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Original Research

Mean Platelet Volume and Risk of Preeclampsia: A Case-Control Study at the Peruvian National Maternal Perinatal Institute

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Abstract

Background: Platelet activation is central to preeclampsia (PE) pathobiology. We evaluated whether mean platelet volume (MPV) is independently associated with PE and quantified its individual discriminatory performance in a hospital-based case-control study in Peru. **Methods**: We included 112 women with PE and 112 normotensive controls who delivered at the National Maternal Perinatal Institute (Lima) in 2024. MPV was obtained from the first complete blood count (CBC) performed at ≥20 gestational weeks. Logistic regression models estimated adjusted odds ratios (aORs) with 95% CIs. Receiver operating characteristic (ROC) analysis provided the area under the curve (AUC) with 95% CI and the optimal cutoff by Youden's index. **Results**: Higher MPV was independently associated with PE (aOR: 2.16 per 1 fL; 95% CI: 1.55–3.01; $p < 0.001$). Gestational obesity (aOR: 2.43; 95% CI: 1.17–5.26; $p = 0.039$) and inadequate prenatal care (<6 visits; aOR: 3.71; 95% CI: 1.27–7.55; $p = 0.006$) were also associated with PE. MPV showed moderate discrimination (AUC: 0.686; 95% CI: 0.616–0.755). Using a cutoff of 8.80 fL, the sensitivity was 61.6%, the specificity was 71.4%, the positive likelihood ratio was 2.16, and the negative likelihood ratio was 0.54. **Conclusions**: MPV is independently associated with PE and provides moderate individual discrimination. As MPV is routinely measured by hematology analyzers at no additional cost, incorporating it into trimester-specific, multivariable antenatal risk models may support cost-effective risk stratification in resource-limited settings.

Keywords: preeclampsia; mean platelet volume; biomarkers; maternal–fetal medicine; SDG 3: good health and well-being

1. Introduction

Hypertensive disorders of pregnancy, particularly preeclampsia (PE), are major contributors to adverse outcomes, causing approximately 76,000 maternal deaths and over 500,000 perinatal and infant deaths each year worldwide [1–3]. Platelet activation, aggregation, and consumption at sites of endothelial injury are central to PE pathobiology, supporting the exploration of platelet-based metrics as accessible tools for risk stratification and screening [4]. A meta-analysis of 25 studies found lower platelet counts [pooled weighted mean difference (WMD): –41.45 $\times$ 10^9/L] and higher mean platelet volume (MPV; pooled WMD: +0.98 fL) in PE versus normotensive pregnancy, reinforcing biological plausibility [5]. Complementarily, pooled diagnostic performance estimates indicate an MPV sensitivity of 0.676, specificity of 0.710, and an area under the curve (AUC) of the summary receiver operating characteristic curve (SROC) of 0.7889 for identifying PE [6]. Altogether, these findings position platelet indices as potential candidates for surveillance in obstetric care.

Despite these advances, uncertainties remain regarding optimal timing, thresholds, and clinical contexts for applying platelet indices [7]. In a large population-based analysis, higher first-trimester MPV categories were associated with gestational hypertension [9.8–10.3 fL: odds ratio (OR): 1.23; ≥10.4 fL: OR: 1.46], whereas associations with PE did not reach statistical significance, raising questions about phenotype-specific utility [8]. At the hospital level in Nepal, a platelet count–to–platelet distribution width (PC/PDW) ratio ≤15.1 yielded an AUC of 0.767, with 70.8% sensitivity and 81.9% specificity for PE detection, and an 11.02-fold increase in odds at this cutoff. These findings underscore the potential of this low-cost triage while highlighting variability across clinical settings [9]. Community and clinical risk profiles also differ. Indeed, in Odisha, India, family history of hypertension and maternal anemia increased the odds of PE by 3.15 and 2.14, respectively, emphasizing context-specific baselines that may interact with biomarker performance [10]. Further, comparative policy analyses note inconsistency in how high-risk criteria are defined and when they are applied, complicating standardized implementation of prediction strategies [11]. In summary, applicability and thresholds for platelet indices likely vary across populations, timelines, and healthcare-system contexts.

Further heterogeneity is observed in cross-sectional data from Ethiopia, where higher MPV (10.6 $\pm$ 1.2 vs. 8.5 $\pm$ 1.0 fL), lower platelet counts (202.4 $\pm$ 71.5 vs. 259.9 $\pm$ 58.4 $\times$ 10^3/µL), and increased PDW (15.2 $\pm$ 2.7 vs. 12.8 $\pm$ 2.5 fL) were documented among women with PE [12]. At the mechanistic level, trimester-specific shifts in platelet indices have been linked to aspirin nonresponsiveness, with increased placental CD62P/CD42b expression observed in PE and persisting uncertainties at the maternal–

fetal interface [13]. Overall, the literature indicates clinical promise yet exposes heterogeneity in effect sizes, endpoints, and practice frameworks, which must be addressed for real-world use. Therefore, the aim of the present study was to evaluate the association between MPV and the risk of PE in a case-control cohort from the Peruvian National Maternal Perinatal Institute.

2. Materials and Methods

2.1 Study Design and Setting

We conducted an analytical, hospital-based case-control study at the Instituto Nacional Materno Perinatal (INMP), a national tertiary referral center for obstetric care in Lima, Peru. The study was conducted in the Obstetrics Hospitalization Service during 2024. The INMP receives high-complexity maternal cases from across the metropolitan area and the national referral network, ensuring access to standardized clinical records and laboratory information relevant to the exposure and outcome under study.

2.2 Population and Sample

Cases comprised pregnant women aged $\geq$18 years who developed PE during hospitalization, underwent prenatal care at the INMP in 2024 and had complete clinical records and a complete blood count (CBC) available. A prenatal control form from the referring facility (initiated before 14 gestational weeks) was required. Controls were normotensive pregnant women aged $\geq$18 years, with prenatal care at the INMP in 2024, complete records and CBC, with no current or previous PE. We excluded patients with comorbidities that could influence MPV (e.g., chronic hypertension, diabetes, or renal disease), those taking anticoagulants/antiplatelet agents, women with coagulation/hematologic disorders, and those with prior blood transfusion at the time of laboratory testing. Sampling was non-probabilistic by convenience, restricted to eligible inpatients meeting inclusion/exclusion criteria. Cases and controls were not individually matched. Controls were selected from the same institution and time frame and met identical eligibility criteria apart from PE status. Potential confounding was addressed through multivariable logistic regression including clinically relevant covariates.

Using Epidat 4.2 and INMP statistical yearbook parameters, assuming a 1:1 case-control ratio, we set: exposure among cases p1 = 0.46, exposure among controls p2 = 0.28, detectable OR = 3.06, 95% confidence, 80% power, and one control per case. This yielded a total sample of 224 participants (112 cases and 112 controls).

2.3 Data Collection

Data were abstracted from medical records and the standardized prenatal control form. The MPV was taken from the first CBC performed at $\geq$20 gestational weeks, and recorded in fL. All variables and codes followed the operational definitions used in the protocol (MPV, PE status, maternal age, parity, pre-/gestational obesity, prior PE, gestational age at onset of PE, prenatal care visits, and adequacy).

All CBCs were processed in the INMP central laboratory using a single automated hematology analyzer (Sysmex XN-1000, Sysmex Corporation, Kobe, Japan), following the institution's routine internal quality control program and participation in external proficiency testing. Peripheral blood samples were collected in K2-EDTA tubes (BD Vacutainer®, Cat. No. 367863; Becton, Dickinson and Company, Franklin Lakes, NJ, USA) and analyzed within a maximum of 2 hours after venipuncture, in accordance with the manufacturer's recommendations. Thus, all MPV measurements were obtained under standardized analytical and pre-analytical conditions within the same platform.

2.4 Variables

The primary outcome was PE, recorded as a binary indicator (case vs. control) based on the institutional protocol and aligned with international guidelines. PE was defined as new-onset hypertension after 20 gestational weeks (systolic blood pressure $\geq$140 mmHg and/or diastolic blood pressure $\geq$90 mmHg on at least two measurements $\geq$4 hours apart in a previously normotensive woman), together with either proteinuria ($\geq$300 mg/24 h, urine protein/creatinine ratio $\geq$0.3, or $\geq$1+ on dipstick) or, in the absence of proteinuria, any of the following: thrombocytopenia (platelet count $<$100,000/µL), renal insufficiency (serum creatinine $>$1.1 mg/dL or doubling of baseline), elevated liver transaminases ($\geq$2 times the upper limit of normal), pulmonary edema, or new-onset headache or visual disturbances not attributable to other causes.

The main exposure was MPV, expressed in fL and obtained from the first CBC at $\geq$20 gestational weeks [14]. MPV was analyzed as a continuous variable (primary specification; effect per 1 fL increase) and summarized descriptively as median (interquartile range, IQR).

Covariates defined a priori were: maternal age (18–20, 21–34, $>$35 years), parity (nulliparous or multiparous), pre-pregnancy obesity (no or yes), gestational obesity (no or yes), history of PE (no or yes), number of prenatal visits (count), and prenatal care adequacy ($<$6 vs. $\geq$6 visits). Unless otherwise specified, categorical variables are presented as n (%) and continuous variables as median (IQR).

Pre-pregnancy obesity was defined as a body mass index (BMI) $\geq$30.0 kg/m^2 calculated from pregestational weight documented at the first prenatal visit and measured height. Gestational obesity was defined as BMI $\geq$30.0 kg/m^2 at the time of the CBC ($\geq$20 gestational weeks), irrespective of pre-pregnancy status. Maternal age was categorized as 18–20, 21–34, and $>$35 years; parity as nulliparous versus multiparous.

2.5 Data Analysis

Analyses were performed in Stata 17.0 (StataCorp, College Station, TX, USA). Categorical variables were summarized as n (%) and continuous variables as median (IQR) given their non-normal distributions. Group comparisons used Pearson's chi-square (or Fisher's exact when appropriate) [15] for categorical variables and the Wilcoxon rank-sum test for continuous variables [16]. Variables with $p < 0.20$ in bivariate analysis were considered for the multivariable logistic regression to estimate adjusted ORs (aORs) with 95% CIs. MPV entered the model as a continuous predictor (per 1 fL). Receiver operating characteristic (ROC) analysis quantified discrimination (AUC with 95% CI), and the optimal cutoff was identified by Youden's index; sensitivity, specificity, and likelihood ratios were reported [17]. Variables exhibiting quasi-complete separation were not entered into multivariable models. Statistical significance was set at two-sided $p < 0.05$.

As a sensitivity analysis to address the potential impact of quasi-complete separation due to the low prevalence of prior PE, we fitted a penalized (Firth) logistic regression model including history of PE as an additional covariate. We report penalized aORs with 95% CIs to evaluate the robustness of the association between MPV and PE.

Given the potential time-dependent variation in MPV, we additionally adjusted the main multivariable model for gestational age at blood sampling. When available, we also evaluated models including systolic and diastolic blood pressure at admission as continuous covariates.

To assess internal validity, the AUC and Youden-derived MPV cutoff were evaluated using bootstrap resampling with 1000 iterations to obtain optimism-corrected estimates and 95% CIs. Model calibration was examined using the Hosmer–Lemeshow goodness-of-fit test and visually inspected with a calibration plot.

There were no missing data for MPV, PE status, or included covariates; all 224 women were retained in the analyses.

3. Results

3.1 Univariate Analysis

The study included 224 women (112 cases and 112 controls). Age distribution was 18–20 years in 12 (5.36%) cases, 21–34 years in 151 (67.41%) cases, and >35 years in 61 cases (27.23%). Most participants were multiparous (178/224, 79.46%). Pre-pregnancy obesity was present in 81 (36.16%) participants, and gestational obesity in 141 (62.95%) individuals. A prior history of PE was documented in 20 (8.93%) participants. Regarding antenatal care, 165 (73.66%) participants underwent adequate prenatal care (≥6 visits) and 59 (26.34%) underwent inadequate care (<6 visits). Continuous variables are summarized as median (IQR): MPV was 8.65 fL (8.10–9.40), and the number of prenatal care visits was 7 (5–10) (Table 1).

Table 1. Baseline characteristics of the study population.

Characteristics	Total n (%)
Age	
18–20 years	12 (5.36)
21–34 years	151 (67.41)
>35 years	61 (27.23)
Parity	
Nulliparous	46 (20.54)
Multiparous	178 (79.46)
Pre-pregnancy obesity	
No	143 (63.84)
Yes	81 (36.16)
Gestational obesity	
No	83 (37.05)
Yes	141 (62.95)
History of PE	
No	204 (91.07)
Yes	20 (8.93)
Prenatal care visits	7.00 (5.00–10.00) *
Prenatal care adequacy (categories)	
Inadequate (<6 visits)	59 (26.34)
Adequate (≥6 visits)	165 (73.66)
MPV (fL)	8.65 (8.10–9.40) *
Gestational age at onset of PE†	
<34 weeks	17 (15.20)
≥34 weeks	95 (84.80)
PE (case/control status)	
No (control)	112 (50.00)
Yes (case)	112 (50.00)

* Median (IQR). † Among women with PE (n = 112). PE, preeclampsia; MPV, mean platelet volume; IQR, interquartile range.

3.2 Bivariate Analysis

In bivariate analysis, PE cases had higher MPV than controls (median 9.05 vs. 8.40 fL; Wilcoxon $p < 0.001$). Gestational obesity was more frequent in PE cases than controls (70.54% vs. 55.36%; χ^2 $p = 0.019$), as was inadequate prenatal care (37.50% vs. 15.18%; χ^2 $p < 0.001$). Pre-pregnancy obesity also differed between groups (42.86% vs. 29.46%; χ^2 $p = 0.037$). Age categories (overall $p = 0.292$) and parity (overall $p = 0.098$) did not differ significantly. History of PE differed by Fisher's exact test due to a zero cell in controls (17.86% vs. 0%; $p < 0.001$) (Table 2).

3.3 Multivariate Analysis

Crude associations showed higher odds of PE per 1-fL increase in MPV (OR: 2.06; 95% CI: 1.51–2.82; $p < 0.001$), for gestational obesity (OR: 1.93; 95% CI: 1.11–3.35; $p = 0.019$), and for inadequate prenatal care (OR: 3.35; 95% CI: 1.76–6.37; $p < 0.001$); pre-pregnancy obesity was also associated with PE (OR: 1.80; 95% CI: 1.03–3.12; $p = 0.038$), while parity was not (OR: 0.57; 95% CI: 0.30–1.11; $p = 0.100$). In the multivariable model (including

Table 2. Bivariate analysis of maternal characteristics by PE status.

Characteristics	Control (n = 112), n (%)	Case (n = 112), n (%)	*p*-value
Age			0.292
18–20 years	5 (4.46)	7 (6.25)	
21–34 years	81 (72.32)	70 (62.50)	
>35 years	26 (23.22)	35 (31.25)	
Parity			0.098
Nulliparous	18 (16.07)	28 (25.00)	
Multiparous	94 (83.93)	84 (75.00)	
Pre-pregnancy obesity			0.037
No	79 (70.54)	64 (57.14)	
Yes	33 (29.46)	48 (42.86)	
Gestational obesity			0.019
No	50 (44.64)	33 (29.46)	
Yes	62 (55.36)	79 (70.54)	
History of PE †			<0.001
No	112 (100.00)	92 (82.14)	
Yes	0 (0.00)	20 (17.86)	
Prenatal care adequacy (categories)			<0.001
Inadequate (<6 visits)	17 (15.18)	42 (37.50)	
Adequate (≥6 visits)	95 (84.82)	70 (62.50)	
MPV (fL) *	8.40 (7.80–9.00)	9.05 (8.30–9.85)	<0.001

* Median (IQR); *p* from Wilcoxon rank-sum for MPV.

† Column percentages; χ^2 tests (Fisher's exact for history of PE).

Table 3. Crude and adjusted associations with PE (logistic regression).

Characteristics	Crude analysis			Adjusted analysis*		
	OR	95% CI	*p*-value	aOR	95% CI	*p*-value
MPV (per 1 fL)	2.06	1.51–2.82	<0.001	2.16	1.55–3.01	<0.001
Parity						
Nulliparous		Reference			Reference	
Multiparous	0.57	0.30–1.11	0.100	0.54	0.25–1.14	0.105
Pre-pregnancy obesity						
No		Reference			Reference	
Yes	1.80	1.03–3.12	0.038	1.45	0.78–2.98	0.315
Gestational obesity						
No		Reference			Reference	
Yes	1.93	1.11–3.35	0.019	2.43	1.17–5.26	0.039
Prenatal care adequacy						
Adequate (≥6 visits)		Reference			Reference	
Inadequate (<6 visits)	3.35	1.76–6.37	<0.001	3.71	1.27–7.55	0.006

* Adjusted for variables with crude $p < 0.20$: parity, pre-pregnancy obesity, gestational obesity, prenatal care adequacy (≥6 vs. <6), and MPV (per 1 fL). History of PE excluded due to quasi-complete separation. OR, odds ratio; aOR, adjusted odds ratio.

variables with crude $p < 0.20$), MPV remained independently associated with PE (aOR: 2.16; 95% CI: 1.55–3.01; $p < 0.001$), as did gestational obesity (aOR: 2.43; 95% CI: 1.17–5.26; $p = 0.039$) and inadequate prenatal care (aOR: 3.71; 95% CI: 1.27–7.55; $p = 0.006$). Parity was not significant after adjustment (aOR: 0.54; 95% CI: 0.25–1.14; $p = 0.105$), and pre-pregnancy obesity lost statistical significance (aOR: 1.45; 95% CI: 0.78–2.98; $p = 0.315$) (Table 3).

In a sensitivity analysis using penalized (Firth) logistic regression including prior PE, the association between higher MPV and PE remained robust (aOR: 2.20 per 1 fL; 95% CI: 1.57–3.09; $p < 0.001$). Gestational obesity (aOR: 2.80; 95% CI: 1.43–5.50; $p = 0.003$), inadequate prenatal care (aOR: 3.03; 95% CI: 1.46–6.30; $p = 0.003$), and prior PE (aOR: 46.45; 95% CI: 2.50–863.82; $p = 0.010$) also remained independently associated with PE.

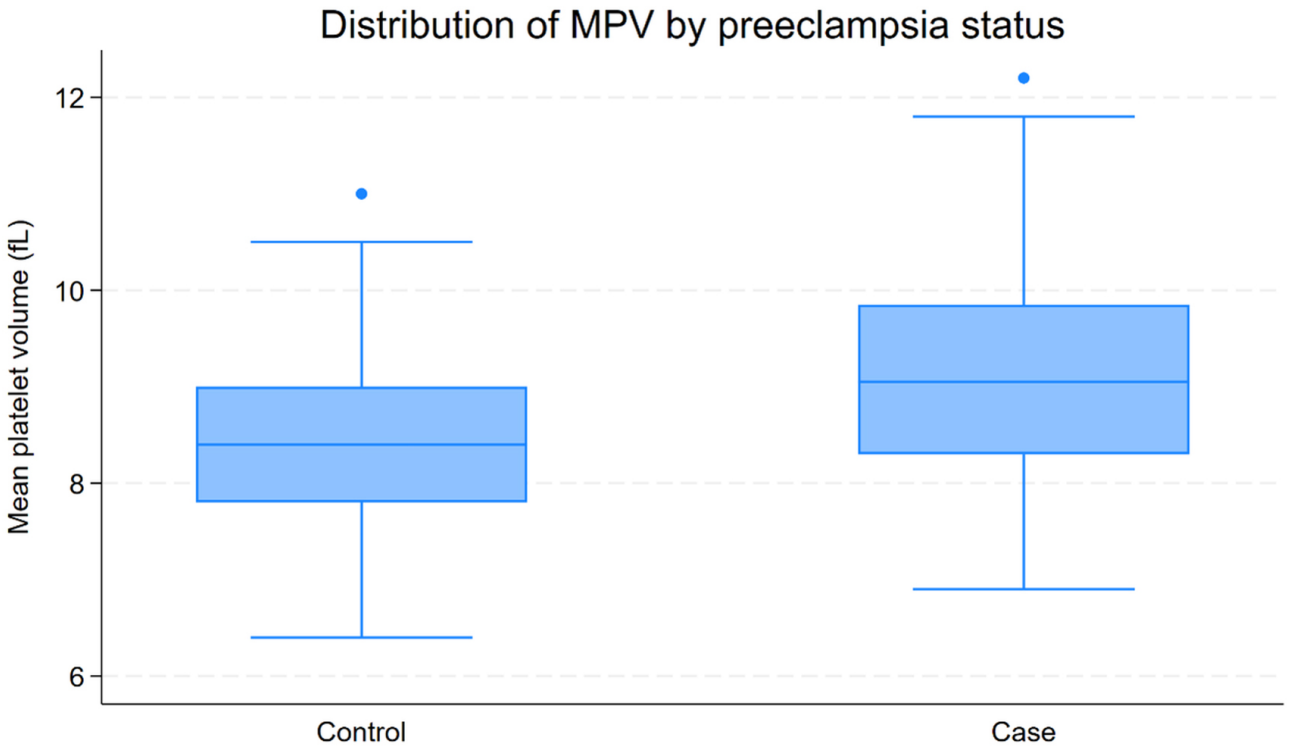

Fig. 1. Distribution of MPV by PE status. Boxplots of MPV (fL) in controls (n = 112) and cases (n = 112). Boxes depict the median and IQR; whiskers denote adjacent values, and points beyond the whiskers (if any) indicate outliers. MPV values were higher in cases than controls, consistent with the bivariate comparison.

Further adjustment for gestational age at blood sampling did not materially modify the association between MPV and PE (aOR: 2.16 per 1 fL; 95% CI: 1.56–2.99). Associations for gestational obesity (aOR: 2.87; 95% CI: 1.50–5.49) and inadequate prenatal care (aOR: 4.00; 95% CI: 1.71–9.34) remained consistent, indicating that the observed effects were not driven by timing of sampling.

In ROC analysis, MPV showed fair ability to discriminate PE, with an AUC of 0.686 (95% CI: 0.616–0.755). Using the Youden-derived threshold of 8.80 fL (classification rule: PE if MPV $\geq$8.80 fL), the test achieved 61.6% sensitivity and 71.4% specificity. At this cutoff, the positive likelihood ratio was 2.16 and the negative likelihood ratio was 0.54 (Table 4).

Bootstrap internal validation with 1000 resamples yielded an optimism-corrected AUC of 0.685 (95% CI: 0.616–0.755), confirming the stability of the discriminatory performance. The multivariable model showed acceptable calibration (Hosmer-Lemeshow $\chi^2 = 6.58$, df = 8, $p = 0.58$), and the calibration plot demonstrated good agreement between predicted and observed risks.

ROC analysis for MPV yielded an AUC of 0.686 (95% CI: 0.616–0.755). The optimal threshold by Youden's index was 8.80 fL, which classified cases as MPV $\geq$8.80 fL and provided 61.6% sensitivity and 71.4% specificity; the corresponding likelihood ratios were likelihood ratio (LR)+ 2.16 and LR– 0.54 (Fig. 1).

Table 4. Diagnostic performance of MPV for classifying PE.

Metric	Value
AUC (95% CI)	0.686 (0.616–0.755)
Optimal cutoff (fL)	8.80
Classification rule	PE if MPV $\geq$8.80 fL
Sensitivity, %	61.6
Specificity, %	71.4
LR+	2.16
LR–	0.54

AUC from ROC analysis. Optimal cutoff selected by Youden's index (sensitivity + specificity – 1). Likelihood ratios are calculated at the optimal cutoff. Positive/negative predictive values are not reported because this is a case-control design. AUC, area under the curve; ROC, receiver operating characteristic; LR, likelihood ratio.

The ROC curve shows moderate discrimination of MPV to classify PE (AUC: 0.686; 95% CI: 0.616–0.755). The Youden-optimal cutoff of 8.80 fL corresponds to 61.6% sensitivity and 71.4% specificity (Fig. 2).

4. Discussion

This case-control analysis indicates that MPV is higher in women with PE and remains independently associated with the condition after adjustment for maternal factors. Furthermore, gestational obesity and inadequate

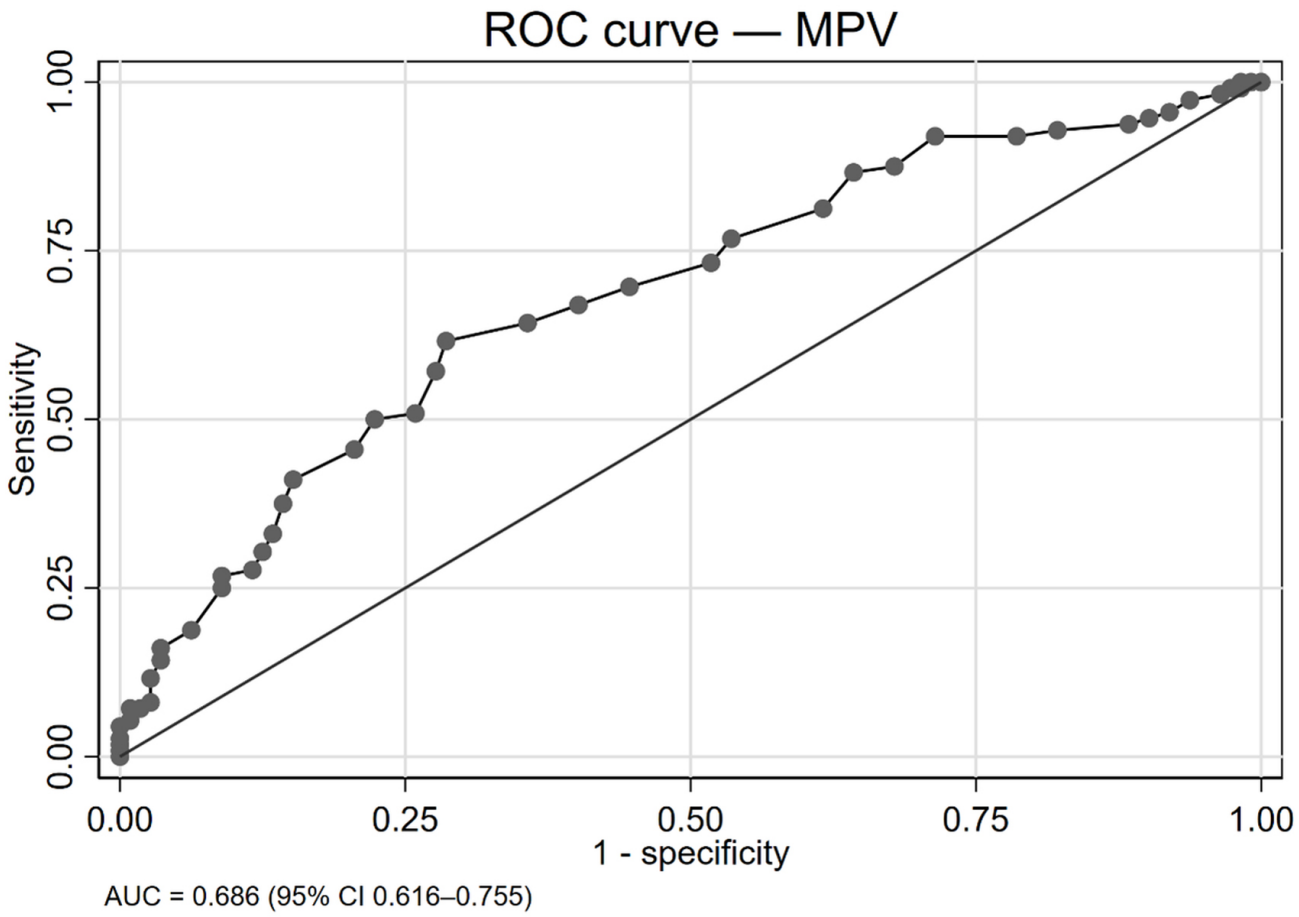

Fig. 2. ROC curve analysis for MPV. ROC curve for MPV for classifying PE (case vs. control). The AUC was 0.686 (95% CI: 0.616–0.755). The optimal cutoff by Youden's index was 8.80 fL, yielding 61.6% sensitivity and 71.4% specificity. Positive/negative predictive values are not reported because this is a case-control design.

prenatal care show independent associations, whereas parity and age do not. Prior PE differentiated groups in unadjusted comparisons but was excluded from multivariable modeling due to quasi-complete separation. As a single biomarker, MPV demonstrates moderate discriminatory capability with a clinically plausible threshold, supporting its value as part of a multivariable risk profile rather than an individual diagnostic test.

Our study indicates that higher MPV is independently associated with PE, in alignment with multiple reports. Li *et al*. [18] observed higher MPV in both mild and severe PE versus healthy pregnancies, as well as a significant univariate association with PE. Similarly, Bawore *et al*. [19] reported elevated MPV in PE with a clear severity gradient. Prospective data corroborate the pattern: Udeh *et al*. [20] found increased MPV among women who later developed PE at 14–18 gestational weeks and at end-of-follow-up, and Thakkar *et al*. [21] reported higher baseline MPV at 14–18 gestational weeks in early-onset PE. Severity-related increases were also confirmed in a prospective study with ROC verification [22]. However, Lin *et al*. [23] observed a partial divergence in timing, as found no group differences in the first trimester, with separation appearing later (e.g., 16–19 weeks), suggesting gestational-age dependence. Methodological factors (prospective vs. case-control design), PE phenotype (early/severe vs. mixed), and analytical variability in hematology platforms may underlie residual heterogeneity. Collectively, converging evidence supports MPV as a biologically plausible marker of platelet-activation in PE. MPV is most informative after the early first trimester and offers an accessible metric with potential to enhance risk stratification in antenatal care, particularly resource-limited settings.

In our settings, MPV alone offered only moderate discrimination for PE using a single cut-point rule. Performance varied across studies, with early-onset cohorts reporting strong accuracy. Udeh *et al*. [20] showed high AUC with a 9.4 fL threshold and near-perfect accuracy in severe early-onset PE at ~10.7 fL, and Thakkar *et al*. [21] reported similarly high AUC with a >10.2 fL threshold. By contrast, Sachan *et al*. [22] found moderate AUCs with a 9.05 fL cutoff, balancing modest sensitivity against higher specificity, and Lin *et al*.'s [23] preterm-PE prediction yielded lower AUCs, closer to moderate ranges. These discrepan-

cies likely reflect phenotype (early/severe disease amplifies signal), gestational-age at sampling (mid-second trimester yields clearer separation than first trimester), and inter-laboratory MPV calibration differences that shift optimal thresholds across platforms. Taken together, MPV's individual diagnostic value appears context-dependent, showing greatest utility in early or severe PE. Its effectiveness is maximized within multivariable, trimester-specific algorithms rather than as a solitary screening tool, a strategy with practical relevance for scalable, tiered PE risk assessment across diverse health systems.

We observed that gestational obesity was independently associated with PE. This aligns with studies showing higher mid-pregnancy adiposity among women with PE. Li *et al*. [18] reported a higher second-trimester BMI in PE alongside elevated systolic and diastolic pressures, and Thakkar *et al*. [21] found higher gestational BMI among PE cases while other baseline factors were comparable. Differences in effect sizes across reports likely reflect the timing and method of BMI assessment, PE phenotype mix (early vs. late onset), and residual confounding by hemodynamics or glycemic status that track with weight gain. From a policy perspective, these convergent findings support integrating routine mid-trimester weight surveillance and metabolic risk counseling into antenatal pathways to control preventable PE burden in resource-constrained settings.

In our analysis, the crude association between pregestational obesity and PE lost significance after multivariable adjustment. External literature largely documents higher baseline BMI among PE cases. Lin *et al*. [23] reported a significant pregestational BMI difference, but does not explicitly test for attenuation after adjustment. Moreover, one cohort restricted pre-pregnancy BMI ($\geq$30 kg/m^2 excluded), limiting evaluation of true baseline effects [18]. Attenuation in our context may arise from collinearity with gestational weight gain or blood pressure, measurement error in recalled pre-pregnancy weight, and phenotype heterogeneity. Clinically, this distinction underscores that dynamic gestational adiposity may be a more actionable target than static preconception BMI alone, informing antenatal counseling strategies with greatest translational impact in primary care.

Parity and maternal age were not associated with PE in our study. The literature is mixed but broadly consistent with a limited role of these demographics in certain cohorts. Lin *et al*. [23] observed older age associated with PE cases but a similar parity distribution without significance. Udeh *et al*. [20] observed no differences in age or gravidity between women who developed PE and those who did not. Thakkar *et al*. [21] also found no group differences among these covariates. Variability likely reflects sampling frames, age ranges, and the dominance of metabolic or placental factors over demographic predictors. Public-health programs should therefore prioritize modifiable cardiometabolic risks over demographic screening alone to improve PE prevention yield.

A prior history of PE differentiated groups in bivariate analysis but could not be retained in multivariable modeling due to quasi-complete separation. The external evidence supports a similar direction of effect. In fact, Lin *et al*. [23] reported a higher proportion of multiparouss with prior pregnancy-induced hypertension in the PE group, whereas Bawore *et al*. [19] mitigated this issue by excluding women with prior PE, precluding its analysis as a predictor. Such handling decisions reflect the well-known strength of recurrence risk and its analytic challenges. In practice, meticulous obstetric history-taking remains a low-cost, high-value measure to identify elevated PE risk early, guiding intensified surveillance in settings with limited health-system resources.

Our case series predominantly comprised later-onset presentations. In contrast, prospective cohorts quantifying early-onset PE report relatively low prevalence but provide detailed distributions of onset timing. Thakkar *et al*. [21] estimated an overall early-onset PE of 5.3%, with most cases clustering between 28–32 weeks, and Udeh *et al*. [20] reported a comparable early-onset frequency of 5.9% with severity stratification. Differences between our hospital-based series and prospective cohorts likely reflect referral patterns, triage thresholds, and regional epidemiology. Recognizing a primarily late-onset profile in our setting argues for scalable second-trimester risk assessment and timely escalation pathways, aligning limited resources to the period of greatest preventable morbidity.

Taken together, our findings support MPV as a pragmatic, laboratory-ready biomarker that captures platelet activation relevant to PE pathophysiology and can be leveraged within routine antenatal workflows. Because MPV is generated automatically by standard hematology analyzers at no additional cost, it offers a scalable tool for risk stratification in settings with limited resources and high disease burden. Clinically, MPV is unlikely to serve as a stand-alone test; rather, its value lies in trimester-specific algorithms that integrate maternal characteristics and blood pressure with hematologic and metabolic indices to identify women who may benefit from closer surveillance or preventive measures. By enabling earlier identification of at-risk pregnancies, particularly beyond the earliest weeks when predictive accuracy improves, MPV-informed pathways could help reduce preventable maternal and perinatal complications and align with global efforts to strengthen low-cost, point-of-care diagnostics in maternal health programs.

This study was conducted at a national tertiary referral center with standardized clinical records and laboratory workflows, enhancing internal validity and consistency of MPV assessment. The case-control design enabled efficient capture of clinically adjudicated PE and appropriate normotensive controls from the same source population and

time frame. We complemented group comparisons with multivariable modeling to isolate the independent contribution of MPV while accounting for key maternal factors. Diagnostic performance was reported transparently using ROC analysis and likelihood ratios at a pre-specified cut-point, with clear acknowledgment of the design-specific constraints (e.g., not estimating predictive values). Together, these features provide a coherent and clinically interpretable evaluation of MPV's association with PE and its potential utility as an accessible component of antenatal risk assessment.

Limitation

This study has several limitations. First, as a single-center hospital-based case-control study, it cannot estimate incidence or predictive values and may be subject to selection bias. Second, we did not perform stratified analyses according to PE severity (mild vs. severe) or timing of onset (early- vs. late-onset PE); and the number of severe and early-onset cases was insufficient to support stable subgroup models, which limits our ability to determine whether MPV behaves differently across phenotypes. Third, although all MPV values were generated in the same accredited laboratory using a single automated analyzer under standardized internal quality control procedures, MPV is inherently sensitive to instrument type, anticoagulant, and sample handling; therefore, the proposed 8.80 fL cutoff should be interpreted as platform-specific and requires calibration in other settings. Fourth, residual confounding cannot be excluded because we lacked inflammatory markers (e.g., C-reactive protein), additional platelet indices (e.g., platelet distribution width, platelet-large cell ratio), and socioeconomic indicators that might influence both MPV and PE risk. Moreover, because PE cases and controls were not matched on age, gestational age at sampling, or other baseline factors, residual confounding cannot be fully excluded despite multivariable adjustment. These constraints mean that our adjusted estimates may still partially capture unmeasured confounding. Future multicenter prospective cohorts with comprehensive phenotyping and extended biomarker and socioeconomic data are warranted to validate our findings and define robust, generalizable MPV-based risk thresholds.

5. Conclusions

In this hospital-based case-control study, higher MPV was independently associated with PE, and as a single biomarker, MPV showed moderate discrimination using a pragmatic cutoff. Gestational obesity and inadequate prenatal care were also associated with PE, whereas parity and age were not. Given that MPV is routinely generated by hematology analyzers at no additional cost, integrating MPV into trimester-specific, multivariable antenatal risk models could help prioritize surveillance and preventive measures, especially in resource-limited settings. Prospective, multicenter studies should establish analyzer- and trimester-specific thresholds and quantify absolute risk to guide implementation and decision-curve–based clinical use.

Availability of Data and Materials

The datasets generated and analyzed during the current study are not publicly available due to institutional and patient confidentiality policies, but are available from the corresponding author upon reasonable request.

Author Contributions

RJR-Y: Data Curation, Investigation, Methodology, Writing Original Draft, and Writing Review & Editing. GD-B: Data Curation, Investigation, Methodology, and Writing Review & Editing. MAA-H: Conceptualization, Methodology, Formal Analysis, Supervision, Validation, Writing Original Draft, and Writing Review & Editing. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Comité Institucional de Ética e Integridad Científica (CIEI) of Universidad Privada Norbert Wiener (Expediente 0995-2024; approval issued 12 November 2024). Informed consent was waived due to the retrospective nature of the study and the use of anonymized medical records without direct patient contact.

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Conflict of Interest

The authors declare no conflict of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT-3.5 in order to check spelling and grammar. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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