Original Article

Predictive value of platelet parameters for early-onset pre-eclampsia: A prospective cohort study in a teaching institution in Gujarat, India

DipenKumar Thakkar[1], Jeel Shihora[1], Rohankumar Gandhi[1], Rahul Parmar[2], Yogesh M[1]

[1]Department of Community Medicine, Shri MP Shah Medical College, Jamnagar, Gujarat, India, [2]Medical Student, Shri MP Shah Medical College, Jamnagar, Gujarat, India

Abstract

Background: Early-onset pre-eclampsia is associated with severe maternal and perinatal complications. Identifying novel biomarkers for early prediction is crucial for timely intervention and improved outcomes. This study aimed to evaluate the predictive value of platelet parameters, namely mean platelet volume (MPV), platelet distribution width (PDW), and platelet count (PC), for early-onset pre-eclampsia. **Methods:** A prospective cohort study was conducted at a tertiary care hospital in Gujarat, India. Pregnant women (n = 712) between 14 and 18 weeks of gestation were enrolled and followed up until delivery. MPV, PDW, and PC were measured at enrollment. The primary outcome was the development of early-onset pre-eclampsia (<34 weeks). Receiver operating characteristic (ROC) curves were used to evaluate the predictive value of platelet parameters. **Results:** The prevalence of early-onset pre-eclampsia was 5.3%. Women who developed early-onset pre-eclampsia had significantly higher MPV and PDW and lower PC at 14–18 weeks compared to those who remained normotensive. The combination of MPV > 10.2 fL, PDW > 16.5 fL, and PC < 180 × 103/μL had the highest predictive value (AUC: 0.951, sensitivity: 71.1%, specificity: 99.1%). Individual platelet parameters also demonstrated good predictive ability. **Conclusion:** Platelet parameters, particularly MPV, PDW, and PC, measured at 14–18 weeks of gestation, have good predictive value for early-onset pre-eclampsia. Incorporating these parameters into routine antenatal screening could improve the early identification of at-risk women. Further research is needed to validate these findings and evaluate the cost-effectiveness of implementation.

Keywords: Early-onset pre-eclampsia, mean platelet volume, platelet distribution width, platelet parameters, predictive biomarkers, pre-eclampsia

Introduction

Pre-eclampsia is a pregnancy-specific disorder characterized by the onset of hypertension and proteinuria after 20 weeks of gestation.[1] It is a leading cause of maternal and perinatal morbidity and mortality worldwide, affecting 2–8% of all pregnancies.[2] In India, the prevalence of pre-eclampsia ranges from 4.8% to 7.5%.[3,4] Early-onset pre-eclampsia, defined as the onset of the disorder before 34 weeks of gestation, is associated with more severe maternal and perinatal complications compared to late-onset pre-eclampsia.[5]

The exact etiology of pre-eclampsia remains unclear; however, it is thought to involve a complex interplay of genetic, immunological, and environmental factors.[6] The pathophysiology

Address for correspondence: Dr. Yogesh M, Department of Community Medicine, Shri MP Shah Medical College, Jamnagar, Gujarat, India.
E-mail: yogeshbruce23@gmail.com

Received: 03-08-2024 **Revised:** 14-09-2024
Accepted: 16-09-2024 **Published:** 13-01-2025

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_1331_24

How to cite this article: Thakkar D, Shihora J, Gandhi R, Parmar R, Yogesh M. Predictive value of platelet parameters for early-onset pre-eclampsia: A prospective cohort study in a teaching institution in Gujarat, India. J Family Med Prim Care 2025;14:327-33.

of pre-eclampsia is characterized by abnormal placentation, systemic inflammation, and endothelial dysfunction.[7] Recent evidence suggests that platelets may play a crucial role in the development of pre-eclampsia as they are involved in the regulation of angiogenesis, inflammation, and coagulation.[8]

Platelet activation and consumption have been observed in women with pre-eclampsia, leading to changes in platelet parameters, such as mean platelet volume (MPV), platelet distribution width (PDW), and platelet count (PC).[9] MPV and PDW are markers of platelet size and reactivity, with higher values indicating the presence of larger, more reactive platelets.[10] Several studies have reported increased MPV and PDW values in women with pre-eclampsia compared to normotensive pregnant women.[11,12]

Despite the growing evidence linking platelet parameters to pre-eclampsia, their predictive value for early-onset pre-eclampsia remains unclear. Early identification of women at risk for pre-eclampsia is crucial for timely intervention and improved maternal and perinatal outcomes.[13] Current screening methods, such as maternal risk factors and uterine artery Doppler, have limited predictive accuracy, particularly for early-onset pre-eclampsia.[14] Therefore, there is a need for novel biomarkers that can accurately predict the risk of early-onset pre-eclampsia and facilitate timely intervention.

This prospective cohort study aimed to evaluate the predictive value of platelet parameters, namely MPV, PDW, and PC, for early-onset pre-eclampsia in a tertiary care hospital in Gujarat, India. We hypothesized that higher MPV and PDW values and lower PC in the early second trimester (14–18 weeks of gestation) would be associated with an increased risk of developing early-onset pre-eclampsia. The findings of this study could contribute to the development of improved screening strategies for early-onset pre-eclampsia and facilitate timely intervention to reduce maternal and perinatal morbidity and mortality.

Methodology

Study design and setting

A prospective cohort study was conducted at a tertiary care hospital in Gujarat, India, to evaluate the predictive value of platelet parameters for early-onset pre-eclampsia.

Study population

Pregnant women attending antenatal care at the tertiary care hospital were recruited between 14 and 18 weeks of gestation. The study included participants who were experiencing a singleton pregnancy with a gestational age between 14 and 18 weeks. Participants were required to have no history of chronic hypertension, diabetes, or renal disease, and there should be no evidence of fetal anomalies or chromosomal abnormalities. Exclusion criteria for the study encompassed multiple pregnancies, known thrombocytopenia or platelet disorders, the use of antiplatelet or anticoagulant medications, and an inability to provide informed consent.

Sample size

Based on an expected 6.2% prevalence of pre-eclampsia in the study population, the sample size was determined. The 95% confidence range for the population prevalence, which had a 95% confidence interval of 2.8–10.6%, an estimated relative risk of 2, and a power of 0.8, indicated that the estimate's precision must be within 5% points. The minimum needed total sample size for a cohort study with the stated parameters was 640, according to the sample size calculator (EPI-info).[15]

Participant recruitment and sample selection

Pregnant women attending antenatal care at the tertiary care hospital were consecutively enrolled in the study between January 2022 and June 2023. The inclusion and exclusion criteria were applied to determine their eligibility.

The study was advertised through posters and pamphlets displayed in the antenatal clinic waiting area. Potential participants were also informed about the study by the clinic staff during their routine antenatal visits. Interested women were provided with detailed information about the study, and those who met the eligibility criteria and provided written informed consent were enrolled.

Participant recruitment continued until the target sample size was reached. A total of 800 pregnant women were screened for eligibility, of which 750 met the inclusion criteria and provided informed consent. During the study, 38 participants were lost to follow-up due to various reasons, such as relocation, withdrawal of consent, or failure to attend scheduled study visits.

As a result, the final study sample consisted of 712 pregnant women who completed the study. This sample size was deemed sufficient to provide the desired precision of the estimate and adequate power to detect significant differences in platelet parameters between the pre-eclampsia and no pre-eclampsia groups.

Data collection

At enrollment, participants underwent a comprehensive medical and obstetric history, physical examination, and routine antenatal investigations. Blood samples were collected for complete blood count analysis, including platelet parameters (MPV, PDW, and PC). Demographic information, medical history, and obstetric data were recorded using a standardized questionnaire.

Platelet parameter measurement

Blood samples were collected in EDTA tubes and analyzed within 2 h of collection to minimize the effect of EDTA on platelet size. Samples were not stored for batch analysis, as immediate processing was crucial to ensure accurate measurement of platelet parameters, particularly MPV and PDW, which can be affected by storage time and conditions.

Platelet parameters were measured using a Sysmex XN-1000 automated hematology analyzer (Sysmex Corporation; Kobe, Japan). This analyzer used fluorescence flow cytometry technology for platelet counting and sizing, providing accurate and reproducible results.

The Sysmex XN-1000 measured MPV in femtoliters (fL), PDW as a coefficient of variation (%), and PC as the absolute number of platelets per microliter of blood ($\times 10^3/\mu L$). The analyzer was calibrated daily using manufacturer-provided controls, and all measurements were performed according to the manufacturer's instructions by trained laboratory technicians.

Follow-up and outcome assessment

Participants were followed up at regular intervals throughout their pregnancy:

1. First trimester (up to 13 weeks):
   - Initial enrollment visit (14–18 weeks)
   - Comprehensive medical history and physical examination
   - Blood sample collection for platelet parameter analysis
2. Second trimester (14–26 weeks):
   - Monthly visits (around 18, 22, and 26 weeks)
   - Blood pressure measurement
   - Urine protein test (dipstick)
   - Fetal growth assessment via ultrasound (at 22 weeks)
3. Third trimester (27 weeks to delivery):
   - Biweekly visits from 27 to 36 weeks
   - Weekly visits from 37 weeks until delivery
   - Blood pressure measurement at each visit
   - Urine protein test (dipstick) at each visit
   - Fetal growth and well-being assessment via ultrasound (at 32 and 36 weeks).

At each follow-up visit, the following assessments were performed:

1. Blood pressure measurement using a calibrated automated device
2. Urine protein test using a dipstick method
3. Maternal weight and BMI calculation
4. Assessment of edema and other clinical signs of pre-eclampsia
5. Fetal heart rate auscultation
6. Review of any symptoms or concerns reported by the participant.

If any abnormalities were detected during these routine visits, additional tests or more frequent follow-ups were scheduled as needed. Participants were also instructed to contact the study team or seek immediate medical attention if they experienced any warning signs of pre-eclampsia between scheduled visits.

Postnatal follow-up

For cases of early-onset pre-eclampsia, additional postnatal follow-up was conducted. These participants were monitored closely during their hospital stay, which typically lasted 3–5 days postpartum. Daily blood pressure measurements and urinalysis were performed to assess the resolution of pre-eclampsia. Participants were also evaluated for complications such as postpartum hemorrhage, thromboembolism, and persistent hypertension.

After discharge, these participants were scheduled for follow-up visits at 2 weeks and 6 weeks postpartum. During these visits, blood pressure was measured, and a urine protein test was performed. If hypertension or proteinuria persisted, participants were referred for further evaluation and management by a specialist.

Data on maternal and neonatal outcomes were collected from hospital records and during follow-up visits. This included information on the mode of delivery, gestational age at delivery, birth weight, Apgar scores, neonatal intensive care unit admissions, and any maternal or neonatal complications.

Outcome measures

The primary outcome was the development of early-onset pre-eclampsia, defined as the onset of pre-eclampsia before 34 weeks of gestation. Pre-eclampsia was diagnosed based on the International Society for the Study of Hypertension in Pregnancy (ISSHP) criteria:

- Systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg on two occasions at least 4 h apart after 20 weeks of gestation

- Proteinuria ≥ 300 mg/24 h or protein/creatinine ratio ≥ 0.3 mg/dL

- In the absence of proteinuria, pre-eclampsia was diagnosed if hypertension was accompanied by any of the following: thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or cerebral or visual symptoms.[16]

Data analysis

Descriptive statistics were used to summarize the characteristics of the study population. Continuous variables are expressed as mean ± standard deviation or median (interquartile range), whereas categorical variables are presented as frequencies and percentages.

The platelet parameters (MPV, PDW, and PC) at 14–18 weeks of gestation were compared between the pre-eclampsia and no pre-eclampsia groups using independent *t*-tests or Mann–Whitney *U* tests, as appropriate. Receiver operating characteristic (ROC) curves were constructed to evaluate the predictive value of each platelet parameter and their combinations for early-onset pre-eclampsia. The area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each parameter and combination.

A P value < 0.05 was considered statistically significant. All analyses were performed using appropriate statistical software.

Ethical considerations

The study protocol was approved by the Institutional Ethics Committee of the tertiary care hospital [ref. no.-06/01/2022]. Written informed consent was obtained from all participants before enrollment. Participants were informed about the purpose, procedures, risks, and benefits of the study. They had the right to withdraw from the study at any time without affecting their care. All data were kept confidential and used only for research purposes.

Results

The prevalence of early-onset pre-eclampsia in our study population was 5.3% (38/712). Among the 38 cases of early-onset pre-eclampsia, the mean gestational age at diagnosis was 30.2 ± 2.8 weeks (range: 24.5–33.6 weeks). The distribution of gestational age at diagnosis was as follows:

- 24–28 weeks: 7 cases (18.4%)
- 28–32 weeks: 21 cases (55.3%)
- 32–34 weeks: 10 cases (26.3%).

Table 1 presents the baseline characteristics of the study participants, comparing those who developed pre-eclampsia to those who did not. Significantly higher BMI, systolic and diastolic blood pressure, mean arterial pressure, and elevated BP category were observed in the pre-eclampsia group. Other factors such as age, parity, family history of PE, education, employment, smoking, alcohol use, marital status, household income, pre-pregnancy diabetes, and chronic hypertension did not differ significantly between the two groups.

Table 2 compares the pre-eclampsia and no pre-eclampsia groups' platelet parameters at 14–18 weeks gestation. Mean platelet volume (MPV) and platelet distribution width (PDW) were significantly higher. In contrast, platelet count (PC) was significantly lower in the pre-eclampsia group compared to the no pre-eclampsia group.

Table 3 presents platelet parameters' receiver operating characteristic (ROC) analysis for predicting early-onset pre-eclampsia. The cut-off values with the best predictive performance were >10.2 fL for MPV, >16.5 fL for PDW, and <180 × 10^3/μL for PC. MPV had the highest area under the curve (AUC) at 0.921, followed by PDW at 0.903 and PC at 0.889, indicating good predictive ability for all three parameters.

Table 4 evaluates the predictive performance of combined platelet parameters for early-onset pre-eclampsia. The combination of MPV >10.2 fL, PDW >16.5 fL, and PC <180 × 10^3/μL had the highest AUC at 0.951, with a sensitivity of 71.1%, specificity of 99.1%, PPV of 87.5%, and NPV of 97.5%. Other combinations also demonstrated good predictive performance, with AUCs ranging from 0.935 to 0.942.

Figure 1 shows the ROC curve of platelet parameters for predicting early-onset pre-eclampsia. The curves for MPV, PDW,

Table 1: Baseline characteristics of study participants

Characteristic	Total (*n*=712)	Pre-eclampsia (*n*=38)	No pre-eclampsia (*n*=674)	*P*
Age (years)	28.5±4.8	29.2±5.1	28.4±4.8	0.32
BMI (kg/m²)	24.8±2.8	25.1±3.6	23.5±3.4	0.003*
Nulliparous	372 (52.2%)	24 (63.2%)	348 (51.6%)	0.16
Family history of PE	56 (7.9%)	6 (15.8%)	50 (7.4%)	0.06
Educational level				0.42
Primary	32 (4.5%)	1 (2.6%)	31 (4.6%)	
Secondary	215 (30.2%)	14 (36.8%)	201 (29.8%)	
Tertiary	465 (65.3%)	23 (60.5%)	442 (65.6%)	
Employment status				0.21
Employed	528 (74.2%)	25 (65.8%)	503 (74.6%)	
Unemployed	184 (25.8%)	13 (34.2%)	171 (25.4%)	
Tobacco usage during pregnancy	26 (3.6%)	3 (8%)	23 (3.4%)	0.14
Alcohol use during pregnancy	4 (0.5%)	1 (2.6%)	3 (0.4%)	0.06
Marital status				0.72
Married	621 (87.2%)	34 (89.5%)	587 (87.1%)	
Single	91 (12.8%)	4 (10.5%)	87 (12.9%)	
Pre-pregnancy diabetes	18 (2.5%)	2 (5.3%)	16 (2.4%)	0.27
Chronic hypertension	24 (3.4%)	3 (7.9%)	21 (3.1%)	0.12
Systolic BP (mmHg)	116±10	118±12	111±10	<0.001**
Diastolic BP (mmHg)	68±8	73±9	67±8	<0.001**
Mean arterial pressure (mmHg)	82±8	88±9	82±8	<0.001**
Pulse pressure (mmHg)	44±7	45±8	44±7	0.41
BP category				<0.001**
Normal	624 (87.6%)	26 (68.4%)	598 (88.7%)	
Elevated	88 (12.4%)	12 (31.6%)	76 (11.3%)	

P<0.05*-significant, *P*<0.001**-highly significant

and PC are all above the reference line, indicating their ability to predict early-onset pre-eclampsia. MPV has the highest AUC, followed closely by PDW and PC.

Figure 2 displays the ROC curve of combined platelet parameters for early-onset pre-eclampsia. The combination of MPV > 10.2 fL, PDW > 16.5 fL, and PC <180 × 10^3/μL had the highest AUC, demonstrating the best predictive performance among the combined parameters. The other combinations also showed good predictive ability, with their curves well above the reference line.

In summary, these tables and figures highlight the significant differences in platelet parameters between women who developed early-onset pre-eclampsia and those who did not. The ROC analyses demonstrate the potential of using platelet parameters, either individually or in combination, as predictors of early-onset pre-eclampsia. These findings support the use of platelet parameters as a simple and accessible screening tool for identifying women at risk of developing early-onset pre-eclampsia.

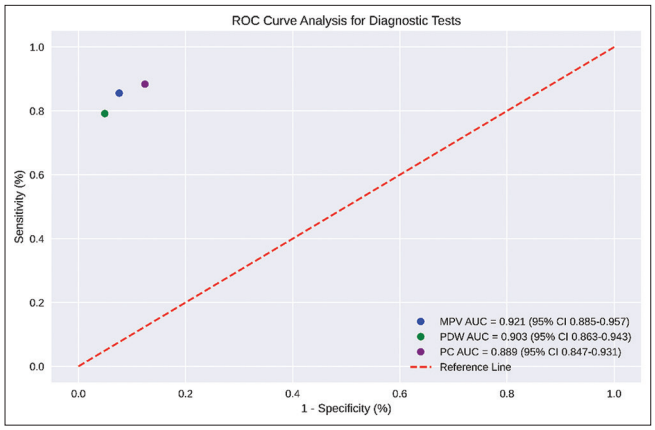

Figure 1: Shows the ROC curve of platelet parameters for predicting early-onset pre-eclampsia

Table 2: Comparison of platelet parameters at 14–18 weeks gestation

Parameter	Pre-eclampsia (*n*=38)	No pre-eclampsia (*n*=674)	*P*
MPV (fL)	11.3±1.2	9.6±0.8	<0.001**
PDW (fL)	17.8±2.1	14.2±1.3	<0.001**
PC (×10^3/μL)	168±32	221±45	<0.001**

P<0.05*-significant, *P*<0.001**-highly significant

Discussion

This prospective cohort study investigated the predictive value of platelet parameters, namely mean platelet volume (MPV), platelet distribution width (PDW), and platelet count (PC), for early-onset pre-eclampsia in a tertiary care hospital in Gujarat, India. The study found significant differences in platelet parameters between women who developed early-onset pre-eclampsia and those who remained normotensive throughout pregnancy.

The prevalence of pre-eclampsia in our study population was 5.3%, which is consistent with other studies that reported a prevalence range of 4.8% to 7.5%, which directly overlaps with your results.[17,18] However, it is valuable to acknowledge the potential for variations due to study design and population specifics.

Women who developed early-onset pre-eclampsia had significantly higher MPV and PDW values and lower PC at 14–18 weeks of gestation compared to those who did not develop pre-eclampsia. These findings are consistent with recent studies that have reported similar associations between platelet parameters and pre-eclampsia risk. A meta-analysis by Ye *et al.* (2023)[19] found that increased MPV values were significantly associated with the development of pre-eclampsia. Similarly, a study by Oğlak *et al.* (2021)[20] reported that high MPV and PDW values in the first trimester were independent risk factors for pre-eclampsia.

The ROC analysis in our study demonstrated that platelet parameters, either individually or in combination, had good predictive value for early-onset pre-eclampsia. The combination of MPV >10.2 fL, PDW >16.5 fL, and PC <180 × 10^3/μL had the highest AUC (0.951), with a sensitivity of 71.1%, specificity of 99.1%, PPV of 87.5%, and NPV of 97.5%. These findings

Table 3: ROC analysis of platelet parameters for predicting early-onset pre-eclampsia

Parameter	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (95% CI)
MPV	>10.2 fL	85.6	92.4	52.7	98.5	0.921 (0.885-0.957)
PDW	>16.5 Fl	79.2	95.1	61.3	97.8	0.903 (0.863-0.943)
PC	<180×10^3/μL	88.4	87.6	42.5	98.7	0.889 (0.847-0.931)

Area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), mean platelet volume (MPV), platelet distribution width (PDW), and platelet count (PC)

Table 4: Predictive performance of combined platelet parameters for early-onset pre-eclampsia

Parameter combination	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (95% CI)
MPV >10.2 fL + PDW >16.5 Fl	76.3	97.5	71.8	97.9	0.938 (0.905–0.971)
MPV >10.2 fL + PC <180×10^3/μL	81.6	95.8	66.1	98.2	0.942 (0.910–0.974)
PDW >16.5 fL + PC <180×10^3/μL	73.7	98.2	77.8	97.7	0.935 (0.901–0.969)
MPV >10.2 fL + PDW >16.5 fL + PC <180×10^3/μL	71.1	99.1	87.5	97.5	0.951 (0.920–0.982)

Area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), mean platelet volume (MPV), platelet distribution width (PDW), and platelet count (PC)

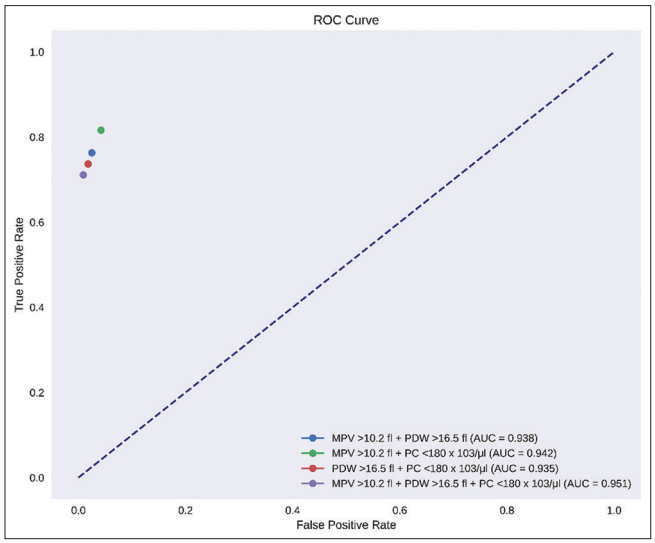

Figure 2: Shows the ROC curve combined platelet parameters for early-onset pre-eclampsia

suggest that incorporating platelet parameters into routine antenatal screening could improve the early identification of women at risk for pre-eclampsia. A previous study by Ozkan *et al.* (2022)[21] also found that the combination of MPV and PDW had a high predictive value for pre-eclampsia.

The pathophysiological mechanisms underlying the association between platelet parameters and pre-eclampsia are not fully understood. However, it is thought that platelet activation and consumption play a role in the development of pre-eclampsia.[22] Increased MPV and PDW values may reflect increased platelet turnover and the presence of larger, more reactive platelets, which could contribute to the endothelial dysfunction and systemic inflammation observed in pre-eclampsia.[23,24]

Limitations and recommendations

Our study has several limitations that should be considered when interpreting the results. Firstly, the single-center design may limit the generalizability of the findings to other settings, particularly those with different population characteristics or healthcare systems. Future studies should aim to validate these findings in larger, multi-center cohorts to ensure their applicability across different settings.

Secondly, although our study demonstrated the predictive value of platelet parameters for early-onset pre-eclampsia, we did not assess the cost-effectiveness of implementing platelet parameter screening in routine antenatal care. Before incorporating these parameters into clinical practice, it is essential to evaluate the economic impact of such screening, considering factors such as the cost of testing, potential benefits of early detection and intervention, and the healthcare resources available in different settings.[25]

Thirdly, our study focused on early-onset pre-eclampsia, which accounts for a smaller proportion of all pre-eclampsia cases compared to late-onset pre-eclampsia. Although early-onset pre-eclampsia is associated with more severe maternal and perinatal complications,[26] future studies should also investigate the predictive value of platelet parameters for late-onset pre-eclampsia to provide a more comprehensive understanding of their utility in predicting this pregnancy complication.

Lastly, although our study identified platelet parameters as potential predictors of early-onset pre-eclampsia, we did not explore the underlying mechanisms driving these associations. Future research should aim to elucidate the pathophysiological pathways linking platelet activation and dysfunction to the development of pre-eclampsia, which may lead to the identification of novel therapeutic targets and prevention strategies.[27]

Conclusion

The present study demonstrates that platelet parameters, particularly MPV, PDW, and PC, measured at 14–18 weeks of gestation, have good predictive value for early-onset pre-eclampsia. Incorporating these parameters into routine antenatal screening could improve the early identification of women at risk for this serious pregnancy complication. Further research is needed to validate these findings in larger, multi-center studies and evaluate the cost-effectiveness of implementing platelet parameter screening in different healthcare settings.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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