

Original Article

Predictive value of platelet indicators and glycolipid metabolism levels for disease severity and adverse pregnancy outcome in patients with early-onset preeclampsia

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Abstract: Objective: To evaluate the predictive value of platelet-related indicators and glycolipid metabolic markers for disease severity and adverse pregnancy outcomes in early-onset preeclampsia (EOPE). Methods: A retrospective analysis was performed on 198 EOPE patients (training cohort) and 56 patients for independent validation. Platelet count, mean platelet volume (MPV), platelet distribution width, triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting plasma glucose (FPG), and 2-hour postprandial plasma glucose (2hPG) were measured. Multivariate logistic regression and receiver operating characteristic curve analyses were used to identify independent factors and evaluate predictive performance. Results: Platelet count was significantly lower in the severe group than in the non-severe group (137.56 ± 29.31 vs. $168.14 \pm 35.22 \times 10^9/L$, $P < 0.001$), while MPV, PDW, and TG were higher, and HDL-C was lower. Delayed gestational week (OR=0.67) and elevated platelet count (OR=0.96) were protective factors against severe preeclampsia, whereas increased MPV (OR=2.28) and elevated TG (OR=1.61) were risk factors. The combined model for severe preeclampsia yielded an AUC of 0.89 (95% CI: 0.84-0.94). For adverse pregnancy outcomes, elevated platelet count (OR=0.97) was protective, while increased LDL-C (OR=3.32) and 2hPG (OR=2.12) were risk factors, with a combined model AUC of 0.88 (95% CI: 0.83-0.92). In the validation cohort, the two models achieved AUCs of 0.92 and 0.90, respectively, with good calibration and clinical applicability. Conclusion: Platelet indicators combined with glycolipid metabolism indicators exhibit favorable predictive value for disease severity and adverse pregnancy outcomes in EOPE, providing an objective basis for early risk stratification and individual management.

Keywords: Early-onset preeclampsia, platelet count, glycolipid metabolism, adverse pregnancy outcomes, predictive value

Introduction

Preeclampsia is a multisystem disease unique to pregnancy. It is defined by new-onset hypertension and proteinuria after 20 weeks of gestation and carries major risks for both mother and baby [1, 2]. Early onset preeclampsia (EOPE) is defined as preeclampsia diagnosed before 34 weeks of gestation [3]. This type is often associated with generalized endothelial damage, coagulation disorders, and metabolic disturbances [4]. The development of this condition can rapidly progress into severe preeclampsia or HELLP syndrome which dramatically increases the risks of preterm delivery,

fetal growth restriction, placental abruption, and maternal multiple organ failure [5]. Currently, EOPE assessment relies primarily on conventional markers such as blood pressure and proteinuria. Sensitive early predictive tools are still lacking for clinical use [6]. Identifying biomarkers that can reliably predict the severity of EOPE and its adverse pregnancy outcomes is important for this reason. The outcome will increase risk assessment, inform patient treatment plans, and ensure safer pregnancies and births.

Endothelial injury is mediated, in part, by platelets [7, 8]. Throughout the pathologic process

of preeclampsia, platelet count and function are altered [7, 8]. Research indicates that pre-eclamptic women have lower platelet counts, abnormal platelet distribution width, and produce larger mean platelet volume (MPV) [9]. The extent of these platelet changes correlates with disease severity, making these indices useful markers of disease activity [10]. Furthermore, impaired glucose and lipid metabolism characterized and contributed to preeclampsia [11, 12]. Affected women have high fasting glucose, insulin resistance, high triglycerides and high low density lipoprotein cholesterol (LDL-C). Metabolic dysfunctions further promote vascular endothelial damage and reduce placental perfusion [13].

In this study, we selected platelet indices (PLT, MPV, PDW) and glycolipid metabolism indicators (TC, TG, HDL-C, LDL-C, FPG, 2hPG) based on their established roles in the pathophysiology of preeclampsia, as well as their widespread availability and low cost in routine clinical practice. These indicators are routinely measured in obstetrics departments, making them highly feasible for developing a practical and generalizable predictive model for early risk stratification. We aim to elucidate the clinical significance of platelet and metabolic test combinations. The findings could facilitate early risk stratification, targeted intervention, and prognosis evaluation in EOPE, whilst refining clinical obstetric care.

Materials and methods

Study subjects

This was a single-center retrospective study. We enrolled patients diagnosed with EOPE who gave birth in the Department of Obstetrics at The Affiliated Shandong Provincial Maternity and Child Health Hospital of Qingdao University between June 2022 and June 2025. A total of 198 eligible patients were included and divided into a severe preeclampsia group (n=86) and a non-severe preeclampsia group (n=112) based on disease severity. To test the external reproducibility and generalizability of the combined models, we recruited an additional 56 patients with EOPE from the same center between July and December 2025 as an independent validation cohort. The same inclusion and exclusion criteria, data collection procedures, and indicator definitions were applied to

both the training and validation cohorts. This study was conducted in full compliance with the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the The Affiliated Shandong Provincial Maternity and Child Health Hospital of Qingdao University (Approval Number: SFYWZLP2026-009).

Inclusion and exclusion criteria

Inclusion criteria: (1) Met the diagnostic criteria for preeclampsia in the Guidelines for the Diagnosis and Treatment of Hypertensive Disorders of Pregnancy (2020) [14]; (2) Onset of disease at gestational age <34 weeks; (3) Singleton pregnancy; (4) Complete clinical data available.

Exclusion criteria: (1) Pre-pregnancy diagnosis of hypertension, diabetes mellitus, thyroid disease, autoimmune disease, or hematological disease; (2) Severe hepatic or renal insufficiency or malignant tumor; (3) Multiple pregnancy, fetal malformation, or chromosomal abnormality; (4) Use of anticoagulants, glucocorticoids, or other medications that may affect platelet or glycolipid metabolism before admission.

Data collection

Clinical data were retrospectively collected from the hospital's electronic medical record system. (1) General data: age, pre-pregnancy body mass index (BMI), gravidity, parity, gestational age at onset, systolic blood pressure (SBP), diastolic blood pressure (DBP), 24-hour urinary protein quantity. (2) Platelet-related indicators: Fasting venous blood samples were collected on admission, and PLT, MPV, PDW, and plateletcrit (PCT) were measured using an automated hematology analyzer. The MPV/PLT ratio was calculated. (3) Glycolipid metabolism indicators: Fasting venous blood was collected on admission. Total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), LDL-C, fasting plasma glucose (FPG), and 2-hour postprandial plasma glucose (2hPG) were measured using an automatic biochemistry analyzer. The TG/HDL-C ratio was calculated. (4) Pregnancy outcome indicators: pre-term birth, fetal growth restriction, neonatal intensive care unit (NICU) admission, placental abruption, postpartum hemorrhage, etc.

Outcome assessment

Disease severity was classified according to the Guidelines for the Diagnosis and Treatment of Hypertensive Disorders of Pregnancy (2020) [14]. Severe preeclampsia was defined by the presence of any of the following: SBP ≥ 160 mmHg or DBP ≥ 110 mmHg; 24-hour urinary protein ≥ 2.0 g or random urine protein $\geq$ (++); serum creatinine >106 $\mu\text{mol/L}$; PLT $<100 \times 10^9/\text{L}$; elevated liver enzymes (alanine aminotransferase [ALT] or aspartate aminotransferase [AST] >70 U/L); persistent upper abdominal pain; headache; or visual disturbances. Thus, patients were assigned to the severe group if they met any single criterion listed above, rather than requiring simultaneous blood pressure elevation and other organ involvement. This multi-indicator definition explains why mean blood pressure differences between the two groups may be relatively modest, as non-blood pressure criteria (e.g., significant proteinuria or thrombocytopenia) alone were sufficient for severe classification. Adverse pregnancy outcome was defined as the occurrence of any of the following: preterm birth (delivery at <34 weeks), fetal growth restriction, placental abruption, NICU admission, or postpartum hemorrhage.

Statistical analysis

All statistical analyses were performed using SPSS 26.0 software. Measured data were tested for normality using the Kolmogorov-Smirnov test. Normally distributed data were presented as mean $\pm$ standard deviation and compared between two groups using an independent-samples t-test. Non-normally distributed data were presented as median and interquartile range and compared using the Mann-Whitney U test. Enumerated data were presented as cases (percentage) and compared using the chi-square test or Fisher's exact test. Multivariate Logistic regression analysis (backward stepwise method) was used to identify the independent factors associated with severe preeclampsia as well as adverse pregnancy outcomes. Odds ratio and its 95% confidence interval (CI) were determined. Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive performance of single indicators and combined models. The AUC, sensitivity, specificity, accu-

racy and cut-off value of ART were calculated. The DeLong test was used for comparing AUCs. The Hosmer-Lemeshow test was used to examine the combined models fit. Decision curve analysis (DCA) was used to assess the models' clinical net benefits. Multiplicative and additive interaction analyses were performed to assess interactions between disease severity and each indicator. Additive interactions were evaluated using the relative excess risk due to interaction (RERI), attributable proportion (AP), and synergy index (SI). Given the multiple between-group comparisons, the False Discovery Rate (FDR) correction using the Benjamini-Hochberg method was applied to control for type I error. All tests were two-sided, and $P < 0.05$ was considered significant.

Results

Baseline characteristics and severity stratification

A total of 198 patients with EOPE were enrolled, including 112 in the non-severe group and 86 in the severe group. There were no significant differences in age, pre-pregnancy BMI, gravidity, or parity between the two groups ($P > 0.05$). Compared to the non-severe group, the severe group had an earlier gestational age at onset (27.77 ± 2.69 weeks vs. 29.38 ± 2.08 weeks, $P < 0.001$). SBP, DBP, and 24-hour urinary protein quantity were also significantly higher in the severe group (162.52 ± 10.31 mmHg vs. 158.28 ± 11.63 mmHg, $P = 0.008$; 99.19 ± 8.93 mmHg vs. 96.71 ± 7.66 mmHg, $P = 0.037$; 2.38 ± 0.72 g vs. 2.18 ± 0.59 g, $P = 0.024$) (Table 1).

Platelet and glycolipid metabolism indices in relation to disease severity

PLT were significantly lower in the severe group than in the non-severe group ($137.56 \pm 29.31 \times 10^9/\text{L}$ vs. $168.14 \pm 35.22 \times 10^9/\text{L}$, $P < 0.001$). In contrast, MPV, PDW, and MPV/PLT ratio were all significantly higher in the severe group (12.29 ± 1.21 fL vs. 11.43 ± 1.14 fL, $P < 0.001$; 17.54 ± 2.27 fL vs. 16.83 ± 2.14 fL, $P = 0.023$; 0.09 [0.08, 0.11] vs. 0.07 [0.06, 0.08], $P < 0.001$). For glycolipid metabolism, TG was significantly higher and HDL-C was significantly lower in the severe group (3.17 ± 0.89 mmol/L vs. 2.89 ± 0.75 mmol/L, $P = 0.017$; 1.26 ± 0.28 mmol/L vs. 1.43 ± 0.31 mmol/L, $P < 0.001$).

Platelets & glycolipids in early-onset preeclampsia

Table 1. Baseline characteristics of patients with early-onset preeclampsia stratified by disease severity

Variable	Total (n=198)	Non-severe (n=112)	Severe (n=86)	Statistic	P
Age (years)	30.21 ± 3.34	29.87 ± 3.49	30.65 ± 3.10	t=-1.65	0.101
Pre-pregnancy BMI (kg/m ²)	22.75 ± 2.65	22.52 ± 2.47	23.04 ± 2.85	t=-1.35	0.180
Gravidity	2.27 ± 1.14	2.24 ± 1.08	2.31 ± 1.21	t=-0.45	0.656
Parity, n (%)				χ ² =0.01	0.943
Primipara	65 (32.83)	37 (33.04)	28 (32.56)		
Multipara	133 (67.17)	75 (66.96)	58 (67.44)		
Onset gestational week (weeks)	28.68 ± 2.49	29.38 ± 2.08	27.77 ± 2.69	t=4.77	<0.001
SBP (mmHg)	160.13 ± 11.24	158.28 ± 11.63	162.52 ± 10.31	t=-2.67	0.008
DBP (mmHg)	97.78 ± 8.31	96.71 ± 7.66	99.19 ± 8.93	t=-2.10	0.037
24 h proteinuria (g)	2.27 ± 0.65	2.18 ± 0.59	2.38 ± 0.72	t=-2.27	0.024

Note: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2. Comparison of platelet and glucose-lipid indices between non-severe and severe groups

Variable	Total (n=198)	Non-severe (n=112)	Severe (n=86)	Statistic	P	FDR (BH)
PLT (× 10 ⁹ /L)	154.86 ± 36.07	168.14 ± 35.22	137.56 ± 29.31	t=6.51	<0.001	<0.001
MPV (fL)	11.80 ± 1.24	11.43 ± 1.14	12.29 ± 1.21	t=-5.17	<0.001	<0.001
PDW (fL)	17.14 ± 2.22	16.83 ± 2.14	17.54 ± 2.27	t=-2.29	0.023	0.040
Plateletcrit (%)	0.17 ± 0.05	0.18 ± 0.05	0.17 ± 0.05	t=1.91	0.058	0.086
MPV/PLT ratio, M (Q1, Q3)	0.08 (0.06, 0.09)	0.07 (0.06, 0.08)	0.09 (0.08, 0.11)	Z=-7.02	<0.001	<0.001
TC (mmol/L)	5.53 ± 1.09	5.42 ± 1.05	5.68 ± 1.12	t=-1.74	0.083	0.111
TG (mmol/L)	3.01 ± 0.82	2.89 ± 0.75	3.17 ± 0.89	t=-2.41	0.017	0.029
HDL-C (mmol/L)	1.36 ± 0.31	1.43 ± 0.31	1.26 ± 0.28	t=3.74	<0.001	<0.001
LDL-C (mmol/L)	3.12 ± 0.59	3.15 ± 0.58	3.08 ± 0.61	t=0.85	0.398	0.430
TG/HDL-C ratio, M (Q1, Q3)	2.24 (1.78, 2.78)	2.09 (1.60, 2.46)	2.59 (2.00, 3.16)	Z=-4.06	<0.001	<0.001
FPG (mmol/L)	5.05 ± 0.82	5.01 ± 0.90	5.11 ± 0.71	t=-0.79	0.430	0.430
2hPG (mmol/L)	6.76 ± 1.13	6.69 ± 1.11	6.85 ± 1.15	t=-1.03	0.304	0.365

Note: MPV, mean platelet volume; PLT, platelet count; PDW, platelet distribution width; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; FPG, fasting plasma glucose; 2hPG, 2-hour postprandial plasma glucose; M (Q1, Q3), median (interquartile range).

After FDR correction, all previously significant differences remained significant (all $q < 0.05$). No significant differences were found between the two groups in TC, LDL-C, FPG, or 2hPG ($P > 0.05$) (**Table 2**).

Incidence of adverse pregnancy outcome and between-group comparisons

The overall incidence of adverse pregnancy outcomes was 37.37% (74/198). The rate was significantly higher in the severe group than in the non-severe group (48.84% vs. 28.57%, $P = 0.004$). Specifically, preterm birth, fetal growth restriction, and NICU admission were all more common in the severe group (36.05% vs. 16.07%, $P = 0.001$; 22.09% vs. 9.82%, $P = 0.017$;

29.07% vs. 12.50%, $P = 0.004$) (**Table 3**). The adverse outcome group had lower PLT ($137.83 \pm 32.64 \times 10^9/L$ vs. $165.02 \pm 34.24 \times 10^9/L$, $P < 0.001$) and higher MPV/PLT ratio (0.08 [0.07, 0.10] vs. 0.07 [0.06, 0.09], $P < 0.001$) compared to the favorable outcome group. In terms of metabolism, LDL-C, FPG, and 2hPG were all significantly higher in the adverse outcome group (3.31 ± 0.61 mmol/L vs. 3.02 ± 0.55 mmol/L, $P < 0.001$; 5.21 ± 0.78 mmol/L vs. 4.95 ± 0.83 mmol/L, $P = 0.031$; 7.24 ± 0.96 mmol/L vs. 6.47 ± 1.13 mmol/L, $P < 0.001$). There were no significant differences in MPV, PDW, plateletcrit, TC, TG, HDL-C, or TG/HDL-C ratio between the two groups ($P > 0.05$). After FDR correction, all previously significant differences remained significant except for FPG

Table 3. Adverse pregnancy outcomes stratified by disease severity

Outcome	Total (n=198)	Non-severe (n=112)	Severe (n=86)	Statistic	P
Overall adverse outcomes	74 (37.37)	32 (28.57)	42 (48.84)	8.54	0.004
Preterm birth	49 (24.75)	18 (16.07)	31 (36.05)	10.42	0.001
Fetal growth restriction	30 (15.15)	11 (9.82)	19 (22.09)	5.70	0.017
NICU admission	39 (19.70)	14 (12.50)	25 (29.07)	8.44	0.004
Placental abruption	7 (3.54)	2 (1.79)	5 (5.81)	-	0.243a
Postpartum hemorrhage	15 (7.58)	6 (5.36)	9 (10.47)	1.81	0.178

Note: NICU, neonatal intensive care unit. A Fisher's exact test.

Table 4. Comparison of clinical indices between favorable and adverse pregnancy outcome groups

Variable	Total (n=198)	Favorable outcome (n=124)	Adverse outcome (n=74)	Statistic	P	FDR (BH)
PLT ($\times 10^9/L$)	154.86 $\pm$ 36.07	165.02 $\pm$ 34.24	137.83 $\pm$ 32.64	t=5.50	<0.001	<0.001
MPV (fL)	11.80 $\pm$ 1.24	11.77 $\pm$ 1.29	11.85 $\pm$ 1.16	t=-0.43	0.666	0.726
PDW (fL)	17.14 $\pm$ 2.22	17.01 $\pm$ 2.20	17.34 $\pm$ 2.24	t=-1.01	0.312	0.535
Plateletcrit (%)	0.17 $\pm$ 0.05	0.18 $\pm$ 0.05	0.17 $\pm$ 0.05	t=0.53	0.596	0.715
MPV/PLT ratio, M (Q1, Q3)	0.08 (0.06, 0.09)	0.07 (0.06, 0.09)	0.08 (0.07, 0.10)	Z=-4.78	<0.001	<0.001
TC (mmol/L)	5.53 $\pm$ 1.09	5.47 $\pm$ 1.02	5.64 $\pm$ 1.19	t=-1.04	0.300	0.535
TG (mmol/L)	3.01 $\pm$ 0.82	3.01 $\pm$ 0.79	3.02 $\pm$ 0.88	t=-0.02	0.982	0.982
HDL-C (mmol/L)	1.36 $\pm$ 0.31	1.37 $\pm$ 0.30	1.33 $\pm$ 0.32	t=0.86	0.393	0.589
LDL-C (mmol/L)	3.12 $\pm$ 0.59	3.02 $\pm$ 0.55	3.31 $\pm$ 0.61	t=-3.42	<0.001	0.002
TG/HDL-C ratio, M (Q1, Q3)	2.24 (1.78, 2.78)	2.20 (1.77, 2.74)	2.30 (1.78, 2.88)	Z=-0.53	0.593	0.715
FPG (mmol/L)	5.05 $\pm$ 0.82	4.95 $\pm$ 0.83	5.21 $\pm$ 0.78	t=-2.17	0.031	0.075
2hPG (mmol/L)	6.76 $\pm$ 1.13	6.47 $\pm$ 1.13	7.24 $\pm$ 0.96	t=-4.84	<0.001	<0.001

Note: MPV, mean platelet volume; PLT, platelet count; PDW, platelet distribution width; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; FPG, fasting plasma glucose; 2hPG, 2-hour postprandial plasma glucose; M (Q1, Q3), median (interquartile range).

(P=0.031, q=0.075), whereas all non-significant differences remained non-significant (all q>0.05) (**Table 4**).

Independent factors for severe preeclampsia and adverse pregnancy outcomes

The results of the single-factor Logistic regression analysis are shown in **Figures 1** and **2**. Multivariate Logistic regression was performed with severe preeclampsia as the dependent variable. Results showed that later gestational age at onset (OR=0.67, 95% CI: 0.55-0.80, P<0.001) and higher PLT (OR=0.96, 95% CI: 0.95-0.98, P<0.001) were protective factors. Larger MPV (OR=2.28, 95% CI: 1.57-3.31, P<0.001) and higher TG (OR=1.61, 95% CI: 1.01-2.56, P=0.045) were independent risk factors. Higher HDL-C was also associated with lower risk of severe preeclampsia (OR=0.14, 95% CI: 0.04-0.50, P=0.002) (**Table 5**). For adverse pregnancy outcomes, regression an-

alysis showed that later gestational age at onset (OR=0.60, 95% CI: 0.50-0.73, P<0.001) and higher PLT (OR=0.97, 95% CI: 0.96-0.98, P<0.001) were protective factors. Higher LDL-C (OR=3.32, 95% CI: 1.67-6.60, P<0.001) and higher 2hPG (OR=2.12, 95% CI: 1.43-3.13, P<0.001) were independent risk factors (**Table 6**). Neither multiplicative nor additive interaction analyses revealed significant interactions between disease severity and gestational age at onset, PLT, LDL-C, or 2hPG (P>0.05). Details are shown in **Tables S1** and **S2**.

Predictive performance and clinical stratification value of combined models

ROC curve analysis showed that PLT (AUC=0.74), MPV (AUC=0.70), gestational age at onset (AUC=0.69), and HDL-C (AUC=0.66) had moderate predictive value for severe preeclampsia, while TG had lower predictive power (AUC=0.59) (**Figure 3**). The combined model

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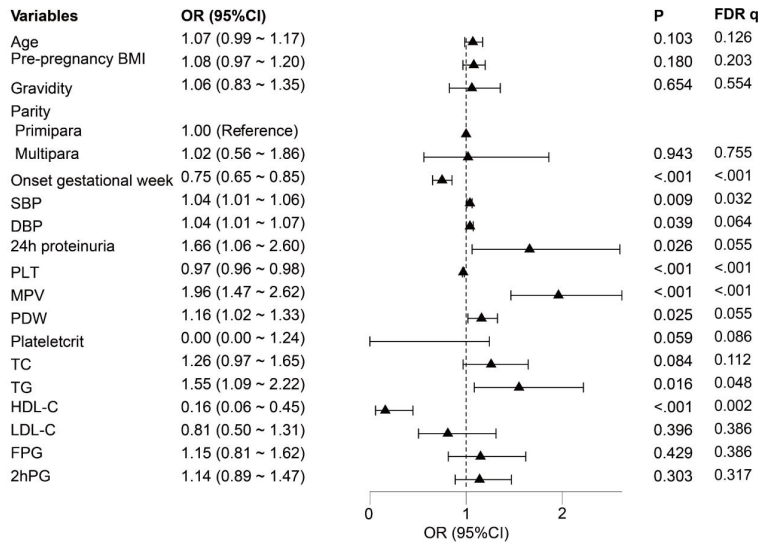


Figure 1. Forest plot of univariate Logistic regression analysis for severe preeclampsia in patients with early-onset preeclampsia. Note: OR, odds ratio; FDR, false discovery rate; CI, confidence interval; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PLT, platelet count; MPV, mean platelet volume; PDW, platelet distribution width; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; 2hPG, 2-hour postprandial plasma glucose. q values were calculated using the FDR Benjamini-Hochberg method.

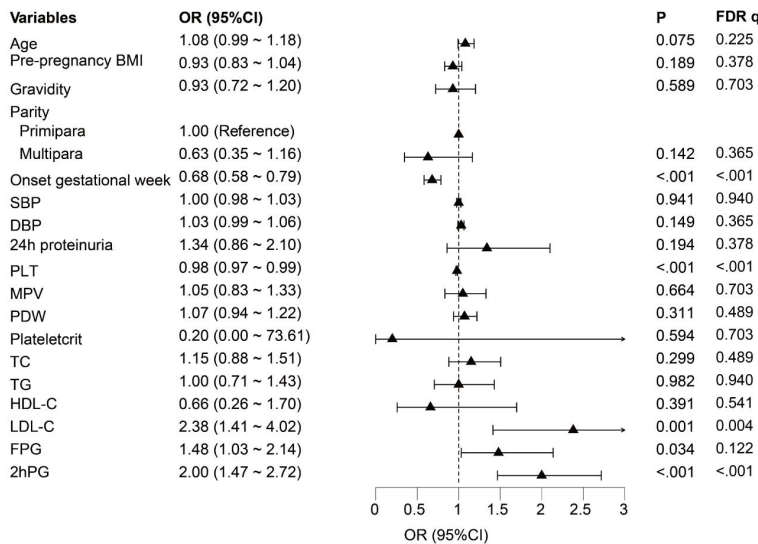


Figure 2. Forest plot of univariate Logistic regression analysis for adverse pregnancy outcomes in patients with early-onset preeclampsia. Note: OR, odds ratio; CI, confidence interval; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PLT, platelet count; MPV, mean platelet volume; PDW, platelet distribution width; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; 2hPG, 2-hour postprandial plasma glucose. q values were calculated using the False Discovery Rate (FDR) Benjamini-Hochberg method.

integrating gestational age at onset, PLT, MPV, TG, and HDL-C achieved an AUC of 0.89 (95% CI: 0.84-0.94), which was significantly better than any single indicator (DeLong test $P < 0.001$) (Table 7). The accuracy, sensitivity, and specificity of the combined model were 0.84, 0.80, and 0.87, respectively. For predicting adverse pregnancy outcomes, gestational age at onset (AUC=0.74), PLT (AUC=0.72), and 2hPG (AUC=0.69) showed moderate predictive value, while LDL-C had lower performance (AUC=0.63) (Figure 4). The combined model (gestational age at onset + PLT + LDL-C + 2hPG) reached an AUC of 0.88 (95% CI: 0.83-0.92), which was significantly superior to single indicators (DeLong test $P < 0.001$) (Table 8). The accuracy, sensitivity, and specificity were 0.81, 0.84, and 0.80, respectively.

Predictive performance of combined models in the independent validation cohort

To test generalizability, we enrolled 56 patients with EOPE as an independent validation cohort (32 severe cases; 21 adverse pregnancy outcomes) between July 2025 and December 2025. The two combined models from the training cohort were directly applied to this validation set. The model for severe preeclampsia (gestational age at onset + PLT + MPV + TG + HDL-C) yielded an AUC of 0.92 in the validation cohort, with sensitivity 0.81, specificity 0.92, and accuracy 0.86. This did not differ significantly from the training cohort (AUC=0.89; DeLong test $P=0.582$). The model for adverse pregnancy outcomes

Table 5. Multivariable logistic regression analysis for severe preeclampsia

Variable	β	S.E	Z	P	OR (95% CI)
Onset gestational week	-0.41	0.09	-4.37	<0.001	0.67 (0.55-0.80)
PLT	-0.04	0.01	-5.13	<0.001	0.96 (0.95-0.98)
MPV	0.82	0.19	4.32	<0.001	2.28 (1.57-3.31)
TG	0.47	0.24	2.00	0.045	1.61 (1.01-2.56)
HDL-C	-1.97	0.65	-3.03	0.002	0.14 (0.04-0.50)

Note: OR, odds ratio; CI, confidence interval; PLT, platelet count; MPV, mean platelet volume; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol.

Table 6. Multivariable logistic regression analysis for adverse pregnancy outcome

Variable	β	S.E	Z	P	OR (95% CI)
Onset gestational week	-0.51	0.10	-5.11	<0.001	0.60 (0.50-0.73)
PLT	-0.03	0.01	-4.54	<0.001	0.97 (0.96-0.98)
LDL-C	1.20	0.35	3.43	<0.001	3.32 (1.67-6.60)
2hPG	0.75	0.20	3.76	<0.001	2.12 (1.43-3.13)

Note: OR, odds ratio; CI, confidence interval; PLT, platelet count; LDL-C, low-density lipoprotein cholesterol; 2hPG, 2-hour post-prandial plasma glucose.

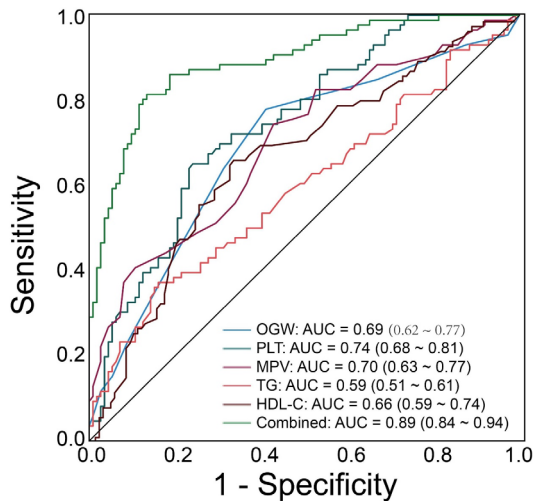


Figure 3. ROC curves of single indicators and the combined model for predicting severe preeclampsia. Note: ROC, receiver operating characteristic; OGW, onset gestational week; PLT, platelet count; MPV, mean platelet volume; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; AUC, area under the curve; CI, confidence interval.

(gestational age at onset + PLT + LDL-C + 2hPG) achieved an AUC of 0.90, sensitivity 0.86, specificity 0.85, and accuracy 0.86. Again, no significant difference was found compared to the training cohort (AUC=0.88; DeLong test $P=0.714$) (Table 9).

Model calibration and clinical applicability

In the training cohort, calibration curves showed good agreement between predicted and observed probabilities for both combined models (Hosmer-Lemeshow $P=0.083$ for severe preeclampsia; $P=0.340$ for adverse pregnancy outcomes) (Figure 5A, 5C). DCA confirmed that both models provided positive net benefit across reasonable threshold probabilities, supporting their clinical usefulness (Figure 5B, 5D). In the validation cohort, calibration remained excellent (Hosmer-Lemeshow $P=0.676$ and $P=0.768$, respectively) (Figure 6A, 6C). DCA also confirmed stable net benefit within clinically relevant ranges, demonstrating good reproducibility and potential for clinical translation (Figure 6B, 6D).

Discussion

This study included a training cohort of 198 patients and an independent validation cohort of 56 patients. We systematically analyzed the predictive value of platelet-related indicators and glycolipid metabolism levels for disease severity and adverse pregnancy outcomes in women with EOPE. We found that lower platelet count, larger MPV, higher TG, and lower HDL-C were independent factors for severe preeclampsia. Lower platelet count, higher LDL-C,

Table 7. Predictive performance of individual indicators and the combined model for severe pre-eclampsia

Indicator	AUC (95% CI)	Accuracy	Sensitivity	Specificity	Cut off	DeLong	
						Z	P
Onset gestational week	0.69 (0.62-0.77)	0.33	0.22	0.41	29.50	5.26	<0.001
PLT	0.74 (0.68-0.81)	0.29	0.35	0.24	143.10	4.30	<0.001
MPV	0.70 (0.63-0.77)	0.65	0.74	0.57	11.75	5.42	<0.001
TG	0.59 (0.51-0.67)	0.64	0.37	0.84	3.57	6.84	<0.001
HDL-C	0.66 (0.59-0.74)	0.34	0.33	0.35	1.37	5.75	<0.001
Combined model	0.89 (0.84-0.94)	0.84	0.80	0.87	-	Ref	Ref

Note: AUC, area under the curve; CI, confidence interval; PLT, platelet count; MPV, mean platelet volume; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol.

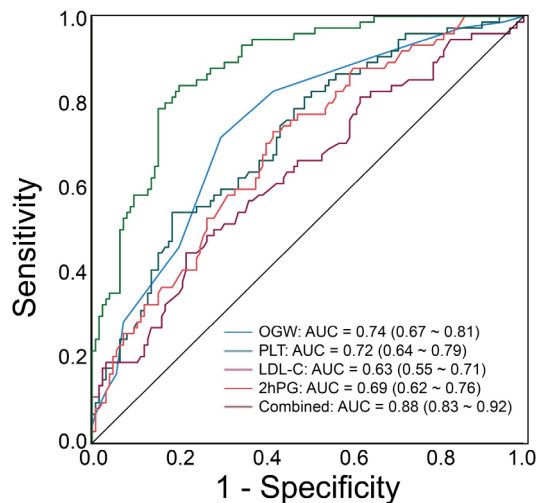


Figure 4. ROC curves of single indicators and the combined model for predicting adverse pregnancy outcome. Note: ROC, receiver operating characteristic; OGW, onset gestational week; PLT, platelet count; LDL-C, low-density lipoprotein cholesterol; 2hPG, 2-hour postprandial plasma glucose; AUC, area under the curve; CI, confidence interval.

and higher 2hPG were independent risk factors for adverse pregnancy outcomes. The combined models showed high predictive performance. The model for severe preeclampsia had an AUC of 0.89 in the training cohort and 0.92 in the validation cohort. The model for adverse pregnancy outcomes had an AUC of 0.88 in the training cohort and 0.90 in the validation cohort. Calibration curves and decision curve analysis further confirmed that these models were well calibrated and clinically applicable. The relatively small mean blood pressure differences between the severe and non-severe groups (SBP 4.24 mmHg, DBP 2.48 mmHg) are explained by the severity definition

used: according to the 2020 Chinese guideline, the presence of any single criterion (e.g., massive proteinuria, thrombocytopenia, or end-organ dysfunction) was sufficient for severe classification, irrespective of blood pressure level.

Abnormalities in platelet indices are considered pertinent in causation of preeclampsia [15]. The primary pathophysiological drivers of EOPE are inadequate placental perfusion and systemic endothelial injury. The release of large amounts of inflammatory mediators and oxidative stress products leads to excessive platelet activation, aggregation, and consumption [16, 17]. Our research found a significant decrease in platelet count among the severe group while observing a significant rise in MPV and PDW. Such findings have been reported before. Sachan et al. [18] reported that as severity of preeclampsia increased, MPV also increased in their prospective case-control study. That study reported a diagnostic accuracy of 74.6% for severe preeclampsia at a cutoff MPV of 9.05 fL (sensitivity 50%). In our study, there was a 2.28-fold higher risk of severe preeclampsia with increased MPV. This implies that MPV could serve as a sensitive marker of platelet activation. Li et al. showed that, after adjusting for age, gestational age, blood pressure, and BMI, PDW and P-LCR were effective predictors of preeclampsia [19]. According to them, MPV, PDW, and P-LCR were significantly higher in the preeclampsia group than healthy controls. Importantly, our combined predictive model included platelet count and MPV. Platelet count and MPV reflect platelet quantity and function, respectively. When combined, it may help explain the dramatic boost in predic-

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Table 8. Predictive performance of individual indicators and the combined model for adverse pregnancy outcome

Indicator	AUC (95% CI)	Accuracy	Sensitivity	Specificity	Cut off	DeLong	
						Z	P
Onset gestational week	0.74 (0.67-0.81)	0.29	0.28	0.30	28.50	4.06	<0.001
PLT	0.72 (0.64-0.79)	0.29	0.46	0.19	137.40	4.72	<0.001
LDL-C	0.63 (0.55-0.71)	0.66	0.45	0.78	3.50	5.82	<0.001
2hPG	0.69 (0.61-0.76)	0.64	0.73	0.58	6.78	5.11	<0.001
Combined model	0.88 (0.83-0.92)	0.81	0.84	0.80	-	Ref	Ref

Note: AUC, area under the curve; CI, confidence interval; PLT, platelet count; LDL-C, low-density lipoprotein cholesterol; 2hPG, 2-hour postprandial plasma glucose.

Table 9. Comparison of predictive performance between training and validation cohorts for severe preeclampsia and adverse pregnancy outcome

Outcome/Model	Cohort	n	AUC (95% CI)	Sensitivity	Specificity	Accuracy	P for DeLong*
Severe preeclampsia							
Combined model	Training	198	0.89 (0.84-0.94)	0.80	0.87	0.84	Reference
	Validation	56	0.92 (0.85-0.97)	0.81	0.92	0.86	0.582
Adverse pregnancy outcomes							
Combined model	Training	198	0.88 (0.83-0.92)	0.84	0.80	0.81	Reference
	Validation	56	0.90 (0.82-0.94)	0.86	0.85	0.86	0.714

*The DeLong test is used to compare the differences in AUC between the validation cohort and the training cohort; a *P* value greater than 0.05 indicates that there is no significant difference in model efficacy.

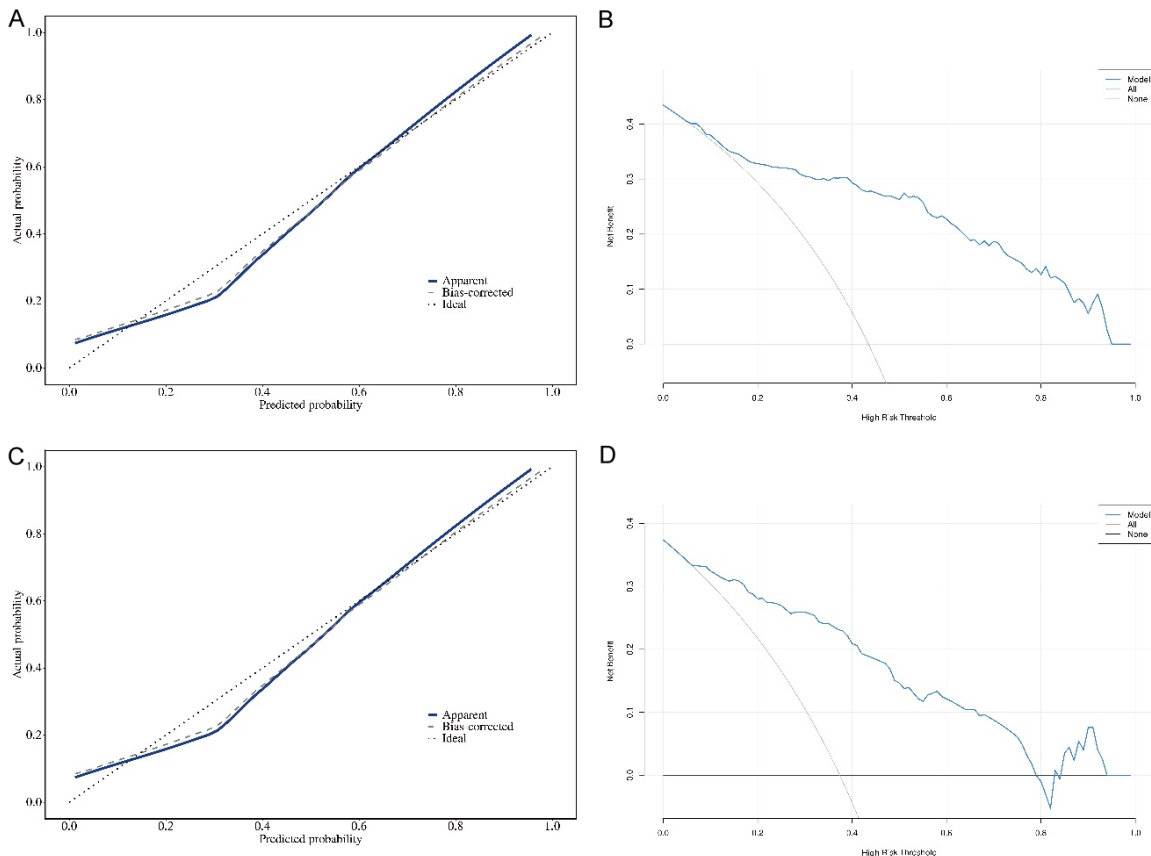


Figure 5. Calibration curves and decision curve analysis of the combined models in the training cohort. Note: (A) Calibration curve of the combined model for severe preeclampsia; (B) Decision curve analysis of the combined model for severe preeclampsia; (C) Calibration curve of the combined model for adverse pregnancy outcome; (D) Decision curve analysis of the combined model for adverse pregnancy outcome.

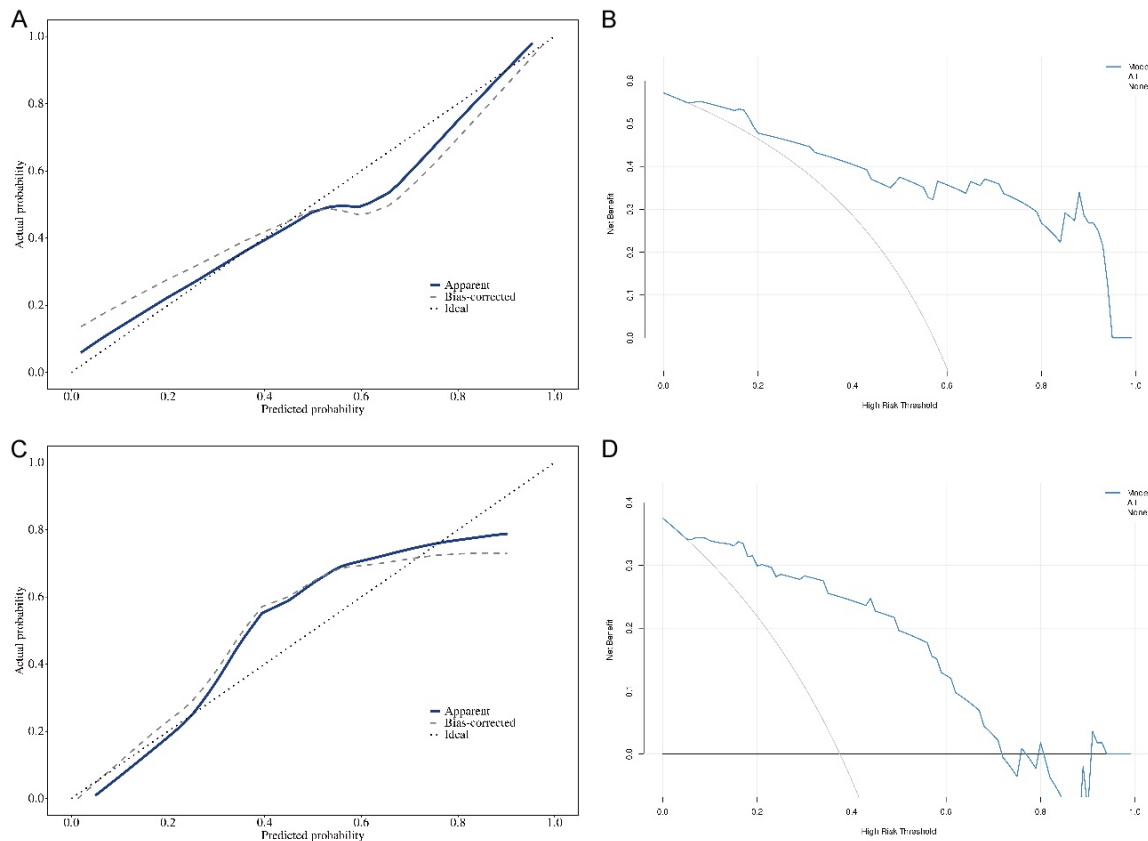


Figure 6. Calibration curves and decision curve analysis of the combined models in the validation cohort. Note: (A) Calibration curve of the combined model for severe preeclampsia; (B) Decision curve analysis of the combined model for severe preeclampsia; (C) Calibration curve of the combined model for adverse pregnancy outcome; (D) Decision curve analysis of the combined model for adverse pregnancy outcome.

tive performance. Our study showed that the AUC of platelet indices for severe preeclampsia (0.74) was slightly lower than the AUC (0.827) of MPV combined with thrombin time (TT) in the study by Zhang et al. [20]. Demographic differences may account for this variation. Early-onset cases are characterized by rapid progression and marked platelet fluctuation, which may reduce the discriminative power of any single indicator. Besides, Arslanoğlu et al. [21] stated that PDW and MPV are advantageous in diagnosis of preeclampsia but are alone insufficient to predict severity. This supports a multi-indicator combined model approach as strategy.

Glycolipid metabolic disorders are involved in the development and progression of EOPE and are closely related to disease severity and pregnancy outcome [22, 23]. Our study showed that the severe group displayed a typical pro-atherogenic lipid profile with high TG and low HDL-C, which matches well with the metabolic pattern of preeclampsia. Elevated TG levels are clinically associated with an increased inflammatory and oxidative stress burden, while reduced HDL-C is associated with diminished antioxidant and endothelial-protective capacity. Together, these lipid alterations represent characteristic features of the severe phenotype in EOPE [24, 25]. Our study confirmed that

higher TG and lower HDL-C were independent factors for severe preeclampsia. These findings are consistent with a meta-analysis by Qin et al., which identified elevated TG and reduced HDL-C as core lipid abnormalities in preeclampsia [26]. For predicting adverse pregnancy outcomes, we found that higher LDL-C and 2hPG were independent risk factors, while TC and FPG had a limited predictive value. This suggests that 2hPG and LDL-C are more sensitive clinical indicators than FPG or TC for capturing the metabolic disturbances associated with adverse pregnancy outcomes [27]. Huang et al. used lipidomics and confirmed that phospholipid metabolism disorders are a core feature of EOPE, supporting the specificity of lipid markers in disease assessment [28]. Elazab et al. supported the lipid-inflammation mechanism and found that TG, TC, and LDL-C were related to disease severity [29]. Furthermore, a longitudinal study by Konrad et al. reported that lipoprotein(a) levels were positively correlated with severity. In mild preeclampsia, lipoprotein(a) >40.5 mg/dL could predict progression to severe disease, highlighting the clinical value of dynamic lipid monitoring [30]. We also performed multiplicative and additive interaction analyses between disease severity and each indicator. We found no significant interactions between severity and gestational age at onset, platelet count, LDL-C, or 2hPG. This indicates that these indicators may affect disease progression independently rather than through synergistic amplification. These results provide statistical support for constructing multi-indicator combined predictive models [31, 32].

Our findings are easy to apply in clinical practice since indicators of platelet and glycolipid metabolism are routinely measured during obstetric care. They are very easy to test, low-cost, and have high reproducibility and hence can be used in all levels of medical institutions. According to a UK clinical document, a predictive model for severe preeclampsia (gestational age at onset, platelet count, MPV, TG, HDL-C) and a predictive model for adverse pregnancy outcome (gestational age at onset, platelet count, LDL-C, 2hPG) aids in the risk stratification of EOPE. According to experts in the field, these tests can enable clinicians to identify which cases are at high-risk for new pregnancy complications. This allows them to initiate in-

tervention in a timely manner, and optimise timing of delivery so that rates of preterm birth, fetal growth restriction and other adverse events can be reduced. Ultimately, the aim is to enhance safety for mother and baby.

This study has several limitations. First, it is a single-center retrospective study with a relatively homogeneous sample, which may lead to selection bias and limit generalizability. Second, we only used single-time measurements at admission, precluding evaluation of dynamic changes or longitudinal trajectories. Third, we did not include other potential biomarkers such as the homeostatic model assessment for insulin resistance (HOMA-IR) or apolipoproteins, inflammatory factors, or placental growth factor, so the completeness of the prediction model can be further improved. The absence of these more direct metabolic indicators limited our ability to explore the mechanistic pathways linking glycolipid metabolism to EOPE severity. Fourth, we did not conduct long-term postpartum follow-up of mothers and infants, so data on long-term metabolic and health outcomes are lacking. Future studies can be designed as multicenter, prospective cohorts with larger sample sizes and dynamic monitoring. Multi-omics indicators can be integrated to optimize predictive models. Long-term follow-up can be performed to fully clarify the impact of platelet and glycolipid metabolism indicators on short- and long-term maternal and infant outcomes. This will help provide higher-level clinical evidence for precise prevention and individualized management of EOPE.

Conclusion

Platelet indicators combined with glycolipid metabolism indices show good predictive value for both disease severity and adverse pregnancy outcome in patients with EOPE. The combined model including gestational age at onset, PLT, MPV, TG, and HDL-C can effectively predict severe preeclampsia, with an AUC of 0.89 in the training cohort and 0.92 in the validation cohort. The combined model consisting of gestational age at onset, PLT, LDL-C, and 2hPG shows reliable performance in predicting adverse pregnancy outcomes, with an AUC of 0.88 in the training cohort and 0.90 in the validation cohort. These routinely available

indicators, when combined in our validated models, demonstrate good generalizability. They can provide an objective evidence-based reference for early risk stratification and individualized clinical management of EOPE.

Disclosure of conflict of interest

None.

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References

- [1] Taageby Nielsen S, Luo J, Tybjaerg-Hansen A, Iversen K, Bundgaard H, Qvist Thomassen J and Frikke-Schmidt R. Preeclampsia, gestational hypertension, and cardiovascular disease risk: a genetic epidemiological study. *Eur Heart J* 2025; 46: 4316-4325.
- [2] Zhang Y, Bao L, Li KZ, Wang BH, He BY and Yin DM. The impact and mechanisms of preeclampsia on offspring neurodevelopment. *Cell Biosci* 2026; 16: 32.
- [3] Karioti M, Katsi V and Tsioufis C. Late vs. early preeclampsia. *Int J Mol Sci* 2025; 26: 11091.
- [4] Kefiyalew D, Aragaw A, Bula K and Etana G. Prevalence and maternal-fetal outcomes of early-onset versus late-onset of preeclampsia: a prospective cohort study at Wallaga university compressive specialized hospital. *BMC Pregnancy Childbirth* 2026; 26: 245.
- [5] Takeda J, Tachibana D, Itakura A, Takagi K, Nakami S, Mano H, Kobayashi T, Kanayama N, Sameshima H, Morikawa M, Sago H, Adachi T, Ohkuchi A, Takeda S, Masuyama H, Seki H and Saito S; KOUNO-TORI Study Group. Randomized study of antithrombin in early-onset preeclampsia: KOUNO-TORI study. *Hypertension*. 2026; 83: e25431.
- [6] Pangesti WD, Sasongko EPS, Pribadi A and Hil-manto D. Evaluation of risk factor screening using the ministry of health's scoring system for the incidence of early-onset preeclampsia in primary health service. *Int J Womens Health* 2025; 17: 4815-4822.
- [7] Kazemi N, Bordbar A, Bavarsad SS, Ghasemi P, Bakhshi M and Rezaeeyan H. Molecular insights into the relationship between platelet activation and endothelial dysfunction: molecular approaches and clinical practice. *Mol Biotechnol* 2024; 66: 932-947.
- [8] Woldeamanuel GG, Tlaye KG, Wang X, Nguyen-Hoang L, Zhou Q, Wang Y, Leung BW, Wang Y, Poon LC and Wang CC. Platelets in preeclampsia: an observational study of indices associated with aspirin nonresponsiveness, activation and transcriptional landscape. *BMC Med* 2025; 23: 346.
- [9] Thakkar D, Shihora J, Gandhi R, Parmar R and 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: 327-333.
- [10] Agarwal M, Singh S, Bhushan D, Ahmad S, Sinha R and Sinha S. Role of platelet-related parameters in prediction of development and severity of preeclampsia (PE): an observational prospective cohort study. *SAGE Open Med* 2025; 13: 20503121251390611.
- [11] Li Q, Zhao C, Liu M, Li M, Zhang Y and Yue C. Association between triglyceride-glucose index in early pregnancy and risk of preeclampsia: a multicenter retrospective cohort study. *Lipids Health Dis* 2025; 24: 152.
- [12] Li S, Zhu J, Zhao Y, An P, Zhao H and Xiong Y. Metabolic disorder of nutrients-an emerging field in the pathogenesis of preeclampsia. *Front Nutr* 2025; 12: 1560610.
- [13] Wang X, Zhang E, Tian Z, Zhao R, Huang K, Gao S, Su S, Xie S, Liu J, Luan Y, Zhang Y, Zhang Z, Yan Y, Yue W, Yin C and Liu R. The association between dyslipidaemia in the first trimester and adverse pregnancy outcomes in pregnant women with subclinical hypothyroidism: a cohort study. *Lipids Health Dis* 2024; 23: 13.
- [14] The Pregnancy Hypertensive Disorders Group of the Obstetrics and Gynecology Branch of the Chinese Medical Association. Guidelines for the diagnosis and treatment of pregnancy hypertensive disorders (2020). *Chin J Obstet Gynecol* 2020, 55: 227-238.
- [15] Er I, Sentürk S, Arpa M and Kuruca N. The thrombopoietic signature of preeclampsia: diagnostic and monitoring insights from the immature platelet fraction. *Diagnostics (Basel)* 2025; 16: 44.
- [16] Singh K, Lia M, Prakasan Sheeja A, Federbusch M, Gupta A, Elwakiel A, Köhler M, Isermann B, Stepan H and Kohli S. Increased platelet activation and thrombo-inflammation in early and late-onset preeclampsia. *Res Pract Thromb Haemost* 2025; 9: 102956.
- [17] Kong H, Ma X, Wang F, Su Y, Chang Y and Xin H. Htra4 promotes vascular endothelial cell injury and is associated with the early-onset of preeclampsia. *Sci Rep* 2025; 15: 11752.
- [18] Sachan R, Patel ML, Vandana, Sachan P and Shyam R. Role of platelet count and mean platelet volume and red cell distribution width

- in the prediction of preeclampsia in early pregnancy. *J Family Med Prim Care* 2021; 10: 838-843.
- [19] Li P, Chen H, Zhang X, Wang J, Li Y, Wang Y, Wang F and Man D. Potential predictive value of platelet parameters in preeclampsia. *Womens Health Rep (New Rochelle)* 2024; 5: 453-460.
- [20] Zhang J, Liu J and Wang P. The platelet and coagulation function parameters in late pregnancy are associated with preeclampsia and its severity: a single-center retrospective study. *PeerJ* 2025; 13: e19916.
- [21] Arslanoğlu T, Kurt-Bilirer K, Çallıoğlu N, Aydın-Şenel S, Turan-Bakırcı I, Koç-Erol İN, Kar E, Bayram Z and Polat I. Can platelet activation markers predict preeclampsia and/or its severity? *Cir Cir* 2024; 92: 52-58.
- [22] Skytte HN, Christensen JJ, Gunnes N, Holven KB, Lekva T, Henriksen T, Michelsen TM and Roland MCP. Metabolic profiling of pregnancies complicated by preeclampsia: a longitudinal study. *Acta Obstet Gynecol Scand* 2023; 102: 334-343.
- [23] Li R, Zhou C, Ye K, Chen H and Peng M. Identification of genes involved in energy metabolism in preeclampsia and discovery of early biomarkers. *Front Immunol* 2025; 16: 1496046.
- [24] Guan P, Su Y, Wang M, Ye X, Hang Y, Li D, Zhang P and Hu W. A wide range of triglyceride levels is sufficient for fetal growth at gestational weeks 12-16, but higher triglyceride levels are associated with gestational hypertension. *Pregnancy Hypertens* 2022; 27: 74-80.
- [25] Stadler JT, van Poppel MNM, Christoffersen C, Hill D, Wadsack C, Simmons D, Desoye G and Marsche G; Dali Core Investigator Group. Gestational hypertension and high-density lipoprotein function: an explorative study in overweight/obese women of the DALI cohort. *Antioxidants (Basel)* 2022; 12: 68.
- [26] Qin X, Ai F, Zhou Q, Zhang Y and Yan X. Preeclampsia, gestational hypertension, and lipid levels during pregnancy: a systematic review and meta-analysis. *Arch Gynecol Obstet* 2025; 312: 385-402.
- [27] Guo J, Qiu H, Wang J, Liu X, Chen S and Li B. Correlation between lipid metabolism levels and pregnancy outcomes. *Front Med (Lausanne)* 2025; 12: 1530525.
- [28] Huang Y, Sun Q, Zhou B, Peng Y, Li J, Li C, Xia Q, Meng L, Shan C and Long W. Lipidomic signatures in patients with early-onset and late-onset Preeclampsia. *Metabolomics* 2024; 20: 65.
- [29] Elazab R, Alkhiary M, Bedairi M and Wageh A. Simultaneous use of tumor necrosis factor, lipid profile, and β -hCG as markers of severity of preeclampsia. *J Obstet Gynaecol India* 2022; 72 Suppl 1: 83-88.
- [30] Konrad E, Güralp O, Shaalan W, Elzarkaa AA, Moftah R, Alemam D, Malik E and Soliman AA. Correlation of elevated levels of lipoprotein(a), high-density lipoprotein and low-density lipoprotein with severity of preeclampsia: a prospective longitudinal study. *J Obstet Gynaecol* 2020; 40: 53-58.
- [31] Lin SS, Wang CR, Wei DM, Lu JH, Chen XJ, Chen QZ, Xia XY, He JR and Qiu X. Incremental predictive value of platelet parameters for preeclampsia: results from a large prospective cohort study. *BMC Pregnancy Childbirth* 2023; 23: 387.
- [32] Huang M, Xie W, Kang L, Luo D, He Q and Yang X. Development and validation of prediction model for pre-eclampsia-related maternal adverse outcome: retrospective cohort study. *Ultrasound Obstet Gynecol* 2025; 66: 762-772.

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Table S1. Multiplicative interaction between disease severity and indicators for adverse pregnancy outcome

Variable	OR01 (mild + high value)	OR10 (severe + low value)	OR11 (severe + high value)	Multiplicative interaction OR (95% CI)	P
Onset gestational week	0.238 (0.100-0.568)	1.763 (0.826-3.763)	0.140 (0.029-0.677)	0.333 (0.057-1.962)	0.2244
PLT	0.294 (0.125-0.694)	1.255 (0.555-2.838)	0.840 (0.298-2.372)	2.277 (0.631-8.209)	0.2086
LDL-C	3.667 (1.471-9.140)	4.442 (1.722-11.460)	6.417 (2.404-17.127)	0.394 (0.113-1.374)	0.1440
2hPG	3.639 (1.494-8.861)	2.798 (1.082-7.232)	8.812 (3.429-22.646)	0.865 (0.247-3.026)	0.8207

Note: LDL-C, low-density lipoprotein cholesterol; 2hPG, 2-hour postprandial plasma glucose; OR, odds ratio; CI, confidence interval. OR01, OR10, and OR11 represent the odds ratios for mild + high value, severe + low value, and severe + high value, respectively, using mild + low value as the reference group.

Table S2. Additive interaction between disease severity and indicators for adverse pregnancy outcome

Variable	RERI (95% CI)	AP	SI	OR01	OR10	OR11
Onset gestational week	-0.8611 (-2.0662-0.3440)	-6.1495	-767.2726	0.238	1.763	0.140
PLT	0.2913 (-0.6518-1.2345)	0.3467	0.3541	0.294	1.255	0.840
LDL-C	-0.6924 (-7.3624-5.9776)	-0.1079	0.8867	3.667	4.442	6.417
2hPG	3.3753 (-5.7852-12.5359)	0.3830	1.7608	3.639	2.798	8.812

Note: RERI, relative excess risk due to interaction; AP, attributable proportion; SI, synergy index; LDL-C, low-density lipoprotein cholesterol; 2hPG, 2-hour postprandial plasma glucose; OR, odds ratio. RERI >0 with a 95% CI excluding 0 indicates positive additive interaction (synergy). OR01, OR10, and OR11 represent the odds ratios for mild + high value, severe + low value, and severe + high value, respectively, using mild + low value as the reference group.