ORIGINAL RESEARCH

# Prediction Model of Adverse Pregnancy Outcome in Pre-Eclampsia Based on Logistic Regression and Random Forest Algorithm

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## ABSTRACT

**Aim** • To construct a prediction model for adverse pregnancy outcomes of preeclampsia (PE). Thus assisting clinicians to identify high-risk patients. Provide guidance for treatment intervention.

**Methods** • A retrospective study was conducted on 319 PE patients admitted to the Huzhou Maternal and Child Health Hospital from April 2021 to December 2022, The patients were divided into an adverse group (93 cases) and a non-adverse group (226 cases) based on whether they had adverse pregnancy outcomes after admission. Collect clinical data from patients, using a single factor analysis to screen statistically significant indicators as input variables, the outcome of the analysis is dependent on the incidence of PE adverse pregnancy outcomes. Divide patients into training and testing sets in a 7:3 ratio, Logistic regression model and random forest model were constructed respectively. Evaluate the predictive performance of two statistical models.

**Results** • Among the 319 PE patients included 93 had adverse pregnancy outcomes after admission. Among them, Age (*OR*: 1.702, 95%*CI*: 1.069~2.710), small gestational age (*OR*: 0.757,95%*CI*: 0.607~0.945), more clinical symptoms (*OR*: 3.618, 95%*CI*: 1.682~7.783), high 24 h proteinuria (*OR*: 2.532, 95%*CI*: 1.290~4.968), low PLT index (*OR*: 0.616, 95%*CI*: 0.419~0.906), high AST index (*OR*: 1.554, 95%*CI*: 1.012~2.387), high D-Dimer index (*OR*:1.966, 95%*CI*: 1.183~3.267) were the influencing factors of adverse pregnancy outcomes in PE patients. The test set found that the random forest model was superior to the Logistic regression model in predicting the risk of adverse pregnancy outcomes in PE patients.

**Conclusions** • The random forest model has good stability in predicting the risk of adverse pregnancy outcomes in PE, and its prediction efficiency is better than the Logistic regression model. (*Altern Ther Health Med.* 2024;30(1):142-147).

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## INTRODUCTION

The global incidence rate of preeclampsia (PE) is about 2%~8%, Approximately 50000 to 60000 maternal PE deaths per year worldwide.[1,2] The etiology of PE is currently unclear, Elevated blood pressure and proteinuria are the first symptoms, and the disease can be progressive and worsened at any time, The risk of adverse pregnancy outcomes, such as maternal pleural and peritoneal effusion, placental abruption, fetal intrauterine hypoxia, premature delivery, postpartum hemorrhage, is high.[3,4] This situation could be linked to premature termination of pregnancy or continued pregnancy in women with PE. Premature termination of pregnancy could lead to poor fetal development, increasing the risk of perinatal complications and even death. On the other hand, continuing with the pregnancy while having PE could increase the risk of malignant outcomes for the mother and her baby. Therefore, we are exploring the influencing factors of PE adverse pregnancy outcomes, the corresponding risk prediction model should also be built to assess the risk of adverse pregnancy outcomes of PE pregnant women, then the medical staff can accurately measure the advantages and disadvantages, and take measures to ensure the maximum benefit of mothers and children.

At present, the prediction model for the risk of adverse pregnancy outcomes of PE pregnant women is mainly based on multivariate regression analysis to draw a nomogram for risk stratification, this method requires high data fitting to align with inclusion criteria and is subjected to bias due to differences between sample and data feature distributions in real clinical scenarios. Therefore, the external data validation effect is often poor. As a typical representative of the machine learning algorithm, the random forest algorithm has made significant progress in the prediction of other diseases and proved its robustness.[5,6] However, the application of a random forest algorithm in the risk prediction of adverse pregnancy outcomes of PE pregnant women is rarely reported. To accurately assess the risk of adverse pregnancy outcomes in PE patients, This study analyzed the factors influencing the risk of adverse pregnancy outcomes of PE pregnant women and constructed a logistic regression model formula, then The data was preprocessed relying on data mining technology by a machine learning algorithm, Draw a nomogram of the logistic regression model, Make it intuitive and practical; Build a random forest model with the help of random forest algorithm, and compare it with Logistic regression model. The study aims to provide medical staff with a more accurate risk prediction model of PE pregnant women's adverse pregnancy outcomes.

## MATERIALS AND METHODS

### Study population

A retrospective study was conducted on 319 PE patients admitted to the Huzhou Maternal and Child Health Hospital from April 2021 to December 2022, Divide patients into adverse and non-adverse groups based on whether they experienced adverse pregnancy outcomes after admission. Inclusion criteria: (1) The diagnostic criteria of PE in the "Guidelines for the Diagnosis and Treatment of Pregnancy-induced Hypertension" issued by the United States in 2013 were met[7]; (2) Complete clinical data; (3) Age ≥ 20 years. Exclusion criteria: (1) Combined with a malignant tumor, chronic hypertension, chronic diabetes, chronic kidney disease, and other complications; (2) In addition to PE, pregnancy anemia, gestational diabetes there are complications such as gestational anemia, gestational diabetes, and gestational thyroid disease; (3) gestational age < 28 weeks; (4) Pregnancy by assisted reproductive technology; (5) Multiple pregnancies; (6) Have a history of uterine surgery; (7) Uterine malformation; (8) Patients with clinical outcomes before collecting predictive data. This study has been approved by the Medical Ethics Committee of Huzhou Maternal and Child Health Hospital.

### Research method

**Material gathering.** Log in to the electronic medical record system of Huzhou Maternal and Child Health Hospital. The PE patient's basic information, age, fertility history, and gestational age at admission, was collected. The number of clinical symptoms at admission, such as headache, vertigo, chest tightness, chest pain, nausea and vomiting, blurred vision, dyspnea, and edema, are recorded. Blood pressure at admission [diastolic blood pressure (DBP), systolic blood pressure (SBP)] is measured. Also, Blood indexes testing [hemoglobin (Hb), platelet count (PLT), albumin (Alb), serum creatinine (Scr), blood urea nitrogen (BUN), total bilirubin (T-BIL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), D-Dimer, fibrinogen (Fib), activated partial thromboplastin time (APTT)] are performed, and 24h proteinuria quantitative indicators are tested.

### Adverse pregnancy outcomes

Any one of the following is judged as an adverse pregnancy outcome.

### Maternal adverse outcomes

Placental abruption, based on ultrasound diagnosis and postpartum placental examination,; Hemolysis, elevated liver enzymes and thrombocytopenia syndrome (Microvascular hemolysis, elevated liver enzymes, PLT count < $100 \times 10^9$); Eclampsia, refers to the new onset of tonic clonus in PE patients without other causes; Retinal detachment, refers to the separation of the patient's retinal nerve sensory layer from the lower retinal pigment epithelium and choroid; Reversible posterior leukoencephalopathy syndrome, refers to the patient's symptoms such as sharp rise in blood pressure, headache, visual impairment, disturbance of consciousness, and neuroimaging suggests reversible edema dominated by bilateral posterior white matter; Renal function was impaired considering if there was no history of kidney disease, creatinine > 150 μmol/L; or there was a history of kidney disease, creatinine > 200 μmol/L; Postpartum hemorrhage, refers to the fetus within 24 h after delivery, vaginal delivery blood loss > 500 mL, cesarean section blood loss > 1000 mL.

### Perinatal infant adverse outcome

Fetal growth restriction where fetal weight or abdominal circumference estimated by ultrasound is lower than the 10th percentile of the same gestational age; Fetal distress, which refers to the fetus in the uterus due to hypoxia and endangered fetal health; Neonatal asphyxia (Apgar score ≤ 7); Neonatal low birth weight, refers to the full-term fetus within 1 h after birth the first weighing less than 2500 g.

### Data preprocessing

The nomogram and random forest of the Logistic regression model are set according to machine learning. All selected patients were randomly divided into a training set (223 cases ) and a test set (96 cases) by a 7:3 ratio.

### Statistical analysis

SPSS version 19.0 software (International Business Machines Corporation) was used for data analysis. The measurement data were expressed as (Mean ± SD). The results of homogeneity of variance between groups were compared by *t* test. Count data are expressed as rates or proportions. The Chi-square ($\chi^2$) test was used for comparison between groups; $P < .05$ indicated that the difference was statistically significant. Multi-factor logistic regression analysis was used to screen the influencing factors. Then the occurrence of adverse pregnancy outcome was taken as the outcome variable. Visualize each influencing factor in the training set to obtain a nomogram; Run Random Forest code using R software (R3.4.3) in the training set and randomly select 70% samples using the Bootstrap

**Table 1**. Characteristics and single factor analysis of PE patients in training centers

| Factors | abnormal group (n = 93) | Non-adverse group (n = 226) | $t/\chi^2$ | P value |
|---|---|---|---|---|
| Age (years) | 29.19±3.07 | 26.94±3.15 | 5.841 | <.001 |
| Primipara | 68/93 | 151/226 | 1.271 | .270 |
| Gestational week (week) | 34.78±3.15 | 36.52±3.09 | 4.545 | <.001 |
| Number of symptoms (pcs) | 3.06±0.72 | 2.51±0.67 | 6.518 | <.001 |
| DBP (mm Hg) | 103.77±14.98 | 101.35±14.53 | 1.340 | .181 |
| SBP (mm Hg) | 155.81±19.63 | 152.93±15.49 | 1.392 | .165 |
| 24-h proteinuria (g) | 3.46±0.82 | 2.73±0.68 | 8.191 | <.001 |
| Hb (g/L) | 117.35±17.59 | 119.06±16.54 | 0.824 | .411 |
| PLT ($\times 10^9$/L) | 130.29±34.81 | 148.75±40.26 | 3.866 | <.001 |
| Alb (g/L) | 29.76±4.58 | 30.21±4.95 | 0.754 | .452 |
| Scr (μmol/L) | 68.01±15.42 | 64.93±15.15 | 1.695 | .091 |
| BUN (mmol/L) | 6.07±1.83 | 5.85±1.76 | 1.003 | .317 |
| T-BIL (μmol/L) | 9.28±2.54 | 8.79±2.38 | 1.638 | .102 |
| ALT (U/L) | 28.92±9.05 | 27.95±8.73 | 0.892 | .373 |
| AST (U/L) | 37.53±11.87 | 32.52±9.98 | 3.850 | <.001 |
| D-Dimer (mg/L) | 0.75±0.16 | 0.58±0.12 | 10.390 | <.001 |
| Fib (g/L) | 3.86±1.08 | 4.07±1.13 | 1.528 | .128 |
| APTT (s) | 30.31±3.78 | 29.83±2.69 | 1.279 | .202 |

**Figure 1**. The expression of the logistic regression model of risk of adverse pregnancy outcome

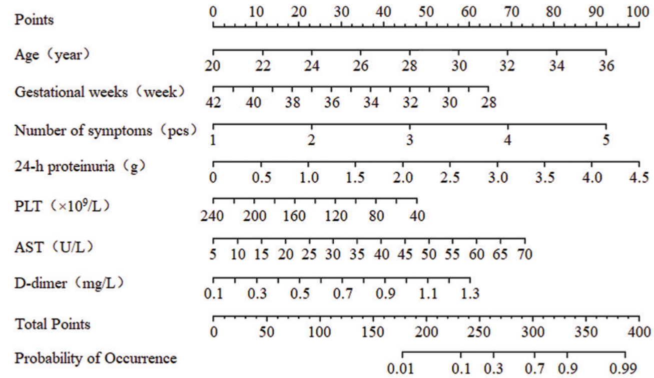
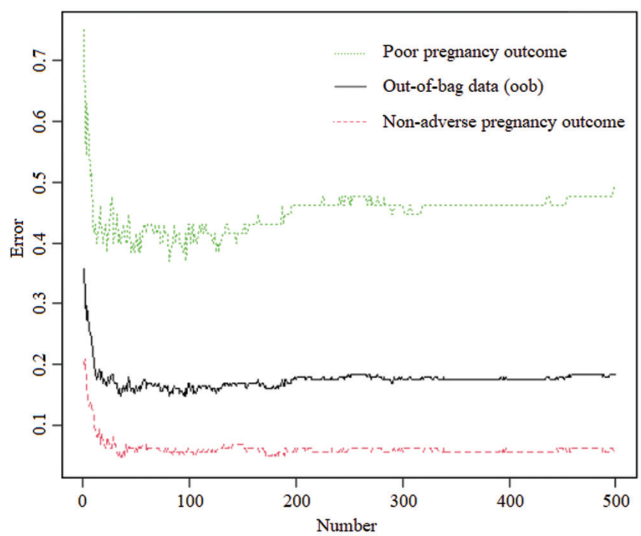



**Table 2**. Multivariate logistic regression analysis of adverse pregnancy outcome in PE patients

| Variable | β | SE | Wald $\chi^2$ | P value | OR (95%CI) |
|---|---|---|---|---|---|
| Age | 0.532 | 0.237 | 5.039 | .025 | 1.702 (1.069 - 2.710) |
| Gestational week | -0.278 | 0.113 | 6.052 | .014 | 0.757 (0.607 - 0.945) |
| Number of symptoms | 1.286 | 0.391 | 10.818 | .001 | 3.618 (1.682 - 7.783) |
| 24-h proteinuria | 0.929 | 0.344 | 7.293 | .007 | 2.532 (1.290 - 4.968) |
| PLT | -0.485 | 0.197 | 6.061 | .014 | 0.616 (0.419 - 0.906) |
| AST | 0.441 | 0.219 | 4.055 | .045 | 1.554 (1.012 - 2.387) |
| D-Dimer | 0.676 | 0.259 | 6.812 | .009 | 1.966 (1.183 - 3.267) |
| Constant | -7.953 | 1.802 | 19.478 | <.001 | - |

**Figure 2.** Random forest prediction model for adverse pregnancy outcome of PE patients: the relationship between model error and random number




method to establish a random forest model, the model construction process mainly includes two important model parameters, they are the decision tree quantity (ntree) and the maximum depth of the number (mtry). Using grid search to optimize the parameters of ntree and mtry, Evaluate the importance of variables through the out-of-pocket error rate to explain the random forest model. The test set was introduced to verify the accuracy, sensitivity, specificity, recall rate, accuracy, and area under curve (AUC) of the prediction model to evaluate the predictive efficacy of the two statistical models.

## RESULTS

### Clinical characteristics and univariate analysis of PE patients

Among the 319 PE patients included 93 had adverse pregnancy outcomes after admission. There was a statistically significant difference between the adverse group and the non-adverse group in terms of age, gestational age at admission, number of clinical symptoms, 24-hour proteinuria quantification, PLT, AST, and D-Dimer indicators ($P < .001$).

### Multivariate logistic regression analysis

The dependent variable was whether PE patients (0 = no, 1 = yes) had adverse pregnancy outcomes. Using statistically significant indicators in univariate analysis as independent variables. Multivariate Logistic regression analysis showed that. Older age, smaller gestational age, more clinical symptoms, higher 24-hour proteinuria, lower PLT index, higher AST index, and higher D-Dimer index were the influencing factors of adverse pregnancy outcomes in PE patients ($P < .05$).

### Construction of logistic regression model

Based on the influencing variables selected in multivariate logistic regression analysis. Logistic regression model equation was constructed: Logit ($p$) = 0.532 × age-0.278 × gestational age + 1.286 × number of clinical symptoms + 0.929 × 24-h proteinuria quantification-0.485 × PLT + 0.441 × AST + 0.676 × D-Dimer-7.953. Among the 319 PE patients included. Bootstrap was used to extract 70% of the sample size. The nomogram of the logistic regression model was obtained by R software (Figure 1). The total score is obtained by visually displaying the corresponding scores of each index value. The total score was converted into the prediction probability of adverse pregnancy outcomes in PE patients.

### Random forest model construction of adverse pregnancy outcomes in PE patients

Among 319 PE patients included, A random forest training model was constructed by bootstrap self-extracting 70% of sample size data, It was found that when ntree=500

**Figure 3.** Random forest model of risk of adverse pregnancy outcome in PE patients: measurement of importance of input variables

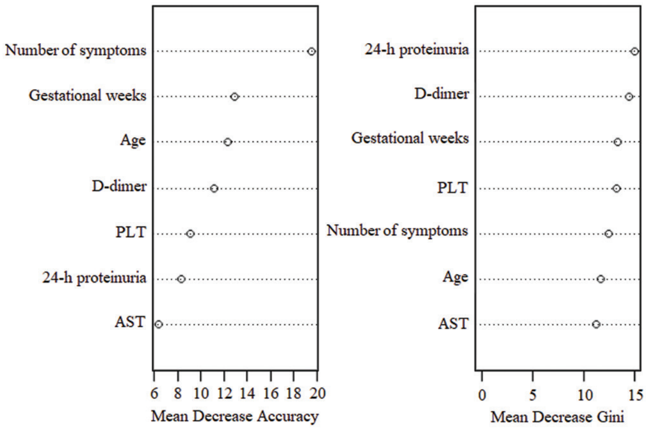
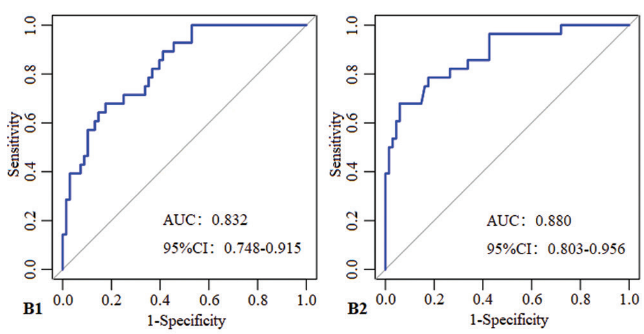



**Table 3.** Comparison of prediction efficiency between logistic regression model and random forest model

| Testing set | Accuracy (%) | Sensitivity (%) | Specificity (%) | Recall (%) | Accuracy (%) | AUC |
|---|---|---|---|---|---|---|
| Logistic regression model | 0.781 | 0.838 | 0.643 | 0.838 | 0.851 | 0.832 |
| Random forest model | 0.854 | 0.956 | 0.657 | 0.956 | 0.855 | 0.880 |

**Figure 4.** ROC curves of the two models verified in the test set (B1 logistic regression model, B2 random forest model)




and mtry=5, the error tends to stabilize, (Figure 2). According to the parameter mtry=5, ntree=500, Build the best model, the random forest model can express the importance ranking of characteristic variables, based on changes in overall prediction accuracy, ranking of influencing variables for adverse pregnancy outcomes in PE patients: 24-h proteinuria > D-Dimer > Gestational weeks > PLT > Number of symptoms > Age > AST, See Figure 3.

**Comparison of model prediction efficiency**

Introducing a test set to validate the effectiveness of two models shows that: The random forest model is superior to the Logistic regression model in identifying adverse pregnancy outcomes in actual patients, the accuracy of the random forest model is 0.854, the sensitivity is 0.956, the specificity is 0.657, the recall rate is 0.956, the accuracy is 0.855, and the AUC is 0.880 (Figure 4), all of which are higher than the Logistic regression model. It shows that the random forest model is more effective in predicting the risk of adverse pregnancy outcomes in PE patients,

## DISCUSSION

PE is one of the three leading causes of maternal mortality.[8-11] To reduce mortality. The severity of the disease must be controlled. The prediction of the occurrence of PE adverse outcomes is critical. Therefore, it is necessary to find out the influencing factors of PE adverse pregnancy outcomes. and build the corresponding risk prediction model. To carry out an individualized and systematic risk assessment for patients and take effective preventive measures.

This study found that factors such as older age, smaller gestational age at admission, more clinical symptoms, higher 24-hour proteinuria, lower PLT index, higher AST index, and higher D-Dimer index were associated with adverse pregnancy outcomes in patients with preeclampsia. The reasons that these factors contribute to adverse pregnancy outcomes are, (1) Advanced age was positively correlated with pregnancy loss, premature delivery, fetal growth restriction, and gestational diabetes mellitus.[12] It can be seen that age is related to adverse pregnancy outcomes. It may be the decline of reproductive system function in elderly pregnant women. Belonging to high-risk groups. Pregnancy complications are prone to occur. Increased risk of adverse pregnancy outcomes.[13] Therefore it is necessary to pay more attention to the management and health care of elderly PE patients during pregnancy. (2) To a certain extent, gestational age can reflect the full degree of fetal development. However, PE patients often terminate pregnancy earlier where delivery can happen before the 34th week, due to the fetus being underdeveloped, premature birth greatly increases the risk of adverse outcomes such as neonatal asphyxia and low birth weight. Additionally, in patients with preeclampsia, blood pressure increases and its fluctuations can have a destructive effect on the blood vessel wall, leading to increased vascular endothelial damage. This can cause the uteroplacental artery to spasm and contract, resulting in ischemia and hypoxia in the placenta and uterus, which ultimately affects fetal development. (3) PE patients with clinical symptoms, such as headache, dizziness, chest tightness, chest pain, nausea and vomiting, blurred vision, dyspnea, and edema, are more likely to have adverse outcomes than asymptomatic patients.[14,15] It may be that PE patients have more clinical symptoms, It indicates that the more serious the disease is, The greater the risk of adverse pregnancy outcomes. The clinical symptoms of PE patients are closely related to the severity of their urine protein. Because proteinuria is caused by the loss of albumin from urine in patients, Hypoalbuminemia can be induced to some extent that makes the body colloid osmotic pressure drop leading to brain edema and fundus edema manifesting in clinical symptoms such as headache and blurred vision.[16] However, the urine protein content of PE patients increased in 24 which can worsen capillary leakage and lead to pleural and peritoneal effusion. It also results in poor fetal nutrition and growth restriction, increasing the risk of premature delivery. In patients with preeclampsia, a high 24-hour urine protein content can significantly reduce the PLT blood cell index, which in turn increases the risk of adverse postpartum hemorrhage outcomes.[17] (4) Systemic small-vessel spasm, activation or injury of vascular endothelial cells, and inadequate placental perfusion are currently considered the basic physiological and pathological changes in the occurrence and development of PE, Among them, systemic vasospasm can directly affect the blood supply of various organs. The liver acts as a detoxifying organ, The decrease of blood supply to other organs will affect the blood supply to the liver, It leads to hepatocyte ischemia, hypoxia, cell swelling, and increased cell membrane permeability, increasing the release of microsomal enzymes in liver cells, Up-regulate AST expression level. The increase in the AST index indicates the damage to liver function, which will increase the adverse pregnancy outcome.[18] (5) During normal pregnancy, The blood in the mother is in a relatively hypercoagulable state, However, there is still a physiological dynamic balance between the coagulation system and the fibrinolytic system. D-dimer is a common indicator of coagulation/fibrinolysis system. The research found that the level of D-dimer in PE patients is higher than that in normal pregnancy.[19] This suggests that patients with PE experience a pathological imbalance between their coagulation and fibrinolytic systems. The body may produce more factors related to coagulation or fibrinolysis due to systemic vasospasm and damage to the vascular endothelium in PE patients. This damages the fibrinolysis process and leads to hypercoagulation in the body.[20] However, a high level of D-dimer can cause intravascular coagulation easily, leading to microthrombosis which makes the surface of vascular endothelial cells form fibrin deposits,[21-23] Thus affecting the transport and exchange of nutrients and oxygen in the capillary bed, resulting in insufficient blood supply to the placenta increasing the risk of adverse pregnancy outcomes such as premature delivery, small for gestational age infants, and placental abruption.

The traditional logistic regression model has very good interpretability where the expression form of nomogram can be obtained from the visualization of features, it enables doctors to intuitively and conveniently calculate the outcome probability of patients or an event.[24] Because the model is simple, it is easy to have problems with fitting bias and low overall efficiency of the model.[25] With the development of intelligent medicine, Machine learning technology has better advantages than traditional statistical methods, it has been widely used in the prediction and diagnosis of diseases.[26] Machine learning selects effective data from large sample data sets, draws a successively distributed framework, and can better fit the data distribution in high-dimensional data space.[27] The clinical data is complex, therefore, its data volume is large. To improve the prediction efficiency of adverse pregnancy outcomes in PE patients, machine learning was employed using the random forest algorithm. The data was fitted and yielded better prediction accuracy compared to the logistic regression model. The random forest model demonstrated higher accuracy, sensitivity, specificity, recall, accuracy, and AUC area of the ROC curve. This proves the superiority of the machine learning algorithm and can aid clinicians in assessing the risk of adverse pregnancy outcomes in PE patients using similar methods.

In summary, the risk of adverse pregnancy outcomes in PE patients was related to age, gestational weeks in the hospital, number of clinical symptoms, 24-hour proteinuria, PLT, AST, and D-Dimer. The prediction model is established based on a machine learning-random forest algorithm, it can accurately predict the risk of adverse pregnancy outcome in PE patients.

The limitation of this study is a single-center retrospective study, conducts model building with a single sample source, and the sample size is too small. Therefore, the clinical practicality and generalizability of this predictive model still need to be further validated and optimized through prospective studies with a large sample size to improve the predictive performance of the model.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest for this article.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions. Nevertheless, all data that is essential to the understanding of our manuscript is included in the Results section and the Tables.

## FUNDING

This study was supported by the Huzhou Science and Technology Bureau Project ( Project number: 2022GYB60).

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