



PREDICTION OF PREECLAMPSIA BASED ON MATERNAL RISK FACTORS, MEAN ARTERIAL PRESSURE AND UTERINE ARTERY PULSATILITY INDEX AT FIRST TRIMESTER OF PREGNANCY: A FIRST DESCRIPTIVE OBSERVATIONAL STUDY FROM NORTHEAST INDIA.

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ABSTRACT

Introduction: Preeclampsia (PE) is a pregnancy disorder and a major factor associated with adverse maternal and neonatal outcomes, including death. Combining maternal risk factors (MF), mean arterial pressure (MAP), and uterine artery Doppler pulsatility index (UtA-PI) provides an effective screening for predicting preterm PE. This study sought to predict the PE based on MF, MAP, and UtA-PI at first trimester of pregnancy.

Methods: The research involves 80 pregnant women, all in their first trimester at 11-13+6 weeks. PE prediction was achieved using MF, MAP, and UtA Doppler measurements. Early trimester GS and ultrasound were performed using a SAMSUNG SonoAce R7 with a 3.5 MHz curvilinear probe.

Results: The PE was diagnosed in 22/80 (27.5%) women. Our study provides evidence that MF ($p=0.018$), an elevated MAP ($p<0.00002$), and UtA-PI ($p<0.00001$) are significant predictors of an increased risk of PE. A combination of MF, MAP, and mean UtA-PI proved to be a useful predictor tool for the detection of PE ($p<0.00001$). MF achieved a sensitivity of 95.45%, a specificity of 29.31%, and a detection rate of 26.25%. MAP produced a sensitivity of 63.64%, a specificity of 84.48%, and a detection rate of 17.50%. UtA-PI demonstrated a high specificity (96.55%), lower sensitivity (68.18%), leading to a detection rate of 18.75%.

Conclusion: The Integrated use of MF, MAP, and UtA Doppler information effectively identified a significant number of patients with preterm PE. Early detection of risk factors, strong screening methods, and regular monitoring are essential for accurately predicting PE and initiating preventive therapy promptly.

Keywords: Preeclampsia, First Trimester, Gestosis Scoring, Maternal Risk Factors, Mean Arterial Pressure, Uterine Artery Pulsatility Index

INTRODUCTION

Preeclampsia (PE) is a complex hypertensive disorder of pregnancy (HDP) that generally emerges after 20 weeks of gestation, defined by new-onset hypertension and end-organ dysfunction. Major risk factors for its development are having a history of the condition, pre-existing diabetes, chronic kidney disease, a high body mass index (BMI), and advanced maternal age.¹ PE is the primary contributor to maternal and perinatal complications and death, impacting 2–4% of pregnancies.² PE is a complex, multisystemic condition linked to significant maternal mortality, with global figures at 14% and a higher incidence in India at 29.54%. The disorder is characterized by dysfunction in the hepatobiliary, renal, neurological, and hematological systems.³

In clinical practice, early detection and precise risk stratification are essential for mitigating preeclampsia-associated morbidity and mortality. Integrating maternal risk factors (MF), mean arterial pressure (MAP), uterine artery Doppler pulsatility index (UtA-PI), and serum placental growth factor, the Fetal Medicine Foundation's triple test effectively screens for preterm preeclampsia, identifying 75% of cases with a 10% false-positive rate.⁴

PE risk factors, as documented in previous studies, encompass a range of MF and conditions such as age, educational attainment, pre-existing hypertension or diabetes, obesity, and certain contraceptives. PE is more frequent in primigravida. However, prior studies present conflicting evidence regarding its association with parity, high BMI, and personal or family history of the disorder.^{5,6} Nevertheless, the accurate prediction of PE remains difficult when using MF as the sole determinant.

Studies have explored multiple blood pressure parameters in early pregnancy, such as systolic BP, diastolic BP, MAP, and 24-hour ambulatory pressure, for their value in predicting PE.⁷ MAP remains a key focus of scientific research in the effort to predict PE. MAP is a feasible tool that is readily incorporated into routine antenatal surveillance. Despite its importance, research on blood pressure patterns in low-risk nulliparous women is scarce.⁸ MAP is a valuable biophysical marker in PE prediction, although model performance varies, possibly due to the diverse measurement techniques employed. It has been demonstrated in a case-cohort study that using an automated device (consistent with the ASPRE trial recommendations) for MAP measurement improves the identification of high-risk women compared to manual devices.⁹

The UtA-PI measurement in the first trimester is a crucial, noninvasive indicator for evaluating the initial stage of placental development and predicting later uteroplacental blood flow. The progression of pregnancy is marked by significant hemodynamic shifts, beginning with the invasion of spiral arteries by cytotrophoblast cells. A key outcome of this uterine adaptation is decreased resistance to blood flow, augmented diastolic velocity, and the resolution of the early diastolic notch around the second trimester.¹⁰ An increase in the PI of the UtA suggests a failure of placental adaptation, a condition often linked to the later development of preterm PE. Using a first trimester UtA-PI assessment can improve the early detection of women who are at a higher risk for preeclampsia, enabling timely intervention.¹¹

The Federation of Obstetric and Gynaecological Societies of India (FOGSI) developed the gestosis score (GS) in 2019 to improve early PE screening. The GS employs a weighted-point system based on clinical risk factors, such as a BMI over 30, a MAP above 85 mmHg, the use of assisted reproductive technology, and pre-existing chronic hypertension to screen patients in their first trimester. A risk assessment score of 3 or greater flags a woman as high-risk for PE, triggering recommendations for more intensive monitoring and prophylactic aspirin before 16 weeks.¹²

Therefore, an early screening for hypertensive disorders is crucial for developing clinical and public health strategies to reduce PE cases. Unfortunately, there is currently no data available on the application of GS and the prediction of PE based on MF, MAP, and UtA-PI during the first trimester of pregnancy within the Northeastern Indian population. Our study, therefore, sought to predict the PE based on MF, MAP, and UtA-PI at the first trimester of pregnancy.

MATERIALS AND METHODS

Setting

The research was carried out at the Department of Obstetrics and Gynecology, Agartala Government Medical College & Govind Ballabh Pant Hospital (AGMC & GBPH) in Tripura, India, covering an 18-month span from November 2020 to April 2022.

Study design and population

We conducted an observational follow-up study at a single centre, selecting a total of 80 pregnant women. The sample consisted of all consecutive women who presented to the AGMC Obstetrics & Gynecology OPD for their routine first trimester antenatal check-up.

Inclusion criteria

The study recruited first trimester antenatal patients who were attending the Obstetrics & Gynecology Outpatient Department (OPD) of AGMC and who consented to participate.

Exclusion criteria

The following criteria excluded pregnant women from participation:

1. Serious mental illness
2. Spontaneous abortion during the first trimester
3. Presence of major fetal malformations or chromosomal abnormalities
4. Inability to maintain follow-up (lost to follow-up)
5. Regular use of Acetylsalicylic Acid (ASA)
6. Diagnosis of unclassified hypertension

Study procedure

Upon enrollment, GS and early-trimester USG were performed on all patients using a SAMSUNG SonoAce R7 machine and a 3.5 MHz curvilinear probe. We performed fetal biometry and UtA Doppler studies on all patients. The ultrasound software performed an automated calculation of the PI. To ensure consistency, one individual performed all Doppler studies. Patients were subsequently followed up until delivery to track the development of PE.

1. Maternal risk factors (MF)

Maternal risk factors were evaluated using GS scoring. A risk score of ≥ 3 was used to identify pregnant women at high risk for PE. GS is an objective, simplified, and dynamic method for quantifying maternal risk of Hypertensive Disorders in Pregnancy (HDP). This system, which involves a questionnaire covering 27 risk factors, assigns scores of 1, 2, and 3 to mild, moderate, and high-risk factors, respectively. The FOGSI-ICOG and Gestosis, India (2019) 'Good Clinical Practice Recommendations' endorse this score for use.

2. Mean Arterial Pressure (MAP)

A MAP of >85 mmHg indicates high risk for PE. Before measurement, the patient was instructed to sit for 2–3 minutes with their feet supported. Bilateral blood pressure readings were obtained at the initial antenatal examination. If no significant difference was observed, the right arm was used for all subsequent measurements. First, the brachial artery was palpated to determine the Systolic Blood Pressure (SBP). The SBP was subsequently measured using the auscultatory method at Korotkoff phase 1 (K1).

The standard measure for Diastolic Blood Pressure (DBP) was Korotkoff phase 5 (K5); phase 4 (K4) was used as an alternative when K5 sounds were not audible. The appropriate cuff size was selected based on arm circumference: a standard cuff for arms ≤ 33 cm, and a large cuff (15×33 cm bladder) for arms >33 cm. The cuff was always placed 2.5 cm above the antecubital fossa, and blood pressure

was measured with the readily available mercury sphygmomanometer, which was the standard in this setting. To calculate MAP, the last two stable measurements were averaged for each arm, and the arm with the higher resulting MAP was used for analysis.

3. Uterine artery doppler

During the transabdominal scan, the transducer was placed in the lower lateral quadrant, angled medially, and Color Doppler was used to locate the common iliac bifurcation. The course of the uterine artery, the main branch of the internal iliac artery, was tracked medially to its destination at the lateral uterine margin.

This artery was then insonated 1 cm beyond its crossover point with the external iliac artery, right as it entered the uterine wall. Waveform acquisition required the optimization of gate, gain, and scale settings. We recorded three consecutive waveforms from both the right and left UtA. The ultrasound machine's software automatically calculated the PI using the standard formula. $PI = \frac{\text{systolic} - \text{diastolic}}{[(\text{systolic} + \text{diastolic})/2]}$. For this study, a mean UtA-PI value >2.6 ($>95^{\text{th}}$ percentile) was defined as abnormal.¹³

Data Analysis

Statistical analysis was carried out with the aid of the SPSS software package (version 21.0) after transferring the data into a Microsoft Excel spreadsheet. Data summarization included the calculation of frequency, mean, standard deviation, and proportion. The Pearson correlation coefficient was utilized to test for linear associations between continuous variables. Statistical significance was set at $p < 0.05$ (two-tailed).

Ethics committee approval

The Institutional Ethical Committee granted its approval for the study protocol before the initiation of the research. Before enrollment, informed written consent was obtained from every participant, with forms translated into the local languages (Bengali and Kokborok). Throughout the study, strict confidentiality was maintained, and all collected data were used solely for research purposes.

RESULTS

A total of 110 subjects were initially evaluated. After excluding 30 cases, 80 subjects remained and were included in the study. Based on the development of PE, subjects were assigned to a control group (58 subjects) and a PE group (22 subjects). In the final study cohort of 80 individuals, participants were stratified into three age groups, with the largest group comprising 65 subjects (81.25%), who were between 19 and 35 years old. A smaller group of 10 subjects (12.5%) was over 35, while the youngest participants, a group of 5 individuals (6.25%), were under 19 years of age. The average age was found to be 24.81 years (standard deviation [SD] = 5.012 years). Among the 80 patients included in the study, 22 (27.5%) developed PE. Of the 22 patients, 12 (54.60%) had late-onset disease (>37 weeks), while 6 (27.27%) were diagnosed between 34 - 37 weeks, and 4 (18.18%) developed early-onset PE (<34 weeks). The distribution of maternal risk factors is summarized in Table 1.

Figure 1 indicates the statistically significant association between gravida status and the development of PE ($p=0.036$), with primigravida patients comprising a higher proportion of the PE group (16/22, 72.72%) compared to multigravida patients (6/22, 27.27%).

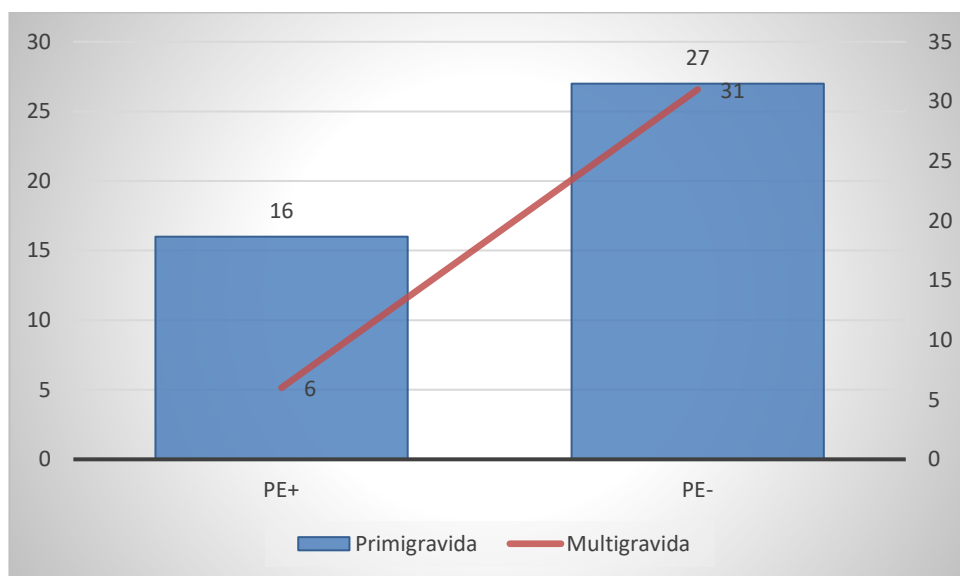


Figure 1: Association between gravida and PE (n=22)

Table 1: Distribution of Maternal Risk Factors

Maternal risk factors	Frequency & percentage	No PE (n=58)	PE Developed (n=22)
Age<19yrs	5 (6.25%)	2	3
Age>35yrs	10 (12.5%)	4	6
Age 19-35yrs	65 (81.25%)	52	13
Maternal anaemia	20 (25%)	16	4
BMI>30kg/m ²	0	0	0
MAP>85mmHg	23 (28.75%)	9	14
Primigravida	43 (53.75%)	27	16
Multigravida	37 (46.25%)	31	6
Women Born as SGA	3 (3.75%)	1	2
Chronic HTN	3 (3.75%)	0	3
Maternal Hypothyroidism	3 (3.75%)	1	2
Chronic Kidney Disease	2 (2.5%)	0	2
Gestational Diabetes Mellitus	1 (1.25%)	0	1
Mental disorder (Bipolar disorder)	1 (1.25%)	0	1
Pre Gestational Diabetes Mellitus	2 (2.5%)	0	2
Cohabitation	2 (2.5%)	2	0
Polycystic Ovarian Syndrome	2 (2.5%)	0	2
Hypertensive disorder in previous pregnancy	1 (1.25%)	0	1
Family history of CAD	1 (1.25%)	1	0
Other factors	18 (22.5%)	17	1

Table 2: Association of MF and PE

MF	Development of PE		Total	X ²	P Value
	Yes	No			
Present	21	41	62 (77.5%)	5.61	0.018
Absent	1	17	18 (22.5%)		
Total	22	58	80 (100%)		

Table 2 indicates that out of 80 subjects, MF were present in 62/80 cases (77.5%), while they were absent in 18/80 cases (22.5%). The predictive utility of MF for PE was assessed, and the findings were statistically significant ($p=0.018$).

Table 3: Association of Mean Arterial Pressure (mmHg) and PE

Mean Arterial BP (mmHg)	Development of PE		Total	X ²	P value
	Yes	No			
>85	14	9	23(28.75%)	18.02	<0.00002
≤85	8	49	57(71.25%)		
Total	22	58	80		

Table 3 demonstrates that of the 80 subjects in the study, 23/80 (28.75%) had a MAP > 85 mmHg, and 14 of these subjects developed PE (17.5% of the total cohort). Among the 57/80 subjects (71.25%) with a MAP ≤85 mmHg, 8 developed PE (10% of the total cohort). An elevated MAP (> 85 mmHg) is significantly linked to an increased risk of developing PE ($p<0.05$).

Table 4: Association of GS (MF + MAP) and PE

GS	Development of PE		Total	X ²	P value
	Yes	No			
≥3	16	2	18 (22.5%)	43.90	<0.00001
<3	6	56	62 (77.5%)		
Total	22	38	80		

Table 4 demonstrates that 18 subjects had received a GS of ≥3, while 62 subjects scored <3, and this was significantly linked to an increased risk of developing PE ($p<0.05$).

Table 5: Association of Mean UtA-PI and development of PE

Mean PI	Development of PE		Total	X ²	P value
	Yes	No			
>2.6	15	2	17 (21.25%)	39.94	<0.00001
≤2.6	7	56	63 (78.75%)		
Total	22	58	80 (100%)		

Table 5 shows that the mean UtA-PI is a statistically significant predictor of PE ($p<0.05$). The incidence of PE was higher in subjects with a mean UtA-PI > 2.6 (15/80, 18.8%) than in those with a mean UtA-PI ≤2.6 (7/80, 8.75%).

Table 6: Detection of PE combining GS (MF+MAP) and Mean UtA-PI

GS & Mean UtA- PI	PE +	PE -	Total	X ²	P value
Any abnormality	17	2	19 (23.75%)	48	<0.00001
Both within normal limits	5	56	61 (76.25%)		
Total	22	58	80 (100%)		

As shown in Table 6, the combined use of the GS and mean UtA-PI for predicting PE resulted in 17 true positives, 2 false positives, 5 false negatives, and 56 true negatives. A combination of MF, MAP, and mean UtA-PI demonstrated significant efficacy in predicting PE.

Table 7: Sensitivity, Specificity, PPV, NPV, Detection rate (DR), DA of MF, MAP, GS, PI, Combination of GS and PI for predicting PE

Statistical parameter	MF	MAP	GS (MF+MAP)	PI	GS+PI
Sensitivity (%)	95.45	63.64	72.73	68.18	77.27
Specificity (%)	29.31	84.48	96.55	96.55	96.55
PPV (%)	33.87	60.87	88.89	88.24	89.47
NPV (%)	94.44	85.96	90.32	88.89	91.80
DR (%)	26.25	17.5	20	18.75	21.25
DA (%)	47.50	78.75	90.00	88.75	91.25

Table 7 indicates that the diagnostic performance of MF for predicting PE indicated a high sensitivity (95.45%), a poor specificity (29.31%), a positive predictive value (PPV) of 33.87%, a negative predictive value (NPV) of 94.44%, and a diagnostic accuracy (DA) of 47.50%. The diagnostic performance of MAP for predicting PE demonstrated 63.64% sensitivity, 84.48% specificity, 60.87% PPV, 85.96% NPV, and 78.75% DA. The diagnostic performance of an HDP-GS (≥ 3) for predicting PE was evaluated, showing 72.73% sensitivity, 96.55% specificity, 88.89% PPV, 90.32% NPV, and 90% DA. The diagnostic performance of mean UtA-PI for predicting PE demonstrated 68.18% sensitivity, 96.55% specificity, 88.24% PPV, 88.89% NPV, and 88.75% DA. This combination of Mean UtA-PI and GS for predicting PE demonstrated 77.27% sensitivity, 96.55% specificity, 89.47% PPV, 91.80% NPV, and 91.25% DA.

DISCUSSION

The GS for hypertensive disorders of pregnancy risk-stratifies patients in their first trimester by analyzing demographic, clinical, and biochemical data. The early identification and categorization of pregnant patients into mild, moderate, or high-risk cohorts allows for the implementation of precise, condition-specific interventions. To minimize potential adverse outcomes, healthcare providers can employ a strategy of enhanced monitoring, lifestyle counseling, and preventative treatments such as low-dose aspirin.¹⁴

This present study sought to predict the PE based on MF, MAP, and UtA-PI during the first trimester of pregnancy by measuring GS and UtA Doppler PI in 80 pregnant women at 11-13+6 weeks of gestation with a singleton fetus.

Comparison with the findings of previous studies

MF and MAP analysis

The demographic analysis of our study revealed that most participants (81.25%) were in the 19–35 age group. This age distribution aligns closely with that of a previous report, which also found a similar prevalence (81.50%) within the same age bracket.¹² Among the 80 women studied, 22 received a diagnosis of PE, with the majority of these cases occurring in primigravida women. This research corroborates the findings presented in the earlier report.¹⁵ Gravida status was a statistically significant predictor for the development of PE. The incidence of PE was markedly higher among primigravida patients compared to their multigravida counterparts.

A statistically significant correlation ($p=0.01$) was found between BMI category and the occurrence of PE. In the PE group, a notably higher percentage of patients were overweight (45.45%) compared to those who were normal weight (36.36%) or underweight (18.18%). The mean BMI observed in our patient cohort closely aligns with a mean BMI of 26.3 ± 4.7 kg/m² documented by Arias et al. (2020).¹⁶ Our study found that the predictive utility of MF for developing PE was assessed and found to be statistically significant.

Our study provides evidence that an elevated MAP (>85 mmHg) was identified as a significant risk factor for PE ($p<0.05$). This suggests that monitoring MAP may be a useful tool for identifying high-risk patients. Prior research has demonstrated that MAP is elevated in women with hypertensive disorders during pregnancy.¹⁷

The effectiveness of a simple, mobile-based GS system in predicting PE is a key finding of our study. The system's high predictive accuracy (90%), with a sensitivity of 72.73% and a specificity of 96.55% for a score of ≥ 3 ($p<0.00001$), can facilitate increased awareness of PE risk and support earlier clinical intervention. This presents a valuable opportunity to improve patient management and prevent adverse outcomes associated with the condition. This aligns with the findings of Gupta et al. (2022), who reported that their HDP-GS System app (score ≥ 3) had a sensitivity of 83.1%, specificity of 97.51%, and a DA of 95.35%.¹⁸

UtA-PI value analysis

The mean UtA-PI was identified as a significant predictor for the development of PE. Our findings highlight the predictive value of first trimester UtA Doppler, demonstrating that increased impedance (mean PI >2.6) can identify nearly 88.75% of patients who later develop PE. The current study confirms the predictive power of UtA Doppler analysis performed in the first trimester. Importantly, this screening method effectively predicted the most severe cases of PE, identifying patients with the earliest manifestations of the disease and the worst pregnancy outcomes. This capability, demonstrated by the presence of abnormal waveforms in 15 of 22 PE patients, reinforces its value for early risk stratification and targeted management. This observation corroborates the results of a previous study.¹⁹

Elevated UtA-PI readings are indicative of increased UtA resistance, a condition that points to inadequate remodeling of the maternal spiral arteries. This defect impairs normal placental blood flow, potentially causing uteroplacental ischemia and contributing to the onset of PE. In our study, a combined screening tool utilizing the GS and UtA-PI value achieved 77.27% sensitivity, 96.55% specificity, and an overall 91.25% DA for the prediction of PE ($p<0.00001$).

An earlier prospective cohort study of pregnant women at 11–14 weeks of gestation included baseline assessments via a questionnaire, blood pressure and MAP measurements, UtA Doppler scans, and collection of serum for PAPP-A analysis. The UtA Doppler PI demonstrated high diagnostic accuracy for predicting PE and intrauterine growth restriction (IUGR) during the 11-to-14-week gestational period. At a cutoff of 1.7, the test yielded a sensitivity of 75.9% and a specificity of 79.6%.²⁰ In an earlier prospective cohort study involving 605 patients, a combined screening approach using MF, MAP, and mean UtA-PI achieved a sensitivity of 71.4% for preterm PE developing before 34 weeks (Group 2) at a fixed false-positive rate of 10%. Lower sensitivities of 50% and 41.2% were observed for preterm PE developing before 37 and 42 weeks, respectively (Groups 3 and 4). The study concluded that this combined method could identify a substantial number of patients with a high risk for developing preterm PE.²

Limitations

The conclusions of this study must be interpreted considering certain limitations. Caution is warranted when interpreting the findings, as the limited sample size may have impacted the statistical power and generalizability. As a single-centre and cross-sectional study, it is susceptible to institutional biases and cannot establish a cause-and-effect relationship. Therefore, a future large-scale, multicenter longitudinal study is warranted to confirm our results.

CONCLUSION

Our study provides evidence that MF, an elevated MAP, and UtA-PI are significant predictors of an increased risk for PE. For effective first trimester PE screening, a risk assessment that integrates MF with MAP and UtA-PI should be prioritized. This early risk stratification is critical for initiating preventive strategies. As the precise mechanisms underlying PE remain elusive and no curative

treatment exists aside from delivery, there is a pressing clinical need to improve predictive accuracy. The identification of effective predictors is crucial for enabling timely intervention and mitigating the serious maternal and fetal complications associated with PE.

Acknowledgement: We gratefully acknowledge the valuable insights and assistance provided by Dr. Sukanta Nath, Research Scientist at Atal Bihari Vajpayee Regional Cancer Centre, Agartala, Tripura, in the preparation of this manuscript.

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