significant factors of pre eclampsia.

4. Receiver operating characteristic curve was used to assess cut off point, sensitivity, specificity, positive predictive value and negative predictive value of pulsatility index for predicting pre eclampsia.

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 25.0.

For statistical significance, p value of less than 0.05 was considered statistically significant.

Results and Discussions

We aimed to perform this study to evaluate the maternal characteristics in order to identify high-risk factors, and to assess the uterine artery doppler pulsatility index as screening modality to predict preeclampsia
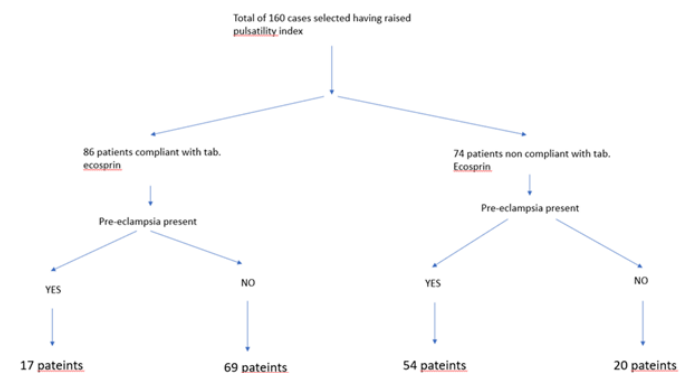
Figure 1: Figure describing that out of all patients having raised pulsatility index 71 developed pre-eclampsia.

Out of 86 patients who were compliant with Tab. Ecosprin only 17 patients developed pre-eclampsia.

Table 1: Multivariate logistic regression to find out significant risk factors of pre-eclampsia

Variables	Beta coefficient	Standard error	P value	Odds ratio	Odds ratio Lower bound (95%)	Odds ratio Upper bound (95%)
Duration of conception since marriage(years)	-1.783	0.473	0.0002	0.168	0.067	0.425
Body mass index(kg/m²)						
18.5 to 24.99 kg/m² {Normal BMI}				1.000		
<18.5 kg/m² {Underweight}	0.196	1.908	0.918	1.217	0.029	51.256
25 to 29.99 kg/m²	1.102	0.840	0.190	3.011	0.580	15.632

{Overweight}						
>=30 kg/m² {Obese}	-0.034	1.054	0.974	0.966	0.123	7.618
Previous history of pre-eclampsia	2.122	1.251	0.090	8.351	0.719	96.997
Socioeconomic status						
II				1.000		
III	3.921	1.939	0.043	50.444	1.128	2255.874
IV	4.340	1.922	0.024	76.742	1.774	3320.732
V	5.302	2.186	0.015	200.748	2.766	14570.023
Family history of pre-eclampsia	2.823	0.793	0.0004	16.820	3.554	79.595
Multiple pregnancy	2.904	1.169	0.013	18.242	1.846	180.229

Table 1 show that in our study among 71 patients developing pre-eclampsia, 36 patients (50.9%) had short duration of exposure to sperm of less than 6 months. Also, maximum patients developing pre-eclampsia were overweight (BMI 25-29.99 kg/m2). Among patients belonging to overweight category 70% developed pre-eclampsia. Pre-eclampsia was more common in patients who had the disease in last pregnancy. The recurrence risk of having pre-eclampsia in our study was 65.71%.

Pre-eclampsia is more common in lower socioeconomic status patients. Among patients belonging to class IV and V of modified kuppuswamy scale 62.9% and 54.29% patients developed pre-eclampsia respectively. Notably, 81.13% patients having family history of hypertension developed pre-eclampsia. Among 13 patients with multiple pregnancy 10 (76.9%) developed pre-eclampsia.

Table 2: Association between uterine artery pulsatility index and pre-eclampsia

Pulsatility index	Patients with pre-eclampsia(n=71)	Patients without pre-eclampsia(n=89)	Total	p value
Mean ± SD	2.74 ± 0.11	2.61 ± 0.18	2.67 ± 0.17	<.0001‡
Median(25th-75th percentile)	2.7 (2.7-2.8)	2.6 (2.5-2.7)	2.7 (2.6-2.8)	
Range	2.5-3	2.3-3	2.3-3	

‡ **Independent t test**

Table 2: In our study all patients having raised uterine artery pulsatility index in their NT/NB scan were selected. Among all patients developing pre-eclampsia the mean uterine artery PI was 2.74 ± 0.11 and among patients not developing pre-eclampsia the mean uterine artery PI was 2.61 ± 0.18.
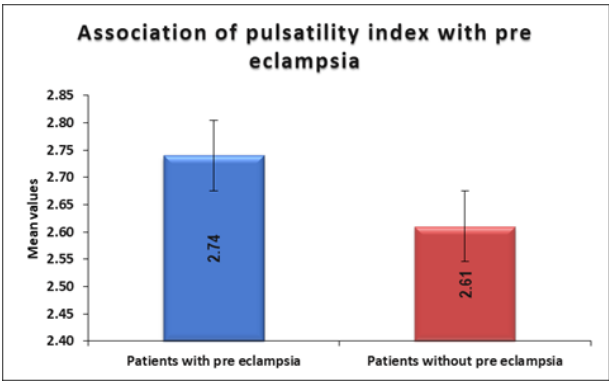
Figure 2: This graph (figure 2) shows that patients developing pre-eclampsia had higher pulsatility index than patients not developing pre-eclampsia.
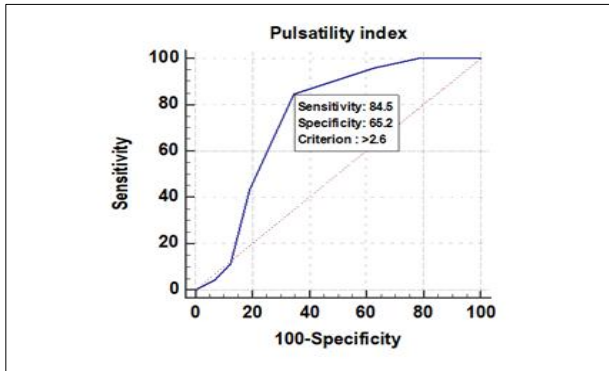

Figure 3: Receiver operating characteristic curve of Pulsatility index for predicting Pre-eclampsia.

The ROC curve (figure 3) shows that at pulsatility index more than 2.6, the sensitivity and specificity of this study is 84.5 and 65.2 respectively.

Similar to our study, Napolitano et. al.(10) also performed pre-eclampsia screening using first trimester UtA PI and found the area under the ROC curve of 0.556 for pre-eclampsia. Plasencia et. al.(9) also studied the receiver-operating characteristics (ROC) curve analysis for pre-eclampsia prediction and found the area under the curve as 0.677.

Table 3:

Variables	Values
Area under the ROC curve (AUC)	0.746
Standard Error	0.039
95% Confidence interval	0.669 to 0.822
P value	<0.0001
Cut off	>2.6
Sensitivity(95% CI)	84.51%(74.0 - 92.0%)
Specificity(95% CI)	65.17%(54.3 - 75.0%)
PPV(95% CI)	65.9%(55.3 - 75.5%)
NPV(95% CI)	84.1%(73.3 - 91.8%)
Diagnostic accuracy	73.75%

This table 3 shows that the Sensitivity (95% CI), Specificity (95% CI), Positive predictive value (95% CI) and Negative predictive value (95% CI) of our study is 84.51% (74.0 - 92.0%), 65.17% (54.3 - 75.0%), 65.9% (55.3 - 75.5%) and 84.1% (73.3 - 91.8%) respectively.

The diagnostic accuracy of this test is 73.75% and the p-value is <0.0001.

Suman Shivrayan et al. found similar results. They studied the relation of high pulsatility index with emergence of pre-eclampsia. The sensitivity and specificity for the study they conducted was 82.1% and 57.4% respectively. They found the PPV and NPV to be 15.7% and 97.1% respectively. (7)

Many other studies found similar results. Van den Elzen et. al.(8) and Plasencia et al.(9) also conducted studies to know the role of Pulsatility index in assessing the risk of pre-eclampsia.

Table 4:

Ecosprin	Pre-eclampsia present (n=71)	Pre-eclampsia absent (n=89)	Total	P value
No	54 (72.97%)	20 (27.02%)	74 (100%)	
Yes	17 (19.76%)	69 (80.23%)	86 (100%)	0.00001†
Total	71 (44.38%)	89 (55.63%)	160 (100%)	

† **Chi square test**

Table 4 shows that among all 160 women with raised PI, 71 women had developed pre-eclampsia and out of these 71 women only 17 women had history of ecosprin intake. In our study out of all 160 women with raised uterine artery pulsatility index in their NT/NB scan, 72.97% women who were not taking ecospirin developed pre-eclampsia while only 17 (19.76%) women who were taking ecosprin had developed pre-eclampsia. Thus, ecosprin intake significantly decreased the occurrence of pre-eclampsia in the study group.

Extensive studies have validated combining maternal high risk factors with uterine artery PI as a promising tool in predicting pre-eclampsia effectively (11,12). Our study employed a relatively small sample size, limiting the generalizability of the outcomes. Carrying out further studies with larger and more diverse set of population would provide strong validation to our findings.

Even though we did not integrated in our study, but various researches have shown that incorporating biomarkers like serum placental growth factor (PlGF) and serum pregnancy-associated plasma protein-A (PAPP-A) further improves the ability of predicting pre-eclampsia (13,14,15,16). Also, we did not sub-categorize development of pre-eclampsia in our study population as either early or late onset.

Therefore, further studies are needed to evaluate the effectiveness of the multi-marker screening model to accurately identify both early onset and late onset pre-eclampsia cases, and ensuring its applicability in clinical settings for better patient care and improved outcomes

Conclusion

Pre-eclampsia represents a significant health concern for pregnant individuals globally, often leading to maternal and perinatal morbidity and mortality.

Our study aimed at early detection of pre-eclampsia using uterine artery pulsatility index as its predictor. We found that combining uterine artery PI with history based high risk factors and maternal characteristic findings, we may improve the accuracy for pre-eclampsia screening.

Uterine artery PI is a good non- invasive and cost effective method to sieve out patients at risk of developing pre-eclampsia. On its basis, initiation of preventive therapy in form of Tab ecosprin, and increased patient surveillance will help save development of pre-eclampsia and its complications.

Thereby, significantly improving the maternal and foetal outcome.

Future studies on larger population will further validate the findings of our study.

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