ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Significance of platelet parameters in pre-eclampsia: A prospective cross-sectional study from a tertiary care center in North India

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Submission: 11-05-2025 Revision: 28-06-2025 Publication: 01-08-2025

ABSTRACT

Background: Pre-eclampsia is a life-threatening disorder that develops after 20 weeks of gestation and is a major cause of maternal morbidity and mortality worldwide. Platelet activation plays a crucial role in its pathogenesis, contributing to end-organ damage. Platelet parameters such as platelet count, mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) are indirect markers of platelet activation and can be evaluated during routine hematological analysis. **Aims and Objectives:** This study aimed to evaluate and compare platelet parameters (platelet count, MPV, PDW, and PCT) in women with pre-eclampsia and normotensive pregnant women, establishing their role in diagnosing and predicting pre-eclampsia. Variations in these parameters in patients with and without severe features were also analyzed. **Materials and Methods:** A prospective cross-sectional study was conducted between August 2022 and February 2024, involving 120 pre-eclamptic and 120 normotensive pregnant women. Platelet parameters were analyzed, and statistical tests such as Mann-Whitney, Independent t-test, Chi-square, and Fisher's exact test were applied. The receiver operating characteristic (ROC) curve analysis evaluated the predictive value of platelet parameters in pre-eclampsia. **Results:** Pre-eclamptic women showed significantly higher MPV (12.73 ± 2.19 fL vs. 11.98 ± 1.78 fL, $P = 0.004$) and PDW ($20.35 \pm 2.98\%$ vs. $16.02 \pm 0.87\%$, $P < 0.0001$) compared to normotensive women. Platelet count ($141.3 \pm 42.47 \times 10^3/\mu L$ vs. $174.32 \pm 27.24 \times 10^3/\mu L$, $P < 0.0001$) and PCT ($0.17 \pm 0.04\%$ vs. $0.22 \pm 0.04\%$, $P < 0.0001$) were significantly reduced. Among 19 pre-eclamptic women with severe features, platelet count and PCT were further decreased, whereas MPV and PDW increased. ROC curve analysis revealed significant discriminatory power for all platelet parameters. PDW had the highest predictive accuracy (area under the curve [AUC] 0.965; 95% confidence interval [CI]: 0.946–0.984) with a sensitivity of 83.33% and specificity of 97.50% at a cut-off value >17.4%. PCT (AUC 0.838; 95% CI: 0.783–0.893) and platelet count (AUC 0.779; 95% CI: 0.719–0.839) also showed notable predictive ability. **Conclusion:** Platelet parameters are significantly altered in pre-eclampsia and serve as reliable, cost-effective biomarkers for diagnosis, monitoring, and assessing severity, particularly in resource-limited settings.

Key words: Pre-eclampsia; Platelet indices; Predictive markers

Access this article online

Website: https://ajmsjournal.info/index.php/AJMS/index

DOI: 10.71152/ajms.v16i8.4611

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Hypertensive disorders affect 2–8% of pregnancies globally and contribute significantly to severe illness, lasting disability, and fatalities for both mothers and infants.[1] Pre-eclampsia and eclampsia are particularly notable among these disorders, as they represent major causes of maternal and perinatal mortality and morbidity.[2] In hospital settings

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in India, the incidence of pre-eclampsia ranges from 5% to 15%, while the incidence of eclampsia is approximately 1.5%. From 1976 to 2014, the risk of eclampsia in India varied between 0.179% and 5%, with an average of 1.5%.[3]

Pre-eclampsia is a complex multisystem disorder characterized by new-onset hypertension (blood pressure ≥140/90 mmHg) that develops after 20 weeks of pregnancy, along with proteinuria or dysfunction of other maternal organs.[4] The pathophysiology of this disorder involves multiple organ systems, and despite years of research, it is poorly understood.

Its pathogenesis is thought to involve defective placentation due to impaired trophoblastic invasion and incomplete spiral artery remodeling, leading to reduced placental perfusion. Placental ischemia and syncytiotrophoblast stress trigger the release of pro-inflammatory cytokines, reactive oxygen species, extracellular vesicles, and anti-angiogenic factors into the maternal circulation, resulting in widespread endothelial dysfunction.[5,6] This damaged endothelium releases tissue factor, activating coagulation and creating a prothrombotic state, which, combined with platelet aggregation, reduces organ perfusion and results in end-organ damage. Platelets get activated by adhering to the damaged endothelium and undergo morphological transformation, increasing the surface area along with degranulation and contributing to platelet aggregation.[7]

The platelet indices, including platelet count, mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT), are routinely assessed in laboratories using blood cell counters and serve as reliable markers of platelet function. In pre-eclampsia, thrombocytopenia, which develops as a result of peripheral consumption, is considered an important sign for diagnosis. The other platelet parameters, such as MPV and PDW, are also altered due to platelet activation and increased bone marrow turnover in pre-eclampsia.[7,8]

Pre-eclampsia requires early diagnosis and appropriate intervention as it can cause adverse fetal and maternal outcomes. There is a need for more sensitive, cost-effective, and easy-to-perform biomarkers for the early detection of pregnant patients at risk of developing pre-eclampsia. Platelet activation occurs before the onset of clinical signs in pre-eclampsia, and platelet indices are simple markers of platelet activation. Therefore, the assessment of platelet indices can be used as a tool for early diagnosis and preventing complications.

Aims and objectives

The purpose of this study is to compare platelet count, MPV, PDW, and PCT between pregnant women with pre-eclampsia and those who were normotensive. In addition, variations in these parameters in patients with and without severe features were also analyzed.

MATERIALS AND METHODS

Study design and participants

A cross-sectional study was conducted over 24 months, from August 2022 to February 2024. The study included 120 women who met the inclusion and exclusion criteria and 120 healthy normotensive pregnant women with gestational age (GA) >20 weeks.

Inclusion and exclusion criteria

All nulliparous women with singleton pregnancy diagnosed with pre-eclampsia, as per the guidelines of the American College of Obstetrics and Gynecology (ACOG)[1] were included in the study. Patients with a history of chronic hypertension, diabetes mellitus, thyroid dysfunction, cardiovascular diseases, and chronic liver disease were excluded from the study.

Sample size calculation

The sample size was calculated by taking the mean difference of platelet count between the pre-eclampsia group and control group as 26.81 ($\times 10^3/\mu L$) as per the study by Khan et al.[9]

Pooled standard deviation (SD) was calculated to be 74.43 ($\times 10^3/\mu L$) using SD1 of 56.59 ($\times 10^3/\mu L$) and sample size (n1) of 102 in the pre-eclampsia group and SD2 of 88.76 ($\times 10^3/\mu L$) and sample size (n2) of 102 in the control group.

The other parameters considered for sample size calculation were 80% power of the study and 5% two-sided alpha error. The following formula was used to calculate the sample size: Sample size, $n=(2SD^2 (Z_{\alpha/2}+Z_{\beta})^2)\div d^2$

Where,

- SD=Pooled SD of the previous study
- $Z_{\alpha/2}=Z_{0.05/2}=1.96$ (From Z table) at 5% alpha error
- $Z_{\beta}=Z_{0.80}=0.84$ (From Z table) at 80% power.

d=effect size=mean difference of the previous study.

The sample size was determined to be 120 cases and 120 controls.

Data collection

The study population underwent detailed clinical examination and relevant laboratory investigations for the diagnosis of pre-eclampsia. The patient group was further divided into two groups: Pre-eclampsia with severe

features and pre-eclampsia without severe features based on ACOG guidelines.[1]

From all study subjects, 2 mL of blood was drawn with minimal stasis from the antecubital vein using a dry sterile disposable syringe and needle. Samples collected in an Ethylenediamine tetraacetic acid vial were labeled with the patient's name, age, and identification number. Samples were tested within 1 h of collection to minimize variations caused by sample aging. Complete Blood Count was analyzed using the five-part differential automated Hematology Analyzer Horiba Pentra XLR. The clinical details, blood pressure, and complete hemogram of the normotensive pregnant women (in >20 weeks of gestation) were noted from the clinical records.

Statistical analysis

Categorical variables were presented as counts and percentages, while quantitative data were shown as means±SD or as medians with interquartile ranges (25th and 75th percentiles). Data normality was assessed using the Shapiro–Wilk test and non-parametric tests were used when data were not normally distributed. For comparisons, the Mann-Whitney test analyzed non-normally distributed quantitative variables, while the Independent t-test was applied to normally distributed ones. Qualitative variables were compared using the Chi-square, or Fisher's exact test if expected cell values were below 5. The receiver operating characteristic (ROC) curve was used to evaluate cut-off points, sensitivity, specificity, positive predictive value, and negative predictive value for platelet count, MPV, PDW, and PCT in predicting pre-eclampsia. Data were entered into Microsoft Excel, and analysis was performed using the Statistical Package for the Social Sciences (IBM, version 25.0). Statistical significance was set at $P<0.05$.

Ethical considerations

This study was conducted following the Declaration of Helsinki after obtaining approval from the Institutional Ethics Committee under reference no. IEC/VMMC/SJH/Thesis/2023-03/CC-231. All the subjects provided their informed written consent for participation in the present study.

RESULTS

The study was a cross-sectional study conducted on 120 pre-eclamptic women and 120 normotensive pregnant women. The mean age was 24.06±4 years in the pre-eclamptic group and 22.85±2.92 years in the normotensive group. The average GA in the pre-eclamptic group was 27.39±5.63 weeks, and 25.8±4.51 in the normotensive group. The mean systolic blood pressure (SBP) of study subjects was 150.98±9.7 mmHg, and diastolic blood pressure (DBP) was 95.75±5.67 mmHg. The mean SBP of the normotensive group was 123.72±9.25 mmHg, and the DBP was 78.71±7.04 mmHg (Table 1).

The platelet indices were compared among pre-eclamptic and normotensive groups. The mean platelet count in the pre-eclamptic group was 141.3±42.47×10^3/μL, significantly lower than in the normotensive group (174.32±27.24×10^3/μL) ($P<0.0001$). MPV was significantly elevated in the pre-eclamptic group with a mean value of 12.73±2.19 fl, and in the normotensive group, it was 11.98±1.78 fl ($P=0.004$). The mean value of PDW in the pre-eclamptic group was 20.35±2.98% and 16.02±0.87% in the normotensive group ($P<0.0001$). PCT in the pre-eclamptic group was 0.17±0.04%, which was significantly lower than the normotensive group, 0.22±0.04% ($P<0.0001$) (Table 2).

The pre-eclamptic group was further divided into pre-eclampsia with and without severe features, and platelet indices were compared between the two groups. Out of 120 pre-eclamptic women, 19 patients had severe features. It was observed that the platelet count and PCT were further reduced in patients with severe features, whereas MPV and PDW showed a significant increase when compared to those without severe features (Table 3).

ROC curve analysis showed that all the platelet parameters had significant discriminatory power to predict pre-eclampsia. Interpretation of the area under the ROC curve showed that the performance of PDW (area under the curve [AUC] 0.965; 95% confidence interval (CI): 0.946–0.984) was outstanding. The discriminatory power of PCT (AUC 0.838; 95% CI: 0.783–0.893) was excellent, and the discriminatory power of platelet count (AUC 0.779; 95% CI: 0.719–0.839) was acceptable. Among all the parameters, PDW was the best predictor of pre-eclampsia at the cut-off point of >17.4%, with a sensitivity of 83.33% and a specificity of 97.50% (Table 4 and Figure 1).

DISCUSSION

Pre-eclampsia is a major leading cause of maternal mortality in low and lower middle-income countries. It is a progressive disorder in which early prediction and diagnosis have an important role in maternal and neonatal outcomes. Much research has been undertaken in this field, and markers such a sFlt-1, and placental growth factor are found to be useful in the prediction of pre-eclampsia.[8] Nevertheless, we need easily available and affordable markers in less developed areas.

It is already established that platelets play an important role in the pathogenesis of pre-eclampsia, and thrombocytopenia is included as a severity indicator. Not only platelet count, but also other platelet parameters, also represent the functional activity of platelets, which can be used as reliable markers for prediction, diagnosis, and assessment of severity.

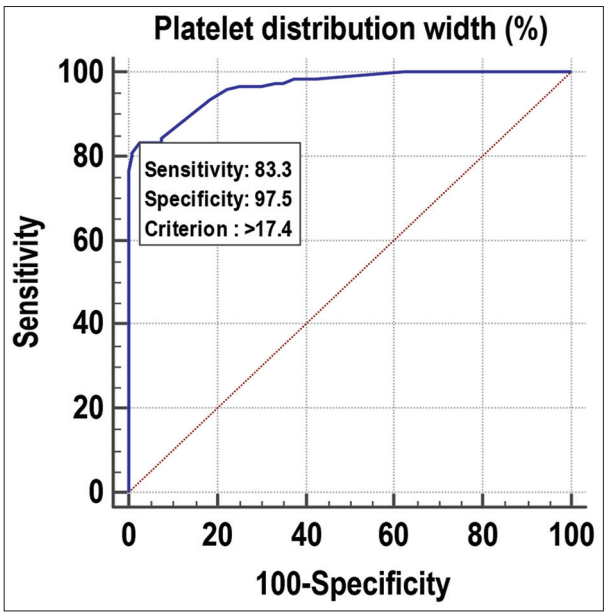

Figure 1: Receiver operating characteristic curve of platelet distribution width for predicting pre-eclampsia

Table 1: Clinical characteristics of study population

Variable	Normotensive (n=120) (Mean±SD)	Pre-eclamptic (n=120) (Mean±SD)	P-value
Age	24.06±4	22.85±2.92	0.008‡
GA in weeks	27.39±5.63	25.8±4.51	0.017‡
SBP (mmHg) (Range)	123.72±9.25 (100–138)	150.98±9.7 (140–200)	
DBP (mmHg) (Range)	78.71±7.04 (60–90)	95.75±5.67 (85–120)	

‡Independent t test. n: Number of samples, GA: Gestational age, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation

The current study included 240 pregnant women, among whom 120 were diagnosed with pre-eclampsia. The comparative group consisted of an equal number of normotensive women with >20 weeks of gestation. The majority of the studied population falls within an age group of 21–30 years, with a mean age of 24.04±4 years in pre-eclamptic and 22.85±2.9 years in the normotensive group. This is comparable with the study population of Dhakre et al.[10] The mean GA at which the sample was collected in the pre-eclampsia group was 27.39±5.6, which was significantly higher than the normotensive group (25.8±4.5).

The SBP and DBP of pre-eclamptic women were within a range of 140–200 mmHg and 85–120 mmHg, respectively; whereas the normotensive women had SBP within 100–138 mmHg and DBP within 60–90 mmHg. This is similar to the study population of Walle et al.,[11] and Mohapatra et al.[12]

Thrombocytopenia occurs in 10% of uncomplicated pregnancies, which is a physiological phenomenon and is more common in the second half of pregnancy. Pre-eclampsia accounts for 20% of thrombocytopenia in pregnancy.[13] The aggravated endothelial dysfunction and interplay of multiple factors result in increased platelet aggregation and turnover. In the current study, we found that platelet count was significantly lower (P<0.0001) in the pre-eclampsia group (141.3±42.4) as compared to normotensive women (174.3±27.2). This goes with findings observed by Khan et al.,[9] Walle et al.,[11] Mohapatra et al.,[12] Kamath and Gomathy.[14]

MPV is a potential marker of platelet activation. The present study showed a significant increase (P=0.004) in MPV among the pre-eclampsia group with a mean value of 12.7±2.19 fl, than normotensive women (mean: 11.98±1.78 fl). This is in line with the findings of other studies.[9,11,14] A systematic review by Ye et al.,[8] suggested that MPV can be used as a promising biomarker in the diagnosis of pre-eclampsia. The release of new larger platelets in response to peripheral depletion and an increase in the number as

Table 2: Comparison of platelet parameters between pre-eclamptic and normotensive group

Parameters	Normotensive			Pre-eclamptic			P-value
	Mean (Mean±SD)	Median (25^{th}–75^{th} percentile)	Range	Mean (Mean±SD)	Median (25^{th}–75^{th} percentile)	Range	
Platelet count (×10^3/μL)	174.32±27.24	171 (152–194.25)	130–250	141.3±42.47	137.5 (111.75–160)	65–290	<0.0001‡
MPV (fl)	11.98±1.78	12 (11–13)	8.4–16	12.73±2.19	12.6 (11.2–13.5)	7.9–20	0.004‡
PDW (%)	16.02±0.87	16 (15.475–16.725)	13–17.9	20.35±2.98	19.55 (18–22)	16–28	<0.0001‡
PCT (%)	0.22±0.04	0.21 (0.2–0.23)	0.16–0.6	0.17±0.04	0.18 (0.15–0.19)	0.08–0.3	<0.0001‡

‡Independent t test, MPV: Mean platelet volume, PDW: Platelet distribution width, PCT: Plateletcrit, SD: Standard deviation

Table 3: Comparison of platelet parameters between pre-eclampsia with and without severe features

Parameters	Preeclampsia with severe features (n=19)			Pre-eclampsia without severe features (n=101)			P-value
	Mean (Mean±SD)	Median (25^{th}–75^{th} percentile)	Range	Mean (Mean±SD)	Median (25^{th}–75^{th} percentile)	Range	
Platelet count (×10^3/μL)	99.42±29.69	90 (87.5–94)	65–180	149.18±39.89	145 (120–160)	94–290	<0.0001‡
MPV (fL)	15.4±2.38	15.9 (13.7–16.7)	10.5–20	12.23±1.76	12.2 (11–13)	7.9–18	<0.0001‡
PDW (%)	22.86±3.87	24 (20.3–25.9)	16.5–28	19.88±2.55	19 (18–22)	16–26.5	0.004‡
PCT (%)	0.14±0.04	0.15 (0.12–0.16)	0.08–0.25	0.18±0.04	0.18 (0.15–0.19)	0.11–0.3	0.0006‡

‡Independent t test, n: Number of samples, MPV: Mean platelet volume, PDW: Platelet distribution width, PCT: Plateletcrit, SD: Standard deviation

Table 4: The diagnostic values of platelet parameters for the diagnosis of pre-eclampsia among pregnant women by ROC curve analysis

Parameters	AUC (95% CI)	Cut off point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic accuracy (%)
Platelet count	0.779 (0.719–0.839)	≤150×10^3/μL	69.17	76.67	74.8	71.3	72.92
MPV	0.594 (0.522–0.666)	>12.1 fL	58.33	65.83	63.1	61.2	62.08
PDW	0.965 (0.946–0.984)	>17.4%	83.33	97.5	97.1	85.4	90.42
PCT	0.838 (0.783–0.893)	≤0.19%	81.67	79.17	79.7	81.2	80.42

AUC: Area under curve, PPV: Positive predictive value, NPV: Negative predictive value, ROC: Receiver operating characteristic, CI: Confidence interval, MPV: Mean platelet volume, PDW: Platelet distribution width, PCT: Plateletcrit

well as the size of pseudopods on activation may be the two major reasons behind the increment of MPV.

PDW indicates platelet heterogeneity in circulation and is increased on platelet activation due to the morphological changes of platelets. We found that PDW is increased in the pre-eclamptic women with a range of 16–28% (20.35± 2.98%) when compared to normotensive women (16.02±0.87%). This difference reached statistical significance (P<0.001), as in previous studies.[9,11,14] In contrast, the study by Temur et al.,[15] stated that there is not much difference in PDW values between cases and controls.

The next parameter studied was PCT, which is a measure of total platelet mass in blood. It is calculated by multiplying the platelet count and MPV, so it is affected by both the number and size of platelets. The present study showed a statistical reduction (P<0.0001) in PCT value in the pre-eclampsia group (0.17±0.04 %) as compared to the normotensive group (0.22±0.04%). This indicates the decreased platelet concentration in circulation. A similar result was observed in the study by Mohapatra et al.[12] On the other hand, Khan et al.,[9] Temur et al.,[15] and Thalor et al.,[16] could not find a statistical difference between the groups, even though PCT was decreased in pre-eclampsia.

In this study, the pre-eclampsia group was further divided into two groups: Pre-eclampsia with severe features and without severe features based on the clinical and laboratory values. 15% of the patients had severe features. It was observed that platelet indices varied with the severity of the disease. Platelet count and PCT showed a significant reduction in pre-eclampsia with severe features than in pre-eclampsia without severe features. The mean platelet count of 99.42±29.69 and PCT of 0.14±0.04% were observed in the severe group. Regarding the indices MPV and PDW, both of them increased further with severity. The mean value of MPV and PDW in the severe group was 15.4±2.38 fl and 22.86±3.87%, respectively. This increase was statistically significant. These findings are consistent with those of Tesfay et al.[17] and Bawore et al.[18] These results emphasize the potential of platelet parameters in monitoring pre-eclamptic patients and in assessing severity.

For this study, the cut-off values of parameters to differentiate pre-eclamptic and normotensive were determined by ROC analysis. The largest AUC was obtained for PDW, indicating that it can act as the best parameter to predict pre-eclampsia with a cut-off value of >17.4% with 90.42% test accuracy. A study by Mahmoud et al.,[19] revealed that PDW can act as the best possible predictor of pre-eclampsia at 20–28 weeks of gestation with a cut-off value of >17.7. There are variations in the cut-off values in other studies.[14,20] These variations may be attributed to differences in automated hematology analyzers used in different studies.

PCT, at a cut-off value ≤0.19%, also showed a better predictive value in our study, whereas Mohapatra et al.,[12] found a cut-off of 0.22%. Many studies have demonstrated MPV as a better predictor among the platelet indices.[11] In this study, despite having the smallest AUC, MPV obtained a sensitivity and specificity of 58.3% and 65.83%, respectively, which shows that it can also be used as a predictor. Platelet count showed good sensitivity and specificity (69.17% and 76.67%) at a cut-off value of

$150\times10^3/\mu m^3$ with an acceptable discriminatory power (AUC: 0.779; 95% CI: 0.719–0.839). Various studies in the literature observed that platelet parameters like MPV, PDW, and PCT have better sensitivity and specificity than platelet count in predicting preeclampsia.[9,12,17]

The findings of this study indicate that platelet parameters are significantly altered in pre-eclampsia, suggesting their potential utility in both early diagnosis and patient monitoring. The observed decrease in platelet count and PCT, along with the increase in MPV and PDW, can also be used to assess the severity of the condition. While platelet count is already an established diagnostic marker and a recognized sign of end-organ damage in pre-eclampsia, this study highlights the importance of considering platelet functionality as well when screening antenatal women at risk. MPV and PDW are direct indicators of platelet activation, and our results further demonstrate that PDW is the most reliable predictor among platelet parameters for detecting pre-eclampsia.

Limitations of the study

The current study has its limitations. As the serial detection of platelet indices at different GAs was not done, the time at which they are altered could not be assessed. This is a single-center study, which limits the generalizability of findings. Hence, a larger multicentre study can provide a wider perspective into the role of platelet parameters in the prediction and diagnosis of pre-eclampsia.

CONCLUSION

This study provides evidence that platelet indices such as platelet count, MPV, PDW, and PCT are significantly altered in pre-eclampsia. These parameters, which serve as biomarkers of platelet activation, can play a pivotal role not only in diagnosis but also in the ongoing monitoring of pre-eclampsia. As pre-eclampsia is a disorder that requires early detection, we need simple, cost-effective, and reliable markers, particularly in resource-limited peripheral healthcare settings. Platelet indices stand out as valuable tools for predicting and diagnosing as well as assessing the severity of pre-eclampsia, making them essential components in the clinical management of the condition.

ACKNOWLEDGMENT

None.

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Authors' Contribution:
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Source of Support: Nil, **Conflicts of Interest:** None declared.