Am J Transl Res 2025;17(4):3074-3084
www.ajtr.org /ISSN:1943-8141/AJTR0162312

Original Article

Combined assessment of placental growth factor, uterine artery pulsation index, and mean arterial pressure for predicting preeclampsia

Xiaozhi Wu, Zhaoyu Xu

Department of Obstetrics and Gynecology, The Third Affiliated Hospital of Zunyi Medical University (The First People's Hospital of Zunyi), Zunyi 563000, Guizhou, China

Received November 27, 2024; Accepted April 3, 2025; Epub April 15, 2025; Published April 30, 2025

Abstract: Objective: To evaluate the clinical significance of combined detection of placental growth factor (PLGF), uterine artery pulse index (UTPI), and mean arterial pressure (MAP) in predicting preeclampsia (PE). Methods: A total of 332 pregnant women who underwent regular prenatal check-ups at The Third Affiliated Hospital of Zunyi Medical University (The First People's Hospital of Zunyi) from January 2022 to December 2023 were retrospectively included in this study. Medical histories and laboratory examination data were collected. The participants were divided into a PE group and a normal group based on the occurrence of PE. Clinical data, including MAP, UTPI, and PLGF were recorded between 11 and 13^{+6} weeks of pregnancy. A multivariate logistic regression analysis was performed with a significance level of $P<0.05$ to construct a predictive model for PE. The diagnostic efficacy of the combined MAP + UTPI + PLGF model for early pregnancy PE was assessed using ROC curves. In addition, 182 pregnant women who underwent regular prenatal check-ups in our hospital between February 1, 2023, and December 31, 2024, were selected for external verification. Results: Multivariate logistic regression analysis identified age, body mass index (BMI), pregnancy associated plasma protein-A (PAPP-A), MAP, UTPI, and PLGF as independent predictors of early pregnancy PE (all $P<0.05$). The AUC values for age, BMI, PAPP-A, MAP, UTPI, and PLGF were 0.660, 0.669, 0.749, 0.869, 0.781, and 0.943, respectively. The AUC of the combined MAP + UTPI + PLGF model was 0.990 (95% CI: 0.938-0.998), with specificity and sensitivity values of 83.98% and 98.80% respectively. Internal validation showed a mean absolute error (MAE) of 0.012, and the consistency index was 0.99 (95% CI: 0.983-0.997). The AUC for external validation of the prediction model was 0.975 (95% CI 0.955-0.995, $P<0.001$). Bootstrap analysis (1000 repetitions) using the Hosmer-Lemeshow test showed a good model fit ($\chi^2=4.039$, $P=0.854$), with the slope of the calibration curve close to 1. Conclusion: Age, BMI, PAPP-A, MAP, UTPI, and PLGF were all effective predictors for early PE. Furthermore, the combined detection of high-risk factors (MAP, UTPI, PLGF) has a high predictive value for PE early in pregnancy.

Keywords: Preeclampsia, placental growth factor, uterine artery pulsation index, mean arterial pressure, prediction effect

Introduction

Preeclampsia (PE) is a pregnancy-specific disorder affecting approximately 2%-8% of pregnant women [1, 2]. It is primarily characterized by hypertension and proteinuria, which can result in organ damage, affecting the heart, brain, liver, kidney, and placenta. This condition poses significant risks to maternal health. For the fetus, there is an increased risk of poor placental function, abnormal fetal development, and adverse pregnancy outcomes, such as stillbirth or fetal demise [3-5]. Early-onset severe PE particularly dangerous, threatening the lives of both the pregnant women and fetuses. Therefore, early prevention and treatment are crucial to reducing maternal and infant mortality rates.

The pathogenesis of PE is not fully elucidated, but accumulating evidence suggests that abnormal levels of angiogenic factors and coagulation dysfunction play a central role. Placental growth factor (PLGF), a pro-angiogenic factor synthesized by syncytiotrophoblast cells and highly homologous to vascular endothelial

https://doi.org/10.62347/JHZE8553

growth factor, has been shown to be closely related to the occurrence and progression of PE [6]. Screening for PE at 11-13^{+6} weeks of gestation using maternal characteristics and biomarkers has demonstrated a high detection rate with low false positive rates [5, 7]. In the past, early termination of pregnancy was often employed to prevent disease progression. However, this approach adversely affected perinatal outcomes, increasing the incidence of respiratory distress syndrome, hypoxic encephalopathy, and mortality risk. The goal in treating early-onset severe PE is to prolong gestation, improve neonatal outcomes, and ensure maternal safety. Low circulating PLGF levels have been shown to have high sensitivity and negative predictive value for PE [8, 9].

For effective prediction of PE, it is recommended to combine multiple indicators, particularly focusing on high-risk factors. The International Federation of Gynecology and Obstetrics (FIGO) advises that women with singleton pregnancies undergo preterm PE screening during the first trimester, incorporating maternal risk factors and biological indicators. The optimal combined screening tests include maternal risk factors, mean arterial pressure (MAP), uterine artery pulsatility index (UTPI), and PLGF [10-12]. Currently, PE prediction mainly relies on the high-risk factors from medical history and biomarkers that are not routinely obtainable in clinical practice. There is still a lack of efficient, accessible, and low-cost prediction schemes. Additionally, the single indicators often lack the specificity or sensitivity needed for comprehensive early pregnancy PE risk assessment. This study aims to explore the predictive value of PLGF, MAP, and UTPI in combination with maternal risk factors for PE of early pregnancy.

Materials and methods

Patient characteristics

This retrospective study included 332 pregnant women who underwent routine antenatal check-ups at The Third Affiliated Hospital of Zunyi Medical University (The First People's Hospital of Zunyi) from January 2022 to December 2023. Inclusion criteria: (1) Singleton pregnancy; (2) Fetal nuchal translucency ultrasound, UTPI, and early Down's syndrome screening were conducted between 11 and 13^{+6} weeks of pregnancy. Exclusion criteria: (1) Fetal chromosomal aneuploidy; (2) Abortion or stillbirth before 24 weeks of pregnancy; (3) Severe fetal abnormalities. Based on the diagnostic criteria for PE in the *Guidelines for the Diagnosis and Treatment of Hypertensive Diseases in Pregnancy (2020)* [13], pregnant women were classified into two groups: the preeclampsia group (including both preeclampsia and chronic hypertension complicated by preeclampsia) and the normal group. This study was reviewed and approved by the Medical Ethics Committee of The Third Affiliated Hospital of Zunyi Medical University (The First People's Hospital of Zunyi).

Methods

A review of relevant literature on PE prediction was conducted, and clinical data were collected from patient records. The collected data included age, pre-pregnancy body mass index (BMI), maternal history (e.g., gestational hypertension, gestational diabetes), systolic blood pressure (SBP), diastolic blood pressure (SDP), method of conception, previous medical history (e.g., diabetes, chronic hypertension, anticardiolipin antibody syndrome, systemic lupus erythematosus), and family history of preecl-ampsia. Laboratory data included fasting blood glucose, blood albumin, prothrombin time (PT), cholesterol, creatinine, and pregnancy associated plasma protein-A (PAPP-A) multiples of the median (MoM) values.

MAP, UTPI, PLGF and other indicators were collected during pregnancy between 11 and 13^{+6} weeks: ① MAP: After the pregnant woman rested for 5 minutes, blood pressure was measured in both upper arms using a regularly calibrated automatic blood pressure cuff. Two measurements were taken from each arm, yielding four blood pressure values. The difference in SBP between the arms should not exceed 10 mmHg (1 mmHg =0.133 kPa), and the differences in DBP should not exceed 6 mmHg. Measurements were repeated after 1 minute, and the average systolic and diastolic blood pressures were used to calculate the mean arterial pressure (MAP) using the formula: MAP =1/3 SBP + 2/3 DBP [14]. ② UTPI: Uterine arteries on both sides were identified by color Doppler mapping at the internal cervical opening plane. A 2 mm sampling window was used to obtain the characteristic uterine artery blood flow spectrum. The scanning angle was kept below 50°, and three similar waveforms were obtained. The UTPI was calculated as the average of both sides [15]. Additionally, the resistance index (RI) and the ratio of peak systolic to end-diastolic flow velocity (S/D) were also calculat-

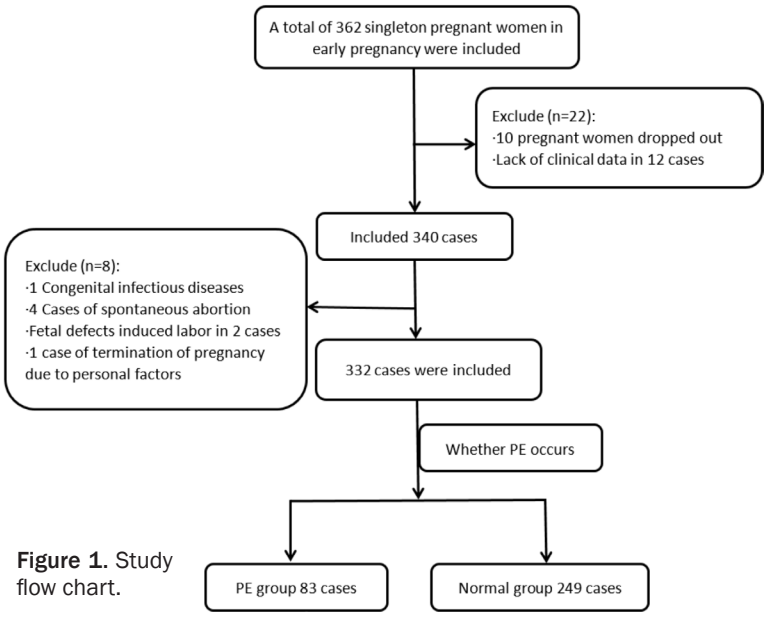

Figure 1. Study flow chart.

ed and averaged. ③ PLGF: During early Down's screening, 2 ml of fasting elbow venous blood was collected and centrifuged at 3000 r/min for 6-10 minutes, and the serum was separated. The PLGF level was determined using an enzyme-linked immunosorbent assay (ELISA).

Statistical methods

Statistical software (IBM SPSS 27.0) was employed for data analysis. Measured data conforming to a normal distribution with homogeneity of variance were expressed as mean ± standard deviation (SD), and comparisons were made using the t-test. Counted data were expressed as n (%) and compared using the χ^2 test. Multiple logistic regression analysis was performed for indicators with $P<0.05$ to establish the PE predictive model. The area under the curve (AUC) of the receiver operating characteristic (ROC) curve was adopted to assess the predictive value of the combined MAP + UTPI + PLGF for PE. R software with rms package was used to construct the nomogram. Bootstrap method was used for internal verification, and the calibration curve was used to evaluate the accuracy of the model. $P<0.05$ was regarded as significant.

Results

Basic information of included cases

362 pregnant women in early pregnancy were included. Among them, 10 pregnant women dropped out, 12 cases had incomplete clinical data, 1 case had a congenital infectious disease, and 7 terminated their pregnancies or had abortions (4 cases of natural abortions, 2 cases of labor induction due to fetal defects, and 1 case of pregnancy termination for personal factors). Ultimately, 332 cases were included in the analysis. Serological and uterine artery blood flow tests were performed on all pregnant women. There were 83 cases (25.00%) in the PE group (63 cases of PE and 20 cases of chronic hypertension combined with PE) and 249 cases (75.00%) in the normal group. The flow chart of patient screening is shown in **Figure 1**.

Comparison of clinical data between the two groups

The average age of pregnant women in the PE group was (29.71±3.79) years, with a BMI of (25.02±2.42) kg/m^2, and the hypertension rate was 39.76%. These values were higher than those in the normal group, where the average age was (27.82±3.40) years, BMI was (23.34±2.87) kg/m^2, and hypertension rate was 17.27% (all $P<0.001$). The PAPP-A level in the PE group was (0.75±0.22) U/L, significantly lower than that in normal group, which had a PAPP-A level of (1.02±0.32) U/L ($P<0.05$). No significant differences were observed between the two groups in terms of parity, mode of conception, diabetes, PE history, kidney disease, systemic lupus erythematosus, PT, cholesterol, creatinine, RI, or systolic-to-diastolic flow velocity ratio (S/D) (all $P>0.05$), as shown in **Table 1**.

Comparison of MAP, UTPI and PLGF between the two groups

The MAP in the PE group was (102.69±6.58) mmHg, and the UTPI was (1.38±0.37), both significantly higher than those of the normal group, where MAP was (90.40±8.63) mmHg and UTPI was (1.04±0.25) ($P<0.05$). The PLGF level in the PE group was (60.12±12.35) pg/mL, significantly lower than (94.82±17.65) pg/mL in the

Table 1. Comparison of baseline data between the two groups

Index	PE group (n=83)	Normal group (n=249)	t/χ^2	P
Age (years)	29.71±3.79	27.82±3.40	4.452	<0.001
BMI (kg/m^2)	25.02±2.42	23.34±2.87	4.802	<0.001
Pregnancy history [n (%)]			0.018	0.895
Primiparity	53 (63.86)	161 (64.66)		
Multiparity	30 (36.14)	88 (35.34)		
Method of Conception [n (%)]			2.613	0.106
Spontaneous Conception	68 (81.93)	182 (73.09)		
Assisted Reproduction	15 (17.07)	67 (26.91)		
Hypertension [n (%)]			17.838	<0.001
Yes	33 (39.76)	43 (17.27)		
No	50 (60.24)	206 (82.73)		
Diabetes mellitus [n (%)]			0.475	0.491
Yes	8 (9.64)	31 (12.45)		
No	75 (90.36)	218 (87.55)		
PE history [n (%)]			1.261	0.261
Yes	8 (9.64)	15 (6.02)		
No	75 (90.36)	234 (93.98)		
Nephropathy [n (%)]			0.625	0.429
Yes	15 (18.07)	36 (14.46)		
No	68 (81.93)	213 (85.54)		
Systemic lupus erythematosus [n (%)]			0.683	0.409
Yes	3 (3.61)	5 (2.01)		
No	80 (96.39)	244 (97.99)		
SBP (mmHg)	134.51±11.22	132.88±11.85	1.094	0.275
SDP (mmHg)	95.35±8.25	94.50±8.26	0.814	0.416
Fasting blood glucose (mmol/L)	4.42±0.95	4.55±0.75	-1.294	0.197
Blood albumin (g/L)	34.65±3.55	33.78±3.75	1.874	0.062
PT (s)	10.68±0.85	10.48±0.82	1.834	0.067
Cholesterol (mmol/L)	6.35±1.45	6.20±0.93	1.095	0.274
Creatinine (μmol/L)	51.83±15.23	48.95±17.25	1.148	0.252
PAPP-A (U/L)	0.75±0.22	1.02±0.32	-6.992	<0.001
RI	0.78±0.13	0.76±0.13	0.659	0.510
S/D	4.88±0.58	4.76±0.58	1.634	0.103

Note: PE, Preeclampsia; SBP, systolic blood pressure; SDP, diastolic blood pressure; PT, prothrombin time; PAPP-A, pregnancy associated plasma protein A; RI, blood flow resistance index; S/D, systolic velocity/diastolic velocity.

normal group (P<0.05). The details are shown in **Figure 2**.

Multivariate logistic regression analysis for PE in pregnant women

The occurrence of PE in pregnant women was taken as the dependent variable, and age, BMI, comorbid hypertension, MAP, UTPI, PLGF, and PAPP-A were used as independent variables for logistic regression analysis. The results of multivariate logistic regression analysis showed that age, BMI, PAPP-A, MAP, UTPI, and PLGF were independent predictive factors for early pregnancy PE (all P<0.05, **Table 2**). Additionally, all these factors were confirmed as independent predictive factors in the external validation cohort, as shown in **Table 3**.

Predictive effect of the combination of MAP, UTPI, and PLGF on PE

Logistic regression prediction models for early pregnancy PE were developed based on these identified significant predictors. The AUCs of age, BMI, PAPP-A, MAP, UTPI, and PLGF we-

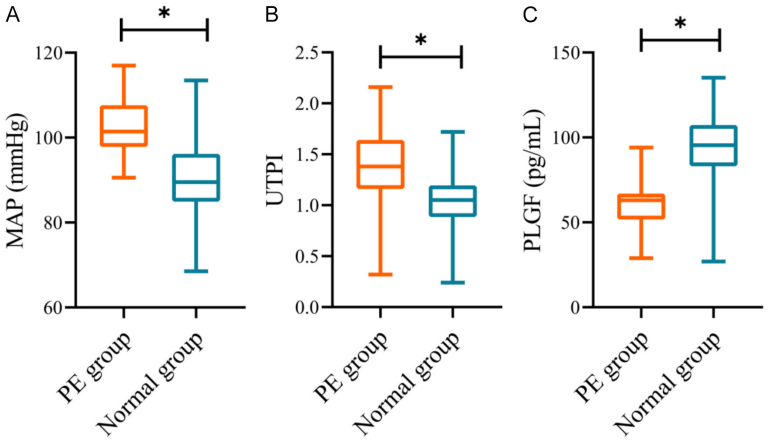

Figure 2. Comparison of MAP (A), UTPI (B), and PLGF (C) between the two groups. MAP, mean arterial pressure; UTPI, uterine artery pulse index; PLGF, Placental growth factor; *P<0.00001.

re 0.660, 0.669, 0.749, 0.869, 0.781, and 0.943, respectively. The AUC of the combined MAP + UTPI + PLGF model was 0.974 (95% CI: 0.957-0.991), with specificity and sensitivity of 95.20% and 93.57%, respectively. The AUC of the combined age + BMI + MAP + UTPI + PLGF model was 0.980 (95% CI: 0.968-0.993), with specificity and sensitivity of 96.40% and 91.97%, respectively. For the model without MAP, UTPI, and PLGF (i.e. age + BMI + PAPP-A), the AUC was 0.835 (95% CI: 0.791-0.879), with specificity and sensitivity being 71.08% and 84.30% respectively. The AUC of the model combining MAP, UTPI, and PLGF was 0.990 (95% CI: 0.938-0.998), with specificity and sensitivity of 83.98% and 98.80%, respectively. These results suggest that the AUC of the combined MAP + UTPI + PLGF model was larger than that of any individual index, significantly enhancing the prediction validity for PEFindings are shown in **Table 4** and **Figure 3**.

Establishment of the PE risk nomogram model

Age, BMI, PAPP-A, MAP, UTPI and PLGF were used as predictors to construct the PE risk nomogram (**Figure 4**). For each 2-year increase in age, the PE risk score increased by 2.5 points, starting from an age of 18. For every 2 kg/m^2 increase in BMI, starting from 14 kg/m^2, the PE risk score increased by 5 points. For every 0.2 U/L decrease in PAPP-A, starting from 2 U/L, the PE risk score increased by 8 points. The PE risk score increased by 8 points for every 5 mmHg increase in MAP, starting from 65 mmHg. For each 0.2 increase in UTPI, starting from 0.2, the PE risk score increased by 3 points. Additionally, for every 10 pg/mL decrease in PLGF, starting from 140 pg/mL, the PE risk score increased by 7.5 points.

Calibration curve of the nomogram model

Internal validation showed that the calibration curve of the nomogram model closely aligned with both the original curve and ideal curves. The mean absolute error (MAE) of the calibration curve was 0.012, and the consistency index was 0.99 (95% CI: 0.983-0.997) (**Figure 5**).

External validation of the predictive model for PE

For external validation, 182 pregnant women underwent regular prenatal examination at our hospital from February 1, 2023 to December 31, 2024 were included, of which 62 women had PE. The external validation results showed that age, BMI, PAPP-A, MAP, UTPI, and PLGF were independent predictors of PE in early pregnant women (all P<0.05). The AUC for the predictive model in the external validation set was 0.975 (95% CI: 0.955-0.995, P<0.001), suggesting that the discriminative ability of the validated nomogram prediction model was excellent (**Figure 6A**). The Bootstrap method, with 1000 repetitions, was used to draw the Hosmer-Lemeshow fitting validity curve. The slope of the calibration curve was close to 1, and the model fit was good (χ^2=4.039, P=0.854) (**Figure 6B**).

Discussion

Preeclampsia (PE) is a serious pregnancy-related condition that contributes significantly to adverse outcomes for both pregnant women and their newborns. Its pathogenesis is complex, and there are currently no effective or specific methods available for its prediction. Both national and international guidelines recommend early screening for PE risk, with aspi-

Table 2. Multivariate logistic regression analysis of PE in pregnant women

Factor	β	SE	Wald χ^2	P	OR	95% CI
Age (years)	0.219	0.102	4.645	0.031	1.245	1.020-1.520
BMI (kg/m^2)	0.424	0.140	9.203	0.002	1.528	1.162-2.010
Hypertension	-0.378	0.675	0.314	0.575	0.685	0.183-2.570
MAP (mmHg)	0.282	0.062	21.051	<0.001	1.326	1.175-1.497
UTPI	3.221	1.034	9.705	0.002	25.041	2.301-189.928
PLGF (pg/mL)	-0.141	0.027	28.637	<0.001	0.868	0.824-0.915
PAPPA	-6.960	1.716	16.444	<0.001	0.001	0.000-0.027
Constant	-32.588	8.287	15.463	0.000	0.000	-

Note: BMI, body mass index; MAP, mean arterial pressure; UTPI, uterine artery pulse index; PLGF, Placental growth factor.

Table 3. Multivariate logistic regression analysis of factors affecting PE in the external validation dataset

Factor	β	SE	Wald χ^2	P	OR	95% CI
Age (years)	0.232	0.104	4.977	0.026	1.261	1.029-1.547
BMI (kg/m^2)	0.512	0.153	11.222	<0.001	1.668	1.237-2.251
MAP (mmHg)	0.324	0.072	19.947	<0.001	1.382	1.199-1.593
UTPI	2.610	1.190	4.808	0.028	13.600	1.319-140.197
PLGF (pg/mL)	-0.129	0.026	23.686	<0.001	0.879	0.835-0.926
PAPPA	-4.597	1.499	9.404	0.002	0.010	0.001-0.190
Constant	-40.745	10.089	16.310	<0.001	0.000	-

Note: BMI, body mass index; mAP, mean arterial pressure; uTPI, uterine artery pulse index; pLGF, Placental growth factor.

Table 4. The predictive value of each influencing factor and their various combinations for PE

Factor	AUC	95% CI	Sensitivity	Specificity	P
Age	0.660	0.593-0.726	69.90%	60.61%	<0.001
BMI	0.669	0.605-0.733	79.50%	44.58%	<0.001
PAPP-A	0.749	0.695-0.803	55.80%	84.34%	<0.001
MAP	0.869	0.832-0.907	90.40%	72.29%	<0.001
UTPI	0.781	0.717-0.845	77.10%	69.48%	<0.001
PLGF	0.943	0.919-0.968	89.20%	89.16%	<0.001
Age + BMI + PAPP-A	0.835	0.791-0.879	71.08%	84.30%	<0.001
MAP + UTPI + PLGF	0.974	0.957-0.991	95.20%	93.57%	<0.001
Age + BMI + MAP + UTPI + PLGF	0.980	0.968-0.993	96.40%	91.97%	<0.001
Age + BMI + PAPP-A + MAP + UTPI + PLGF	0.990	0.938-0.998	98.80%	93.98%	<0.001

Note: BMI, body mass index; MAP, mean arterial pressure; UTPI, uterine artery pulse index; PLGF, Placental growth factor; PE, Preeclampsia.

rin administration advised for high-risk patients starting from 11-14 weeks of pregnancy to prevent PE [2, 16, 17]. Therefore, early prediction of preeclampsia is of great significance. Literature has shown that the detection rate of PE in preterm pregnancies is low (40% and 35%) when relying solely on clinical risk factors during early pregnancy [18]. A study using a nomogram to predict threatened PE among pregnant women revealed that BMI, blood pressure, uterine artery ultrasound parameters, and serological indicators were effective for individualized prediction of PE [19]. However, most predictive models rely on serological markers such as sFlt-1, PlGF, and sEng, which are not routinely tested in many hospitals in China. In contrast, this study constructed a model using clinically accessible indicators to better align with primary diagnosis and treatment settings.

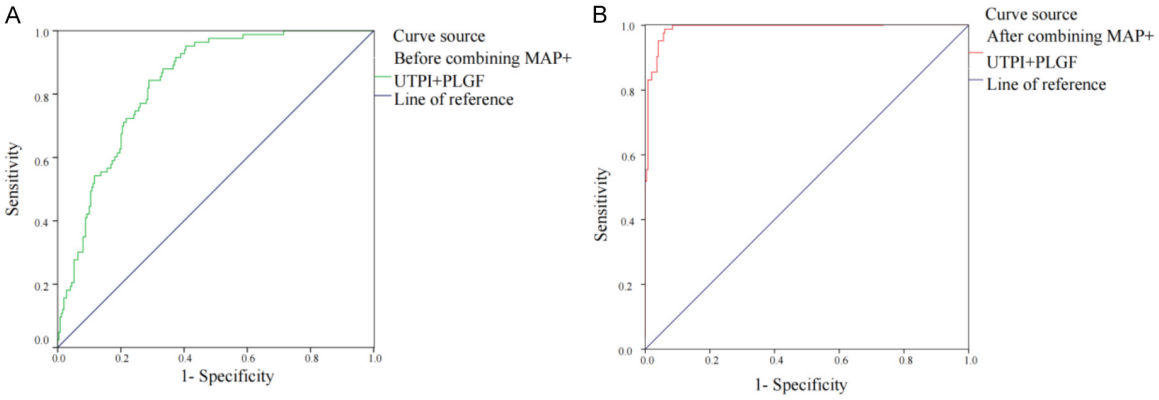

Figure 3. Predictive performance of risk models for PE in early pregnancy. A. Predictive performance of model excluding MAP, UTPI, and PLGF for PE in early pregnancy; B. Predictive performance of model incorporating MAP, UTPI, and PLGF for PE in early pregnancy. PE, Preeclampsia.

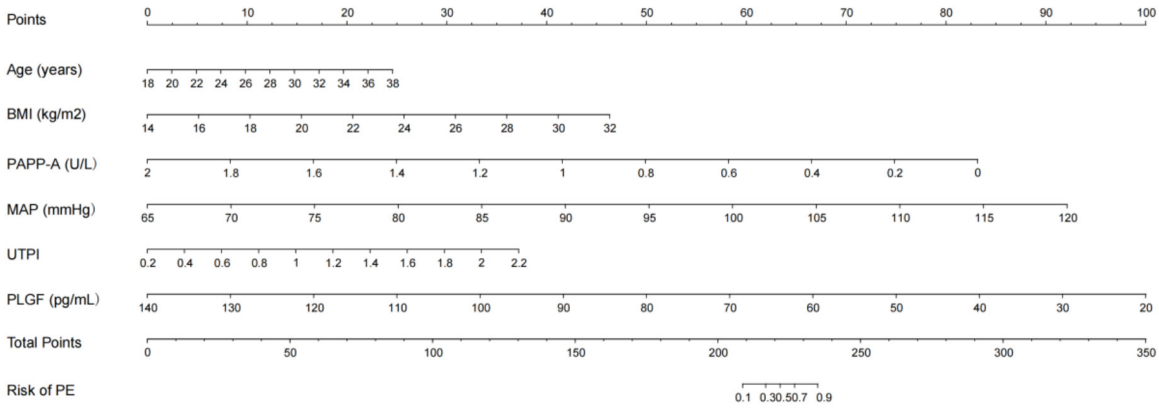

Figure 4. Nomogram predictive model for PE. BMI, body mass index; MAP, mean arterial pressure; UTPI, uterine artery pulse index; PLGF, Placental growth factor; PE, Preeclampsia.

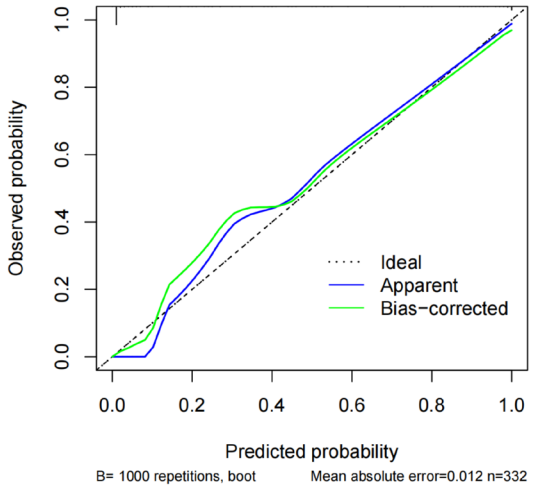

Figure 5. Calibration curve of the nomogram model for predicting PE. PE, Preeclampsia.

The FIGO guidelines on screening and prevention of early pregnancy PE highlight that, although the pathogenesis of PE is not fully understood, current theories suggest that it occurs in two stages. The first stage involves shallow trophoblast invasion, leading to inadequate remodeling of the spiral arteries. This results in the second stage, where maternal endothelial dysfunction and an imbalance between angiogenesis and anti-angiogenic factors lead to the clinical manifestations of the disease [20]. Pregnant women who develop PE exhibit alterations in maternal vascular elasticity during early pregnancy, manifesting as abnormal blood pressure levels. Notably, MAP demonstrates a predictive value that surpasses that of isolated systolic or diastolic pressure. In early stages of pregnancy, trophoblast cell invasion into the placenta disrupts the remodeling of uterine spiral arteries, resulting in increased vascular resistance and elevated UTPI [12, 21]. Numerous studies have confirmed that PLGF plays an important role in nor-

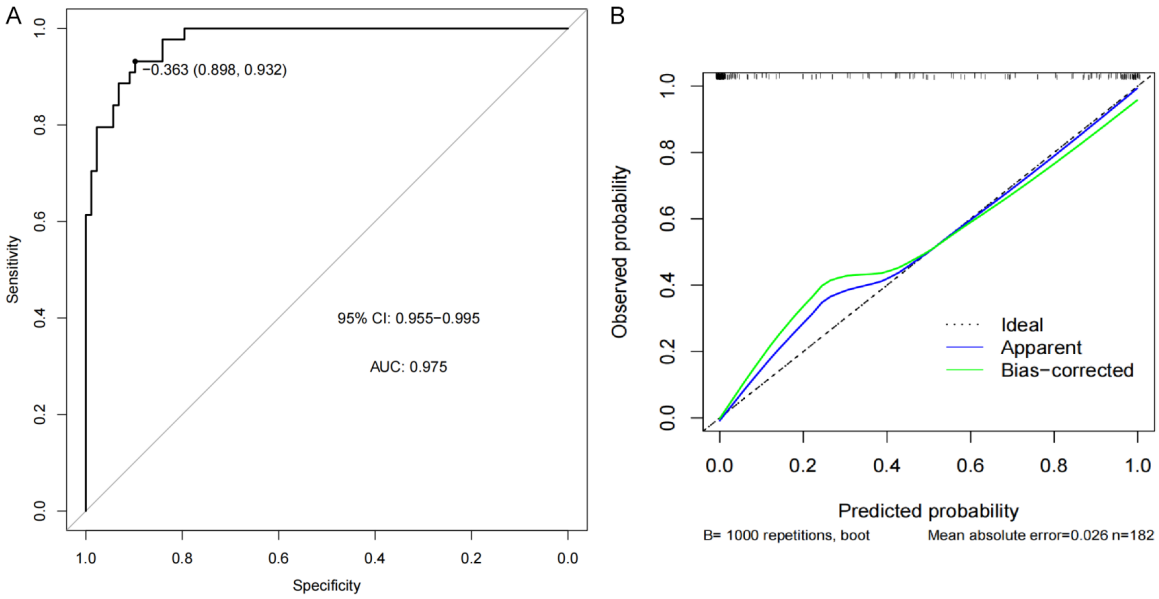

Figure 6. ROC curve and calibration curve of predictive model in the external validation set. A. ROC curve; B. Calibration curve; BMI, body mass index; MAP, mean arterial pressure; UTPI, Uterine artery pulse index; PLGF, Placental growth factor; ROC, receiver operating characteristic.

mal placental formation and development during pregnancy, with its abnormal secretion closely linked to PE [6, 8, 22]. PLGF is a glycosylated dimeric glycoprotein from the vascular endothelial growth factor subfamily. In uncomplicated pregnancies, PLGF is crucial for the development of placental blood vessels and for maintaining maternal vascular endothelial function. In PE patients, PLGF levels are significantly reduced, contributing to abnormal vascular endothelial function and inadequate blood perfusion, which exacerbates the development of PE [23, 24]. This study supports these findings, since results showed that in the PE group, MAP and UTPI were both significantly higher, while PLGF levels were lower compared to the normal group.

With increasing age and BMI, the likelihood of pregnant women developing hypertension and kidney disease also increases, which in turn increases the risk of PE [25]. The level of PAPP-A rises with gestational weeks, and this elevation can reduce IGF levels and inhibit the fibrinolysis activity within the physiologic system. Such changes may result in metabolic abnormalities that affect placental function, ultimately increasing susceptibility to PE [26]. This study shows that early pregnancy age, BMI, and PAPP-A MoM individually predict PE with AUCs of 0.660, 0.669, and 0.749 respectively, serving as indicators for combined prediction. Elevated blood pressure is a core indicator for diagnosing PE. MAP reflects the average arterial pressure over one cardiac cycle and is commonly included in various predictive models. When combined with other early pregnancy indicators, MAP shows higher predictive value for PE [4]. The results of this study demonstrate that MAP exhibits stable performance for predicting PE, with an AUC of 0.869 when used alone. UTPI indirectly reflects uteroplacental circulation perfusion, thus predicting the risk of PE [27]. Previous studies have reported that UTPI, combined with maternal high-risk factors, can predict PE in 30% of patients [28]. This study demonstrates that early pregnancy UTPI alone predicts PE with an AUC of 0.781, and it can be used as a combined predictive indicator. PLGF, mainly synthesized and secreted by trophoblasts and vascular endothelial cells, promotes cell proliferation, activation, and migration, while also facilitating placental remodeling during pregnancy [29]. In PE cases, basal membrane spiral artery sclerosis can lead to ischemia and hypoxia in the placenta, damaging vascular endothelial cells and trophoblast function, which in turn causes a significant reduction in PLGF levels [30]. The results of this study show that PLGF predicts PE with an AUC of 0.943.

The pathogenesis of PE remains unclear, and there is still a lack of specific clinical indicators to predict the occurrence and severity of PE. Therefore, combining multiple biological markers related to PE should theoretically improve the sensitivity and specificity of prediction. In this study, MAP, UTPI and PIGF were combined to predict PE, with the AUC for PE prediction being 0.974. The AUC for the model combining age, BM, PAPP-A, MAP, UTPI, and PLGF was 0.990 (95% CI: 0.938-0.998), with specificity and sensitivity values of 83.98% and 98.80%, respectively. These findings suggest that the AUC of the combined MAP + UTPI + PLGF model was higher than the individual diagnostic AUCs of each marker, and the integration of age, BMI, and PAPP-A enhanced the predictive validity for PE. Based on these predictive indicators, a risk model for predicting PE was initially constructed and visually represented through a nomogram. Both internal and external verification confirmed that the model had good predictive value and broad potential for use.

This study still has several limitations, mainly related to the following aspects: (1) This study was limited by a relatively small sample size included in a specific time frame. All early-pregnancy participants were normal prenatal patients from the obstetrics and gynecology department at our hospital. Further verification requires a large sample size; (2) The sensitivity of screening for MAP, UTPI, and PIGF levels in this study may have been overestimated. The purpose of this study was to evaluate the predictive efficacy of these indicators for PE, rather than to dynamically assess changes in pregnant women's conditions. Therefore, further research should expand the sample size, foster cooperation between hospitals, and employ double data entry and processing for analyzing images and data to provide more robust scientific evidence for exploring early pregnancy screening strategies by using combined indicators like MAP, UTPI, and PLGF for PE prevention.

Conclusion

Age, BMI, PAPP-A, MAP, UTPI, and PLGF were all effective indicators for predicting early PE. Furthermore, the combined detection of high-risk factors, including MAP, UTPI, and PLGF, significantly enhanced the predictive value for PE during early pregnancy.

Disclosure of conflict of interest

None.

Address correspondence to: Xiaozhi Wu, Department of Obstetrics and Gynecology, The Third Affiliated Hospital of Zunyi Medical University (The First People's Hospital of Zunyi), No. 98, Fenghuang North Road, Zunyi 563000, Guizhou, China. Tel: +86-0851-28925231; E-mail: wuxiaozhi0621@163.com

References

[1] Yang Y, Le Ray I, Zhu J, Zhang J, Hua J and Reilly M. Preeclampsia prevalence, risk factors, and pregnancy outcomes in Sweden and China. JAMA Netw Open 2021; 4: e218401.

[2] Pasokpuckdee K and Boriboonhirunsarn D. Incidence of preeclampsia and cesarean section rate according to the Robson classification. Cureus 2023; 15: e49845.

[3] Tsakiridis I, Giouleka S, Arvanitaki A, Giannakoulas G, Papazisis G, Mamopoulos A, Athanasiadis A and Dagklis T. Gestational hypertension and preeclampsia: an overview of national and international guidelines. Obstet Gynecol Surv 2021; 76: 613-633.

[4] Chang KJ, Seow KM and Chen KH. Preeclampsia: recent advances in predicting, preventing, and managing the maternal and fetal life-threatening condition. Int J Environ Res Public Health 2023; 20: 2994.

[5] Chaemsaithong P, Sahota DS and Poon LC. First trimester preeclampsia screening and prediction. Am J Obstet Gynecol 2022; 226: S1071-S1097, e2.

[6] Stepan H, Galindo A, Hund M, Schlembach D, Sillman J, Surbek D and Vatish M. Clinical utility of sFlt-1 and PlGF in screening, prediction, diagnosis and monitoring of pre-eclampsia and fetal growth restriction. Ultrasound Obstet Gynecol 2023; 61: 168-180.

[7] Slade LJ, Syngelaki A, Wilson M, Mistry HD, Akolekar R, von Dadelszen P, Nicolaides KH and Magee LA. Blood pressure cutoffs at 11-13 weeks of gestation and risk of preeclampsia. Am J Obstet Gynecol 2025; 232: 214.e1-214.e10.

[8] Tanner MS, de Guingand D, Reddy M, Rowson S, Rolnik DL, Davey MA, Mol BW, Wallace EM, Da Silva Costa F and Palmer KR. The effect of comorbidities on the sFLT-1:PlGF ratio in preeclampsia. Pregnancy Hypertens 2022; 29: 98-100.

[9] Savka RF, Mykolaiovych Berbets A, Mykhailovych Barbe A, Mykhailovych Yuzko O and Radu MR. Changes in concentrations of melatonin, PlGF, and cytokines in women with preeclampsia. J Med Life 2023; 16: 471-476.
[10] Zhu J, Zhang J, Syaza Razali N, Chern B and Tan KH. Mean arterial pressure for predicting preeclampsia in Asian women: a longitudinal cohort study. BMJ Open 2021; 11: e046161.
[11] Suksai M, Geater A, Phumsiripaiboon P and Suntharasaj T. A new risk score model to predict preeclampsia using maternal factors and mean arterial pressure in early pregnancy. J Obstet Gynaecol 2022; 42: 437-442.
[12] Xu X, Yan G, Liu J, Li X, Zhang B, Meng X, Chen H, Han B, Shao K, Zhao X, Liu J and Yan Y. Clinical application of multi-index combined risk assessment in early pregnancy for screening of preeclampsia. Evid Based Complement Alternat Med 2022; 2022: 5089442.
[13] Lin JH and Lyu X. Difficulties and confusion concerning the management of hypertensive disorders in pregnancy--interpretation of the guidelines for the diagnosis and treatment of hypertensive disorders in pregnancy (2020). Sichuan Da Xue Xue Bao Yi Xue Ban 2022; 53: 1007-1011.
[14] He Y, Xie J, Guo Y, Ma J, Wang X, Lv Y, Wu S, Wei S, Xie X and Wang B. The potential of repeated mean arterial pressure measurements for predicting early- and late-onset pre-eclampsia in twin pregnancies: prediction model study. Int J Gynaecol Obstet 2025; 168: 196-204.
[15] Gana N, Sarno M, Vieira N, Wright A, Charakida M and Nicolaides KH. Ophthalmic artery Doppler at 11-13 weeks' gestation in prediction of pre-eclampsia. Ultrasound Obstet Gynecol 2022; 59: 731-736.
[16] Khanijo P, Nautiyal R, Mangla M, Rajput R and Saini M. Diagnostic accuracy of gestosis score in comparison to multi-marker screening as a predictor of preeclampsia at 11-14 weeks of pregnancy: a cohort study. Curr Hypertens Rev 2023; 19: 187-193.
[17] Valenzuela-Muhech YL, Cervantes-Ricaud AJ, Carrasco-Blancas ER, Cortes-Martinez MA and Oviedo-Cruz H. Definition of normal blood pressure at 11 to 14 weeks' gestation according to risk. Arch Cardiol Mex 2023; 93: 62-68.
[18] Magee LA, Nicolaides KH and von Dadelszen P. Preeclampsia. N Engl J Med 2022; 386: 1817-1832.
[19] Yue CY, Gao JP, Zhang CY, Ni YH and Ying CM. Development and validation of a nomogram for the early prediction of preeclampsia in pregnant Chinese women. Hypertens Res 2021; 44: 417-425.
[20] Poon LC, Shennan A, Hyett JA, Kapur A, Hadar E, Divakar H, McAuliffe F, da Silva Costa F, von Dadelszen P, McIntyre HD, Kihara AB, Di Renzo GC, Romero R, D'Alton M, Berghella V, Nicolaides KH and Hod M. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: a pragmatic guide for first-trimester screening and prevention. Int J Gynaecol Obstet 2019; 145 Suppl 1: 1-33.
[21] Tousty P, Fraszczyk-Tousty M, Golara A, Zahorowska A, Slawinski M, Dzidek S, Jasiak-Jozwik H, Nawceniak-Balczerska M, Kordek A, Kwiatkowska E, Cymbaluk-Ploska A, Torbe A and Kwiatkowski S. Screening for preeclampsia and fetal growth restriction in the first trimester in women without chronic hypertension. J Clin Med 2023; 12: 5582.
[22] Burwick RM and Rodriguez MH. Angiogenic biomarkers in preeclampsia. Obstet Gynecol 2024; 143: 515-523.
[23] Xie X, Chen D, Yang X, Cao Y, Guo Y and Cheng W. Combination of maternal serum ESM-1 and PLGF with uterine artery doppler PI for predicting preeclampsia. J Clin Med 2023; 12: 459.
[24] Tomkiewicz J and Darmochwal-Kolarz DA. Biomarkers for early prediction and management of preeclampsia: a comprehensive review. Med Sci Monit 2024; 30: e944104.
[25] Toloza FJK, Derakhshan A, Mannisto T, Bliddal S, Popova PV, Carty DM, Chen L, Taylor P, Mosso L, Oken E, Suvanto E, Itoh S, Kishi R, Bassols J, Auvinen J, Lopez-Bermejo A, Brown SJ, Boucai L, Hisada A, Yoshinaga J, Shilova E, Grineva EN, Vrijkotte TGM, Sunyer J, Jimenez-Zabala A, Riano-Galan I, Lopez-Espinosa MJ, Prokop LJ, Singh Ospina N, Brito JP, Rodriguez-Gutierrez R, Alexander EK, Chaker L, Pearce EN, Peeters RP, Feldt-Rasmussen U, Guxens M, Chatzi L, Delles C, Roeters van Lennep JE, Pop VJM, Lu X, Walsh JP, Nelson SM, Korevaar TIM and Maraka S. Association between maternal thyroid function and risk of gestational hypertension and pre-eclampsia: a systematic review and individual-participant data meta-analysis. Lancet Diabetes Endocrinol 2022; 10: 243-252.
[26] Wang Q, Zhang W, Li W and Yu C. The early predictive value of maternal serum PAPP-A concentration at 11-14 weeks of pregnancy for preeclampsia. Folia Neuropathol 2024; 54257.
[27] Chen JY, Yu BL, Wu XJ, Li YF, Zhong LY and Chen M. A longitudinal and cross-sectional study of placental circulation between normal and placental insufficiency pregnancies. Placenta 2024; 149: 29-36.
[28] Monckeberg M, Arias V, Fuenzalida R, Alvarez S, Toro V, Calvo A, Kusanovic JP, Monteiro LJ,

Schepeler M, Nien JK, Martinez J and Illanes SE. Diagnostic performance of first trimester screening of preeclampsia based on uterine artery pulsatility index and maternal risk factors in routine clinical use. Diagnostics (Basel) 2020; 10: 182.

[29] Hackeloer M, Schmidt L and Verlohren S. New advances in prediction and surveillance of preeclampsia: role of machine learning approaches and remote monitoring. Arch Gynecol Obstet 2023; 308: 1663-1677.

[30] Rolnik DL, Syngelaki A, O'Gorman N, Wright D, Nicolaides KH and Poon LC. Aspirin for evidence-based preeclampsia prevention trial: effects of aspirin on maternal serum pregnancy-associated plasma protein A and placental growth factor trajectories in pregnancy. Am J Obstet Gynecol 2024; 231: 342.e1-342.e9.