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Original Article

Serum creatinine, uric acid, and D-dimer levels as predictors of disease severity in hypertensive disorders of pregnancy

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Abstract: Objective: This study aims to explore the association between serum creatinine (Scr), uric acid (UA), D-dimer (D-D) levels and disease severity in patients with hypertensive disorders of pregnancy (HDP), and to establish a nomogram model for risk stratification and prediction of adverse pregnancy outcomes (APO). Methods: We retrospectively analyzed 230 HDP patients, categorizing them into two groups based on the occurrence of APO: the APO group (n=75) and the non-APO group (n=155). The predictive value of biomarkers for disease severity was evaluated, and a composite risk model incorporating both severity and biomarkers was constructed to assess APO risk. Then we checked different clinical indicators between the two groups to find which ones might be linked to APO. We used this information to make a nomogram model that showed the risk of APO in HDP patients. We tested how well the model worked. Results: Out of 230 HDP patients, 75 had bad pregnancy results (32.61%). The univariate logistic regression analysis showed several factors linked to APO: maternal age, disease severity, D-D levels, Scr, and UA (all $P<0.05$). Further multivariate logistic regression identified four independent risk factors: disease severity, D-D, Scr, and UA (all $P<0.05$). Using these, we built a nomogram model. The model exhibited good calibration and goodness-of-fit ($P=0.230$). A receiver operating characteristic analysis showed the model worked well, with an area under the curve of 0.888 (95% confidence interval: 0.844-0.932). The model had a sensitivity of 89.0%, a specificity of 74.7%, and an overall accuracy of 84.35%. A decision curve analysis showed that the model was helpful for doctors in making clinical decisions. Conclusion: We developed a nomogram model to help predict APO in women with HDP. The results showed that the model performed well in terms of accuracy and consistency.

Keywords: Hypertensive disorders of pregnancy, adverse pregnancy outcomes, nomogram, risk factor, prediction model

Introduction

Hypertensive disorders of pregnancy (HDP) are a common group of complicating problems during pregnancy, affecting about one in ten pregnant women [1, 2]. HDP includes several subtypes, such as gestational hypertension, preeclampsia, and eclampsia. Once the condition worsens, especially when it progresses to preeclampsia or eclampsia, pregnant women may experience severe symptoms like convulsions, altered consciousness, or even coma. Clinical observations have shown that these severe symptoms often indicate a series of adverse pregnancy outcomes (APO), including fetal growth restriction (FGR), placental abruption, preterm birth, and even stillbirth [3]. As such, identifying key risk factors associated with APO, detecting high-risk patients early, and applying timely, evidence-based interventions are essential for improving maternal and fetal safety in clinical settings.

HDP can cause serious problems for both mother and baby. There are many reasons for these problems, which involve a number of changes in the body's functioning. One of the main problems is that blood vessels remain too constricted for long periods of time. This reduces the oxygen and blood supply to the placenta. Re-

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cent studies have found that this blood flow impairment may be related to abnormal expression of angiotensin II receptors and dysregulation of their downstream signaling pathways [4]. Patients with HDP usually present with multiorgan involvement, including ischemia, hypoxia, and edema in vital organs such as the heart, brain, liver, and kidneys. In severe cases, these symptoms can progress to organ damage and even organ failure [5]. A hallmark of preeclampsia is defective remodeling of the uterine spiral arteries [6]. Under normal conditions, extravillous trophoblasts invade and transform these arteries into low-resistance, high-capacitance vessels to ensure adequate placental perfusion. However, when maternal immune regulation is altered, particularly involving uterine natural killer cells, trophoblast differentiation may be impaired. This limits arterial transformation, resulting in chronic placental hypoxia and restricted blood flow [7]. This situation is very likely to lead to a series of pregnancy complications.

It has been suggested that the age of the mother, as well as the severity of the condition, may be associated with the occurrence of APO [8, 9]. To improve the detection of these risks, recent studies have explored the combined use of multiple biomarkers instead of relying on a single indicator [10]. Among them, uric acid (UA), as an end product of purine metabolism, has received attention for its association with vascular endothelial damage and decreased placental function [11]. Serum creatinine (Scr), which indicates kidney filtration capacity, is another important marker. In women with HDP, declining renal function often results in elevated Scr, which can worsen blood pressure control and raise the risk of organ damage [12, 13]. Similarly, higher levels of D-dimer (D-D) may suggest a prothrombotic state that could impair placental blood flow [14]. Therefore, dynamic monitoring of UA, Scr, and D-D levels can help clinicians identify high-risk patients earlier. However, the current combined multi-indicator prediction model still faces some problems, such as insufficient sensitivity, poor reproducibility, and the stability of clinical application needs to be further verified.

This study focused on exploring the association between UA, Scr and D-D levels and APO in HDP patients. A nomogram model was developed for the study. Subsequently, the predictive effect of the model was evaluated using calibration curve, receiver operating characteristic curve and decision curve analysis (DCA). The results of the study are expected to inform clinical work and assist healthcare professionals in more effectively identifying high-risk HDP patients and developing individualized intervention strategies to optimize maternal and infant outcomes.

Materials and methods

General information

Clinical data were retrospectively collected from 230 patients with HDP who were treated at Peking University First Hospital Ningxia Women and Children's Hospital (Ningxia Hui Autonomous Region Maternal and Child Health Hospital) between June 2021 to June 2024. Inclusion criteria: (1) diagnosis of HDP; (2) singleton pregnancy; (3) post-diagnosis antihypertensive treatment with good adherence; (4) gestational age ≥28 weeks at delivery. Exclusion criteria: (1) communication difficulties or psychiatric disorders, including anxiety, depression, or schizophrenia; (2) severe cardiac, hepatic, or renal dysfunction; (3) coexisting pregnancy-related complications; (4) incomplete medical records. This study was approved by the Ethics Committee of Peking University First Hospital Ningxia Women and Children's Hospital (Ningxia Hui Autonomous Region Maternal and Child Health Hospital).

Basic data collection

Patient data were collected, including age, pre-pregnancy body mass index, educational background, number of pregnancies, gestational week, pre-conception screening, disease severity, history of miscarriage, family history of hypertension, fetal presentation, delivery method, and consistent folic acid supplementation during early pregnancy. APO were defined in this study according to the 2009 World Health Organization maternal near-miss criteria and the Pre-eclampsia Integrated Risk Score model proposed by Von Dadelszen et al. [15]. APO was characterized by the presence of one or more conditions during pregnancy or postpartum: maternal death, disseminated intravascular coagulation, acute heart failure, hemolytic

anemia, hemolysis, elevated liver enzymes, and low platelets syndrome, placental abruption, posterior reversible encephalopathy syndrome, exudative retinal detachment, non-cardiogenic acute pulmonary edema, acute liver failure, FGR, intrauterine fetal death, stillbirth, preterm birth (<37 weeks), low birth weight (<2500 g), neonatal asphyxia, or neonatal intensive care unit admission.

Clinical data collection

On the second day after admission, 6 mL of fasting peripheral venous blood was collected from all patients for the assessment of various laboratory parameters, including high-density lipoprotein, low-density lipoprotein, triglycerides, total cholesterol, D-D, Scr, UA, platelet count, and hemoglobin.

Statistical analysis

Data analysis was conducted using SPSS version 22.0. The normality of continuous variables was assessed with the Kolmogorov-Smirnov test. Normally distributed data were expressed as $\bar{x} \pm s$, and intergroup comparisons were performed using the *t*-test. For non-normally distributed data, results were expressed as [M (Q_1, Q_3)], and comparisons were conducted using the Mann-Whitney U test. Categorical variables were presented as frequencies and percentages [n (%)], with group differences assessed by the χ^2 test or Fisher's exact test. Predictive model variables were selected through univariate logistic regression analysis, while independent predictors were identified using multivariate logistic regression analysis. A two-tailed significance level of α=0.05 was applied, with P<0.05 considered statistically significant. A nomogram prediction model was developed based on multivariate logistic regression analysis. The model's diagnostic accuracy and clinical utility were evaluated through calibration curve, receiver operating characteristic curve analysis, and DCA.

Results

Comparison of basic data

This study included 230 patients, among whom 75 experienced APO, resulting in an incidence rate of 32.61% (75/230). The mean age in the APO group was 30.43±3.15 years, which was significantly higher than that in the non-APO group (29.58±2.81 years; P<0.05). A statistically significant difference was observed in the distribution of disease severity between the two groups (P<0.001). No significant differences were found in other baseline characteristics (all P>0.05) (**Table 1**).

Comparison of clinical data

The D-D level in the APO group was 0.93 (0.72, 1.09) mg/L, which was significantly higher than the 0.67 (0.51, 0.79) mg/L observed in the non-APO group (P<0.001). The Scr level in the APO group was 49.39±11.43 μmol/L, significantly higher than 42.85±10.15 μmol/L in the non-APO group (P<0.001). Similarly, the UA level was 361.38±55.39 μmol/L in the APO group, significantly exceeding the 315.19± 61.47 μmol/L recorded in the non-APO group (P<0.001). No significant differences were found in other clinical parameters between the two groups (all P>0.05) (**Table 2**).

Univariate logistic regression analysis of factors associated with APO in patients with HDP

For variable assignment in the regression analysis, continuous variables including age, body mass index, number of pregnancies, gestational week, high-density lipoprotein, low-density lipoprotein, triglycerides, total cholesterol, D-D, Scr, UA, platelet count, and hemoglobin were entered using their actual measured values. Categorical variables were assigned as follows: educational background was coded as 0 for primary school, 1 for middle and high school, and 2 for college. Pre-conception screening, history of miscarriage, family history of hypertension, and consistent folic acid supplementation during early pregnancy were coded as 0 for no and 1 for yes. Fetal presentation was coded as 0 for cephalic presentation and 1 for breech presentation. Delivery method was coded as 0 for vaginal birth and 1 for cesarean delivery. In order to reflect clinical progression of HDP, the diagnostic categories of gestational hypertension, preeclampsia, and eclampsia were consolidated into a categorical variable labeled "the severity of the disease" (**Table 3**). A univariate logistic regression analysis was conducted using the occurrence of APO in HDP patients as the dependent variable and various clinical indicators as independent variables. The analysis revealed that age (odds

Table 1. Comparison of basic data ($\bar{x}\pm s$)/[n (%)]

	APO (n=75)	Non-APO (n=155)	t/χ^2	*P*
Age	30.43±3.15	29.58±2.81	2.057	0.041
Pre-pregnancy BMI (kg/m^2)	21.48±2.01	20.96±2.15	1.751	0.081
Educational background			0.656	0.721
Primary school	15 (20.00)	27 (17.42)		
Middle and high school	26 (34.67)	49 (31.61)		
College	34 (45.33)	79 (50.97)		
Number of pregnancies	1.65±0.51	1.79±0.53	1.906	0.058
Gestational week	37.51±1.21	37.78±1.48	1.390	0.166
Pre-conception screening			2.189	0.139
No	21 (28.00)	30 (19.35)		
Yes	54 (72.00)	125 (80.65)		
Disease severity			-	<0.001[a]
Gestational hypertension	37 (49.33)	114 (73.55)		
Preeclampsia	34 (45.33)	40 (25.81)		
Eclampsia	4 (5.33)	1 (0.65)		
History of miscarriage			1.524	0.217
No	63 (84.00)	139 (89.68)		
Yes	12 (16.00)	16 (10.32)		
Family history of hypertension			1.204	0.273
No	59 (78.67)	131 (84.52)		
Yes	16 (21.33)	24 (15.48)		
Fetal presentation			0.457	0.499
Cephalic presentation	65 (86.67)	139 (89.68)		
Breech presentation	10 (13.33)	16 (10.32)		
Delivery method			1.078	0.299
Vaginal birth	56 (74.67)	125 (80.65)		
Cesarean delivery	19 (25.33)	30 (19.35)		
Consistent folic acid supplementation during early pregnancy			3.426	0.064
No	21 (28.00)	27 (17.42)		
Yes	54 (72.00)	128 (82.58)		

Note: APO, adverse pregnancy outcomes; BMI, body mass index; [a]Fisher's exact tests.

Table 2. Comparison of clinical data ($\bar{x}\pm s$)/[M (Q_1, Q_3)]

	APO (n=75)	Non-APO (n=155)	*t/Z*	*P*
HDL (mmol/L)	1.85±0.34	1.94±0.35	1.899	0.059
LDL (mmol/L)	3.70±0.53	3.60±0.80	0.917	0.360
TG (mmol/L)	3.94±1.24	3.83±1.05	0.752	0.453
TC (mmol/L)	5.94±0.64	5.84±0.68	1.065	0.266
D-D (mg/L)	0.93 (0.72, 1.09)	0.67 (0.51, 0.79)	6.539	<0.001
Scr (μmol/L)	49.39±11.43	42.85±10.15	4.401	<0.001
UA (μmol/L)	361.38±55.39	315.19±61.47	5.515	<0.001
PLT (×10^9/L)	233.85±41.62	222.37±43.59	1.901	0.059
Hb (g/L)	124.69 (116.79, 137.56)	123.05 (113.38, 133.43)	1.502	0.133

Note: APO, adverse pregnancy outcomes; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; TC, total cholesterol; D-D, D-dimer; Scr, Serum creatinine; UA, uric acid; PLT, platelet count; Hb, hemoglobin.

Table 3. Assignment of each factor

	Assignment
Age	Enter the actual value
Pre-pregnancy BMI	Enter the actual value
Educational background	0= Primary school, 1= Middle and high school, 2= College
Number of Pregnancies	Enter the actual value
Gestational week	Enter the actual value
Pre-conception screening	0= no, 1= yes
The severity of the disease	0= Gestational hypertension, 1= Preeclampsia, 2= Eclampsia
History of miscarriage	0= no, 1= yes
Family history of hypertension	0= no, 1= yes
Fetal presentation	0= Cephalic presentation, 1= Breech presentation
Delivery method	0= Vaginal birth, 1= Cesarean delivery
Consistent folic acid supplementation during early pregnancy	0= no, 1= yes
HDL	Enter the actual value
LDL	Enter the actual value
TG	Enter the actual value
TC	Enter the actual value
D-D	Enter the actual value
Scr	Enter the actual value
UA	Enter the actual value
PLT	Enter the actual value
Hb	Enter the actual value

Note: BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; TC, total cholesterol; D-D, D-dimer; Scr, Serum creatinine; UA, uric acid; PLT, platelet count; Hb, hemoglobin.

ratio [OR]=1.104, 95% confidence interval [CI]: 1.003-1.215, *P*=0.042), preeclampsia (OR= 2.619, 95% CI: 1.454-4.718, *P*=0.001), eclampsia (OR=12.324, 95% CI: 1.335-113.754, *P*=0.027), D-D (OR=115.701, 95% CI: 25.542-524.103, *P*<0.001), Scr (OR=1.061, 95% CI: 1.031-1.091, *P*<0.001), and UA (OR=1.014, 95% CI: 1.008-1.019, *P*<0.001) were significant predictors of APO in HDP patients (**Table 4**).

Multivariate logistic regression analysis of factors associated with APO in patients with HDP

Using the occurrence of APO in patients with HDP as the dependent variable, variables with *P*<0.05 from the univariate logistic regression analysis (**Table 4**) were included as independent variables in the multivariate logistic regression analysis to further identify independent risk factors for APO. The results showed that preeclampsia (OR=2.443, 95% CI: 1.116-5.348, *P*=0.025), eclampsia (OR=44.086, 95% CI: 1.706-1139.549, *P*=0.023), D-D (OR= 410.744, 95% CI: 55.268-3052.610, *P*<0.001), Scr (OR=1.099, 95% CI: 1.057-1.142, *P*<0.001), and UA (OR=1.021, 95% CI: 1.013-1.029, *P*< 0.001) were identified as independent risk factors for APO in HDP patients (**Table 5**).

Construction of nomogram prediction model

A nomogram prediction model was developed based on the independent risk factors for APO in patients with HDP identified through multivariate logistic regression analysis, including disease severity, D-D, Scr, and UA (**Figure 1**). Each predictive factor was assigned a score according to its contribution to the outcome. The total score can then be used to estimate the risk of APO in HDP patients. **Figure 1** visually represents the contribution of each predictor to the total risk score. Each variable is aligned with a corresponding point scale, and the cumulative total points can be mapped to an estimated probability of APO at the bottom of the chart. This tool allows for intuitive bedside risk estimation.

Calibration analysis

The Hosmer-Lemeshow test indicated that the nomogram model demonstrated satisfactory goodness-of-fit and calibration (*P*=0.230), sug-

Table 4. Univariate logistic regression analysis of factors associated with APO in patients with HDP

	B	*SE*	*P*	OR (95% CI)
Age	0.099	0.049	0.042	1.104 (1.003-1.215)
Pre-pregnancy BMI (kg/m^2)	0.133	0.072	0.064	1.143 (0.992-1.316)
Educational background				
Primary school				Reference
Middle and high school	0.061	0.407	0.881	1.063 (0.478-2.361)
College	-0.186	0.388	0.631	0.830 (0.388-1.776)
Number of Pregnancies	-0.511	0.271	0.059	0.600 (0.353-1.020)
Gestational week	-0.144	0.104	0.166	0.866 (0.707-1.061)
Pre-conception screening				
No				Reference
Yes	-0.483	0.328	0.141	0.617 (0.325-1.173)
The severity of the disease				
Gestational hypertension				Reference
Preeclampsia	0.963	0.300	0.001	2.619 (1.454-4.718)
Eclampsia	2.512	1.134	0.027	12.324 (1.335-113.754)
History of miscarriage				
No				Reference
Yes	0.504	0.411	0.220	1.655 (0.739-3.703)
Family history of hypertension				
No				Reference
Yes	0.392	0.359	0.274	1.480 (0.733-2.991)
Fetal presentation				
Cephalic presentation				Reference
Breech presentation	0.290	0.430	0.500	1.337 (0.575-3.106)
Delivery method				
Vaginal birth				Reference
Cesarean delivery	0.346	0.334	0.301	1.414 (0.734-2.723)
Consistent folic acid supplementation during early pregnancy				
No				Reference
Yes	-0.612	0.333	0.066	0.542 (0.282-1.042)
HDL (mmol/L)	-0.791	0.421	0.061	0.454 (0.199-1.036)
LDL (mmol/L)	0.181	0.197	0.359	1.198 (0.814-1.763)
TG (mmol/L)	0.096	0.127	0.451	1.101 (0.858-1.412)
TC (mmol/L)	0.248	0.223	0.266	1.281 (0.828-1.983)
D-D (mg/L)	4.751	0.771	<0.001	115.701 (25.542-524.103)
Scr (μmol/L)	0.059	0.014	<0.001	1.061 (1.031-1.091)
UA (μmol/L)	0.014	0.003	<0.001	1.014 (1.008-1.019)
PLT (×10^9/L)	0.006	0.003	0.060	1.006 (1.000-1.013)
Hb (g/L)	0.016	0.010	0.132	1.016 (0.995-1.037)

Note: APO, adverse pregnancy outcomes; HDP, hypertensive disorders of pregnancy; OR, odds ratio; CI, confidence interval; SE, standard error; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; TC, total cholesterol; D-D, D-dimer; Scr, Serum creatinine; UA, uric acid; PLT, platelet count; Hb, hemoglobin.

gesting that the model accurately represents the actual data distribution (**Figure 2**).

Diagnostic performance evaluation

The area under the curve for the model was 0.888 (95% CI: 0.844-0.932), indicating strong discriminative capacity (**Figure 3**). The model demonstrated a sensitivity of 0.890, a specificity of 0.747, and an overall accuracy of 84.35%, highlighting its high diagnostic efficacy.

Clinical utility evaluation

The DCA, which plots net benefit on the y-axis and threshold probability on the x-axis, demonstrated that the net benefit remained above zero when the threshold probability ranged

Table 5. Multivariate logistic regression analysis of factors associated with APO in patients with HDP

	B	*SE*	*P*	OR (95% CI)
The severity of the disease				
Gestational hypertension				Reference
Preeclampsia	0.893	0.400	0.025	2.443 (1.116-5.348)
Eclampsia	3.786	1.659	0.023	44.086 (1.706-1139.549)
D-D (mg/L)	6.018	1.023	<0.001	410.744 (55.268-3052.610)
Scr (μmol/L)	0.094	0.020	<0.001	1.099 (1.057-1.142)
UA (μmol/L)	0.021	0.004	<0.001	1.021 (1.013-1.029)

Note: APO, adverse pregnancy outcomes; HDP, hypertensive disorders of pregnancy; OR, odds ratio; CI, confidence interval; SE, standard error; D-D, D-dimer; Scr, Serum creatinine; UA, uric acid.

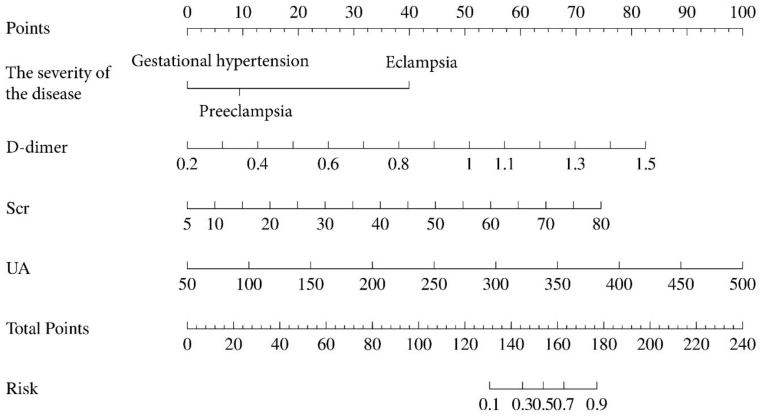

Figure 1. Nomogram prediction model. Note: Scr, Serum creatinine; UA, uric acid.

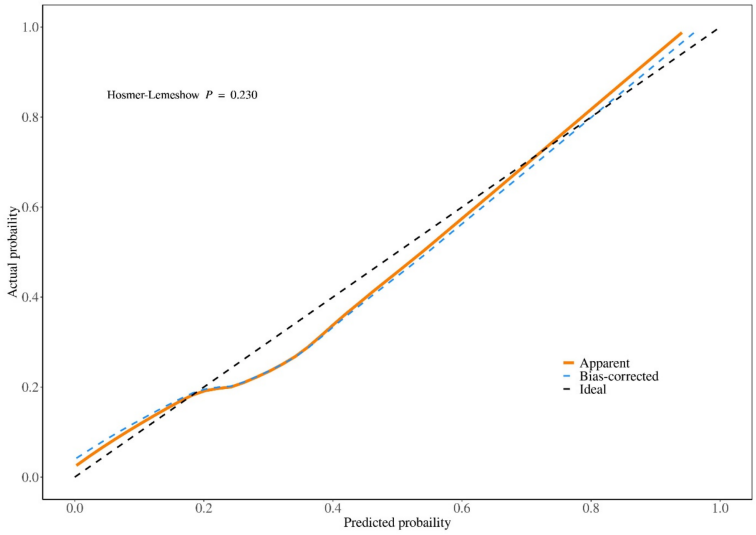

Figure 2. Calibration curves.

from 0.1 to 1. This finding suggested that the nomogram risk prediction model possessed favorable clinical utility (**Figure 4**).

Discussion

HDP are one of the most common complications during pregnancy and a significant contributor to APO. In this study, the incidence of APO among HDP patients was found to be 32.61%, which closely aligns with the 37.5% reported by Yan et al. [16]. This consistency highlights the elevated risk of APO in HDP patients. Identifying the main risk factors and building practical tools for early prediction plays a critical role in improving both maternal and neonatal outcomes. We analyzed the clinical data of 230 HDP patients and grouped them based on whether they experienced APO. We used multivariate logistic regression and found that disease severity, D-D, Scr, and UA were all independently linked to APO. Nomograms built on these variables excel in accuracy and clinical utility. They offer a robust tool for early identification of high-risk patients and support the development of personalized intervention strategies to enhance maternal and neonatal health outcomes.

As the disease progresses, the hemodynamic regulation of vital maternal organs and the placenta deteriorates, significantly increasing the

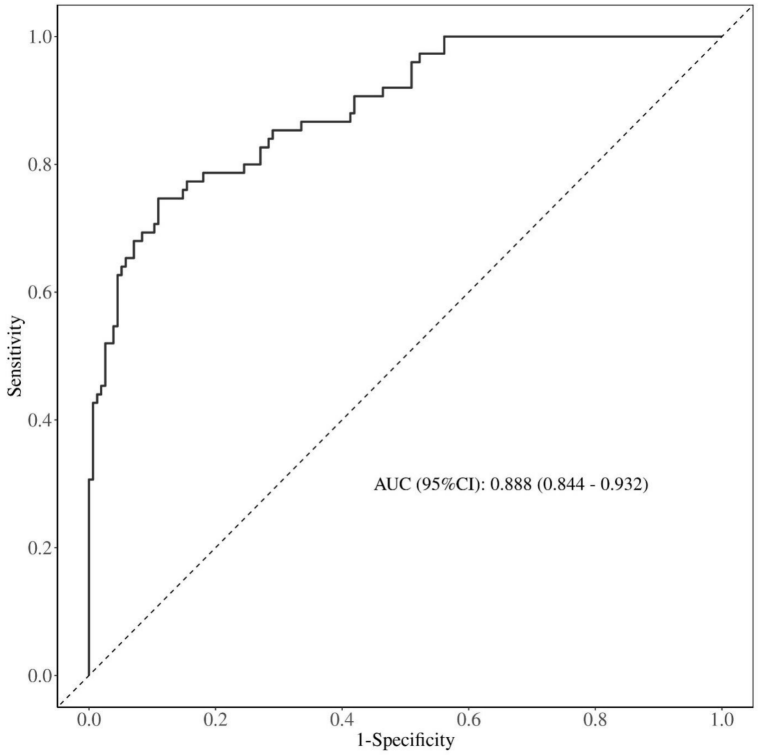

Figure 3. ROC curves. Note: ROC, receiver operating characteristic; AUC, area under curve; CI, confidence interval.

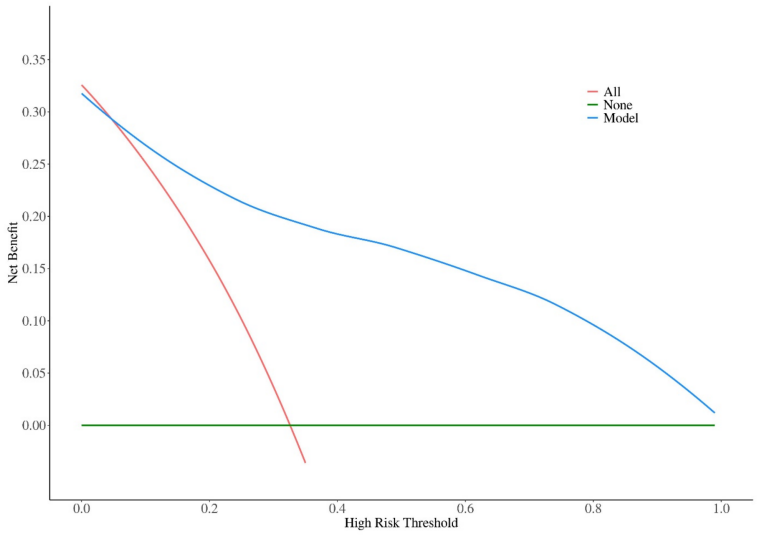

Figure 4. DCA. Note: DCA, decision curve analysis.

risk of APO. Our findings indicated that the progression of HDP was closely linked to an increased risk of pregnancy-related complications. In preeclamptic patients, endothelial dysfunction was especially pronounced. Endothelial cells pumped out too many inflammatory signals, setting off body-wide inflammation. This made blood vessels leaky, causing familiar problems like swelling and high blood pressure [17]. Furthermore, in preeclampsia, a localized chronic inflammatory state of the placenta might interfere with normal blood flow regulation mechanisms by disrupting vascular endothelial integrity, ultimately leading to reduced placental perfusion. This disrupted normal perfusion to the placenta and maternal organs, ultimately contributes to placental dysfunction. Poor placental blood flow, in turn, was closely linked to FGR, placental abruption, and higher rates of perinatal death [4, 18]. Burwick et al. reported that the risk of perinatal death was noticeably higher in women with severe preeclampsia compared to those with milder forms of the condition [19]. Razaz et al. [20] further emphasized that disrupted regulation of cerebral blood vessels during eclamptic seizures could cause sharp increases in perfusion pressure. This led to brain swelling and hemorrhage, two major contributors to maternal death in eclampsia.

To better understand how disease progression affects pregnancy outcomes through blood function disorders, it is necessary to focus on the impact of coagulation abnormalities in patients with HDP. Previous research has demonstrated that elevated blood pressure could easily damage the vascular endothelium. Once this protective barrier was compromised, normal coagulation balance was often disturbed as well [13]. In this study, we observed that D-D levels were significantly elevated in patients with APO. D-D is widely recognized as a marker of hypercoagulability, and its elevation may

also signal the early formation of microthrombi. Although the shift may appear minor, it carries real risks for both maternal and fetal health. In addition, platelet activation and impaired fibrinolysis in preeclampsia significantly increase the risk of thrombosis, further worsening placental perfusion disorders [21]. Several studies have also linked elevated D-D levels to the severity of preeclampsia, suggesting an increased risk of thromboembolic complications as the disease progresses [14, 22]. These findings emphasized the critical role of hemodynamic instability and impaired organ perfusion in the progression of HDP. Together with endothelial dysfunction and increased vascular resistance, these factors appear to drive the development of APO. Therefore, monitoring and managing disease progression in patients with HDP is essential to improve maternal and neonatal prognosis.

It is worth noting that the OR for both D-D and eclampsia in our multivariate model were exceptionally high, with wide CIs. This may indicate a degree of instability in the risk estimates, particularly for eclampsia, where the sample size is very limited. As such, the predictive value of eclampsia in the model should be interpreted with caution. This statistical limitation has been acknowledged as a potential source of reduced robustness in the model and highlights the need for validation in larger and more diverse patient populations.

This study demonstrated that Scr and UA were strongly associated with APO in patients with HDP, and supported the idea that attention to these markers during pregnancy could help identify potential risks in a timely manner. UA is a product of purine metabolism and is excreted mainly through the renal tubules [23]. In preeclampsia, prolonged arterial constriction affects placental blood supply, leading to hypoxia and metabolic disturbances and elevated lactate levels [24]. Increased lactate decreases the acid-excretory capacity of the renal tubules, making it difficult to excrete UA, ultimately resulting in elevated serum UA concentrations [25]. Ahmed et al. reported that elevated UA induced inflammatory responses and hyperactivated the immune system, thereby worsening systemic maternal inflammation and significantly increasing the risk of APO [26]. Natural killer cells are essential in early pregnancy, where they regulate immune balance and promote spiral artery remodeling through trophoblast invasion, ensuring adequate placental perfusion [27]. Elevated UA levels, however, may impair natural killer cell function and reduce their numbers, disrupting the remodeling process and exacerbating placental blood flow impairments [28]. This mechanism is thought to play a critical role in the pathogenesis of both HDP and preeclampsia. Scr serves as a key indicator of glomerular filtration rate, primarily excreted through glomerular filtration [12]. During normal pregnancy, Scr levels typically demonstrate a physiological decline due to increased blood volume and elevated glomerular filtration rate [29]. However, in patients with HDP, especially those with preeclampsia or eclampsia, renal function is often impaired to varying degrees, and Scr levels tend to be elevated [30]. Rising Scr values generally reflect reduced glomerular filtration capacity, potentially stemming from multiple pathological mechanisms, including renal ischemia, vascular endothelial damage, and microangiopathy [31, 32]. Previous studies have found that reduced renal perfusion in preeclampsia could lead to glomerular injury, which in turn lead to excretory dysfunction and accumulation of metabolic waste products [33, 34]. Furthermore, persistently elevated Scr may signify chronic hypertension-induced kidney damage [35]. Kang et al. demonstrated that increased Scr was significantly correlated with organ failure risk in preeclampsia patients, establishing it as an independent predictor of APO [36]. Thus, combined monitoring of Scr, D-D, and UA levels enables dynamic assessment of disease progression in HDP patients.

This study affirms that APO are closely linked to the severity of HDP and elevated levels of D-D, UA, and Scr. Based on these variables, we established a nomogram model that may serve as a useful clinical tool for early risk detection and tailoring individualized treatment strategies. Nonetheless, several limitations should be acknowledged. First, the selected biomarkers are limited in scope, primarily reflecting hematologic and renal functions, while ignoring placental indicators such as blood flow and perfusion. This exclusion may have led to the omission of important pathological mechanisms associated with APO. Incorporating imaging or Doppler studies in future research may

offer a more layered understanding. Second, the number of patients with eclampsia in our dataset is very small, which may have led to overestimated ORs and wide CIs in the regression model. This limitation affects the stability and generalizability of the predictive value associated with eclampsia. Next-phase research is expected to recruit larger, multi-center cohorts across different regions. Splitting data into training and validation sets will prove crucial information for building reliable tools that work for all populations.

Disclosure of conflict of interest

None.

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