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Hypertension Progression, Preeclampsia, Postpartum, Influencing Factors, Nomogram

**Abstract**

Introduction
Preeclampsia is a pregnancy-related hypertensive disorder with long-term cardiovascular risks. The aim of this study was to explore the influencing factors of hypertension progression in preeclampsia patients within five years postpartum, and to construct a nomogram.

Material and methods
A retrospective study of 280 preeclampsia patients, grouped by hypertension progression status within 5 years postpartum. Differential analyses compared: 1) demographic/pregnancy characteristics, and 2) late-pregnancy, 1-week-postpartum,and 6-week-postpartum blood indicators between groups. Multiple logistic regression and generalized estimating equations (GEE) identified hypertension progression factors. Significant factors built a nomogram evaluated via calibration and receiver operating characteristic (ROC) curves in training/test sets.

Results
Patients who progress to hypertension have higher pre-pregnancy and postpartum body mass index (BMI), a greater proportion of early-onset and severe preeclampsia, and a higher incidence of adverse pregnancy outcomes compared to those who do not progress to hypertension. Additionally, they have lower platelet levels during late pregnancy and postpartum, while levels of aspartate aminotransferase, alanine aminotransferase, 24-hour urinary protein, uric acid, and C-reactive protein are higher in patients who do not progress to hypertension. Multivariate logistic regression identified placental abruption, oligohydramnios, and umbilical artery pulsatility index as significant factors, while the generalized estimating equation highlighted uric acid, platelet, and alanine aminotransferase as key predictors. The nomogram demonstrated good predictive performance, as shown by calibration and ROC curves.

Conclusions
Hypertension progression correlates with placental abruption, oligohydramnios, elevated UA-PI, elevated UA, decreased PLT, elevated ALT, and specifically postpartum 1-week AST. The nomogram aids early identification of high-risk patients.

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## Running Title: Postpartum Hypertension Prediction Model

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**Author's contribution**

Yanli Xu and Huafang Liu designed the research study; Yanli Xu, Huafang Liu, Xiaodi Kang, Hongli Jiang, and Wenjing Wang performed the research; Yanli Xu and Huafang Liu collected and analyzed the data. Yanli Xu and Xiaodi Kang has been involved in drafting the manuscript and all authors have been involved in revising it critically for important intellectual content. All authors give final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all

aspects of the work in ensuring that questions related to its accuracy or integrity

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**Conflict of Interest**

The authors declare that there is no competing interest associated with the manuscript.

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**Ethics Clearance**

This paper has been reviewed by relevant departments of our hospital, such as the Science and Education Department, Medical Department and Ethics Committee of Beijing Ditan Hospital Affiliated Capital Medical University. The research content involved in this research meets the requirements of medical ethics and academic morality of our hospital, and the research content is reasonable, the risks are controllable, and there are no violations. The relevant research carried out is in line with the safe, standardized and true scientific research guiding principles, and in line with the requirements of the clinical research ethics code.

**Availability of Data and Materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Hypertension progression correlates with placental abruption, oligohydramnios, elevated UA-PI, elevated UA, decreased PLT, elevated ALT, and specifically postpartum 1-week AST. The nomogram aids early identification of high-risk patients.

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## 1. Introduction

Preeclampsia (PE) is a pregnancy-related hypertensive disorder that typically develops after twenty weeks of gestation, characterized by high blood pressure and damage to multiple organs [1], [2]. This disease poses a serious threat to the health of pregnant women and infants, and may lead to hypertension, cardiovascular damage [3], kidney damage [4], liver damage, multiple organ failure, etc. And it may also continue to affect the cardiovascular health of the mother after childbirth. The exact cause of preeclampsia is not yet fully understood, but it is currently believed to be the result of multiple mechanisms such as placental dysfunction, maternal endothelial dysfunction [5],

immune abnormalities [6], and genetic factors working together [7], [8]. Its global incidence rate is about 2%~8% [9]. In the past 20 years, with the increase of advanced maternal age and the application of assisted reproductive technology [10], the overall incidence rate has increased [11].

In recent years, studies have shown that some preeclampsia patients do not recover normal blood pressure after delivery, but continue to maintain a state of hypertension, and even progress to chronic hypertension (CH) [12]. According to statistics, approximately 15% -25% of preeclampsia patients still have postpartum hypertension [13], [14], and these patients have a significantly increased risk of developing cardiovascular diseases in the future, including hypertension, coronary heart disease, stroke, etc. Therefore, identifying the risk factors for postpartum hypertension progression in preeclampsia patients and developing effective predictive models is of great clinical significance for optimizing pregnancy and postpartum follow-up management.

At present, multiple studies have shown that preeclampsia is a risk factor for various cardiovascular diseases [15], [16], but the factors that affect the progression of preeclampsia patients to cardiovascular diseases such as hypertension, have not been fully studied. Factors such as age and body mass index (BMI), as well as the subtypes of preeclampsia, have been shown to be closely related to the development of the disease, but it remains unclear whether these factors will continue to impact patients' vascular and other organ functions after delivery. Moreover, the incidence of hypertension and cardiovascular diseases is increasing globally year by year, making it of significant clinical and public

health importance to identify the factors that contribute to the progression of preeclampsia patients to hypertension postpartum. The purpose of this study is to address this gap. We expect to identify significant influencing factors for the progression of hypertension through multiple logistic regression analysis and generalized estimating equations, and further construct a nomogram model to predict the probability of individuals with preeclampsia progressing to hypertension.

## 2. Materials and Methods

### 2.1 Research Object

This retrospective study included 280 preeclampsia patients who gave birth in our hospital from January 2017 to January 2019. The inclusion criteria were: 1) Age $\geqslant$ 18 years; 2) Pregnant women over 20 weeks of gestation; 3) Diagnosed with preeclampsia according to the American College of Obstetricians and Gynecologists (ACOG) 2013 criteria; 4) Complete clinical data. The exclusion criteria were: 1) having hypertension or other cardiovascular diseases that may interfere with the study before pregnancy; 2) Major immune system and other coagulation disorders; 3) Severe liver and kidney dysfunction; 4) Serious mental illness or poor compliance; 5) Follow up not completed.

### 2.2 Data Collection

We collected baseline data such as age, pre pregnancy BMI, postpartum BMI, subtypes of preeclampsia, severity of preeclampsia, family history of cardiovascular disease, and pregnancy related data such as the occurrence of fetal growth restriction and the presence of hemolysis, elevated liver enzymes, and low platelets syndrome (HELLP) syndrome.

We collected production-related data, such as whether the patient had a premature birth or underwent a cesarean section. We also collected Edinburgh Postnatal Depression Scale (EPDS), Generalized Anxiety Disorder-7 (GAD-7), Uterine Artery Pulsatility Index (UtA-PI), and Umbilical Artery Pulsatility Index (UA-PI) from late pregnancy. We also collected the levels of platelets (PLT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), 24-hour urinary protein (24-hour UP), uric acid (UA), and C-reactive protein (CRP) in the late pregnancy, one week postpartum, and six weeks postpartum.

Hypertension was defined as an interval of at least one day and a systolic blood pressure of $\geqslant$ 140 mmHg or a diastolic blood pressure of $\geqslant$ 90 mmHg. The measurement method is to sit still for at least 5 minutes, use a suitable cuff to measure upper arm blood pressure, and take the average of 2-3 measurements. Document the diagnosis of hypertension in all patients within 5 years postpartum.

**2.3 Statistical analysis**

All analyses in this study were conducted using R 4.4.0 software. For continuous data, Mann Whitney U test or t-test is used, represented by median (minimum maximum). For categorical data, chi square test or Fisher's exact test is used, represented by frequency (percentage). Using multiple logistic regression analysis to calculate the odds ratio (OR) value and 95% confidence interval (CI), explore the influencing factors of hypertension progression. The generalized estimating equations (GEE) was applied to conduct a longitudinal analysis of blood indicators (including platelet count, uric acid, and ALT)

measured in the third trimester, one week postpartum, and six weeks postpartum, in order to explore their dynamic changes and association with the development of postpartum hypertension. Subsequently, a nomogram prediction model was constructed based on significant factors identified by multivariate logistic regression and GEE. The model's discriminative ability and predictive performance were evaluated in both the training and testing sets using receiver operating characteristic (ROC) curves and the area under the curve (AUC), verifying its clinical utility. All statistical tests are two-sided tests, and $P<0.05$ is considered statistically significant.

## 3. Results

### 3.1 Differences in demographic and disease characteristics between preeclampsia patients who have progressed to hypertension and those who have not progressed to hypertension

Patients who progressed to hypertension had significantly higher pre-pregnancy BMI (30.4 vs 28.7, P=0.0469) and postpartum BMI (31.4 vs 29.4, P=0.0052), as well as a higher proportion of early-onset preeclampsia (30.61% vs 17.03%, P=0.0134) and severe preeclampsia (40.82% vs 21.43%, P=0.0010).

They also had a significantly higher incidence of fetal growth restriction (33.67% vs 20.33%, P=0.0206), placental abruption (15.31% vs 3.3%, P=0.0007), preterm birth (27.55% vs 11.54%, P=0.0013), and oligohydramnios (25.51% vs 9.34%, P=0.0006). Additionally, their EPDS score (11 vs 9, P=0.0105), GAD-7 score (12 vs 10, P=0.02), UtA-PI (1.9 vs 1.8, P=0.0062), and UA-PI (1.9 vs 1.9, P=0.0255) were significantly

higher than those who did not progress to hypertension (Table 1).

**3.2 Differences in blood indicators between patients with and without hypertension during late pregnancy, one week postpartum, and six weeks postpartum**

The results showed that patients who progressed to hypertension in late pregnancy (128 vs 137 × $10^9$/L, P=0.0112), The platelet levels at one week postpartum (170 vs 188 × $10^9$/L, P=0.0251) and six weeks postpartum (201 vs 230 × $10^9$/L, P=0.00764) were significantly lower than those in patients who did not progress to hypertension. The AST levels in patients who progressed to hypertension were significantly higher at one week postpartum (48.6 vs 46.0 U/L, P=0.00495) and six weeks postpartum (36.3 vs 34.1 U/L, P=0.0267) compared to those who did not. Similarly, ALT levels were significantly higher in the hypertension group at late pregnancy (72.2 vs 66.3 U/L, P=0.0161), one week postpartum (46.9 vs 43.6 U/L, P=0.0297), and six weeks postpartum (38.6 vs 34.1 U/L, P=0.0023). 24-hour urinary protein levels were also significantly higher in the hypertension group at late pregnancy (710.4 vs 634.4 mg/24h, P=0.0154), one week postpartum (352.1 vs 325.5 mg/24h, P=0.0383), and six weeks postpartum (245.7 vs 229.2 mg/24h, P=0.0319). Uric acid levels were significantly higher at late pregnancy (6.4 vs 6.2 mg/dL, P=0.0132), one week postpartum (5.5 vs 5.4 mg/dL, P=0.0213), and six weeks postpartum (4.4 vs 4.2 mg/dL, P=0.00841) in patients who developed hypertension. Similarly, CRP levels were significantly higher in the hypertension group at late pregnancy (22.1 vs 20.5, P=0.0191), one week postpartum (9.8 vs 8.7, P=0.0118), and six weeks postpartum (4.2 vs 3.7, P=0.0263) (Table 2).

### 3.3 Multivariate logistic regression screening for independent influencing factors of hypertension

The results showed that postpartum BMI (OR=1.019, 95% CI: 1.004-1.035, P=0.016), pregnancy depression (EPDS) (OR=1.019, 95% CI: 1.005-1.033, P=0.007), pregnancy anxiety (OR=1.016, 95% CI: 1.004-1.028, P=0.010), uterine artery pulsatility index (UtA-PI) (OR=1.229, 95% CI: 1.078-1.401, P=0.002), and the umbilical artery pulsatility index (UA-PI) (OR=1.239, 95% CI: 1.023-1.500, P=0.029) were all significantly positively correlated with the progression of hypertension. There was also a significant positive correlation between placental abruption (OR=1.438, 95% CI: 1.196-1.728, P=0.000), premature birth (OR=1.200, 95% CI: 1.052-1.368, P=0.007), oligohydramnios (OR=1.255, 95% CI: 1.092-1.442, P=0.002), and the development of hypertension. Additionally, the severity of the disease (OR=1.180, 95% CI: 1.057-1.317, P=0.003) was significantly positively correlated with the development of hypertension, and the subtypes of preeclampsia (OR=0.866, 95% CI: 0.770-0.973, P=0.017) were significantly negatively correlated with the development of hypertension, indicating a lower likelihood of late-onset preeclampsia progressing to hypertension (Table 3). The top three most significant factors are placental abruption, oligohydramnios, and umbilical artery pulsatility index.

### 3.4 Screening Progress of Generalized estimating equations for Influencing Factors of Hypertension

The results showed that platelet count (PLT) was significantly negatively correlated with

the progression of hypertension ( β =-0.008, p<0.001). Alanine aminotransferase (ALT) was significantly positively correlated with the progression of hypertension ( β =0.034, p<0.001). Uric acid (UA) was significantly positively correlated with the progression of hypertension ( β =0.671, p<0.001). C-reactive protein (CRP) was significantly positively correlated with the progression of hypertension (β=0.110, p<0.001). One week postpartum was significantly positively correlated with the progression of hypertension ( β =4.194, p<0.001). Six weeks postpartum was significantly positively correlated with the progression of hypertension ( β =6.517, p<0.001). The interaction analysis with time showed that AST ( β =0.060, p=0.043) at one week postpartum (T2), ALT ( β =0.040, p=0.086) and CRP ( β =0.226, p=0.093) at six weeks postpartum (T3) were significantly positively correlated or nearly significantly positively correlated with the progression of hypertension (Table 4). Among them, the top three factors with the highest significance (ranked by Wald size) are UA, PLT, ALT.

### 3.5 Construction of Nomogram

We selected factors with high significance in both multivariate logistic regression and generalized estimating equations. These included placental abruption, oligohydramnios, umbilical artery pulsatility index (UA-PI), uric acid (UA), platelet count (PLT), and alanine aminotransferase (ALT). Based on these factors, we constructed a nomogram using the training and test sets to predict the probability of developing hypertension. Each patient's six indicators will find their corresponding scores on the corresponding scale line. By calculating the total score of these six indicators, the total score and

corresponding risk probability can be obtained. For example, in the training set, a patient's total score is 112, and the probability of developing hypertension is 17%. In the test set, a patient's total score is 236, and the probability of developing hypertension is 43.4% （Figure. 1 A,B）. The calibration curve and ROC curve indicate that the nomogram has good predictive ability in both the training and test set（Figure. 2 A-D）.

**4. Discussion**

Through univariate and multivariate analysis, we identified six factors—namely placental abruption, oligohydramnios, umbilical artery pulsatility index, uric acid (UA), platelet (PLT), and alanine aminotransferase (ALT)—that were significantly associated with the development of hypertension. Placental abruption is a pregnancy complication that can endanger the lives of both the mother and the fetus, commonly occurring after 20 weeks of pregnancy. Preeclampsia patients are prone to vascular spasm or endothelial damage, leading to insufficient blood supply to the placenta, ischemia or hematoma formation, resulting in placental separation[17]. The risk of preeclampsia patients with placental abruption progressing to hypertension within five years postpartum was significantly increased. This may be due to placental abruption causing vascular damage and endothelial dysfunction in the mother, which exacerbates oxidative stress and inhibits endothelial nitric oxide synthase (eNOS) activity. If not fully repaired postpartum, this may result in a sustained reduction in nitric oxide (NO) levels, an increase in inflammatory cytokines, and potentially lead to long-term progression to hypertension [18].

Preeclampsia patients are also prone to oligohydramnios [19], which may be due to placental ischemia leading to fetal hypoxia. This triggers neuroprotective mechanisms that prioritize blood supply to the brain and heart, reduce renal perfusion, decrease fetal urine output, and ultimately result in oligohydramnios. When the fetus suffers from chronic hypoxia, it secretes more antidiuretic hormone (ADH), further reducing urine output and leading to oligohydramnios. Pathological analysis of placenta with oligohydramnios may result in widespread infarction, thrombosis, and ischemic necrosis of villi, indicating that preeclampsia patients also face endothelial damage and imbalance of active substances. Prolonged postpartum vascular damage can easily progress to hypertension.

The umbilical artery pulsatility index is commonly used to monitor fetal blood flow and oxygen supply in utero [20]. Preeclampsia patients may experience impaired remodeling of the spiral arteries, leading to increased placental vascular resistance. Therefore, the umbilical artery pulsatility index is usually higher. Placental hypoxia releases anti angiogenic factors (such as sFlt-1) and inflammatory mediators (TNF-α, IL-6) into the maternal circulation, leading to vascular damage.. Even if production is carried out, the damage may not be fully recovered, leading to an increase in vasoconstrictors (such as endothelin-1) and causing hypertension. Placental ischemia can also lead to overactivity of the renin-angiotensin system, elevated levels of angiotensin II, and trigger hypertension.

Uric acid is crucial in the pathogenesis of preeclampsia, as it can exacerbate

oxidative stress by activating NADPH oxidase, increase inflammation levels by activating NLRP3 inflammasome, and stimulate placental vascular smooth muscle to cause vasoconstriction, thereby exacerbating disease progression [21]. Persistent high uric acid levels after childbirth can crystallize and deposit in the renal tubules, increasing the burden on the kidneys and thus increasing the risk of postpartum hypertension. Thrombocytopenia is a common complication in preeclampsia patients [22], [23], and endothelial injury promotes platelet adhesion to exposed collagen, forming microthrombi and consuming large amounts of platelets. The excessive activation of the coagulation system caused by placental ischemia can also form microthrombi, consume platelets, and lead to a structural reduction in the capillary network. The decrease in postpartum platelet levels reflects the persistence of symptoms such as vascular damage, imbalance of the coagulation fibrinolysis system, and microvascular rarefaction, thereby increasing the risk of hypertension. Alanine aminotransferase is a hallmark of liver injury [24] , and sFlt-1, along with the release of inflammatory factors (TNF-α) and angiotensin II, leads to systemic small artery vasospasm and liver microcirculation disorders. Overactivation of the coagulation system can lead to blockage of sinusoidal blood flow and damage to liver cells. The intensified oxidative stress response produces reactive oxygen species (ROS) and other peroxides, which enter the liver through the portal vein circulation, exacerbating liver cell damage and increasing ALT levels. The continuous increase in postpartum ALT levels suggests that liver inflammation and oxidative stress are progressively worsening vascular damage. Abnormal liver metabolism may lead to excessive triglycerides

deposited in the vascular wall, promoting atherosclerosis. Metabolic disorder can also cause insulin resistance, activate the sympathetic nervous system, promote vascular contraction, and increase the risk of development of hypertension.

The innovation of this study lies in the analysis of the interaction between blood markers and time. The results showed that AST levels one week after delivery were significantly correlated with the progression of hypertension. This suggests the importance of postpartum monitoring. Early postpartum intervention may be an important time point for hypertension intervention. Monitoring AST levels during this period and early intervention for patients with high AST can reduce the risk of developing hypertension in preeclampsia patients. This also indicates that preeclampsia not only affects pregnancy, but also plays an important role in postpartum vascular damage and oxidative stress, providing early identification strategies for predicting the risk of hypertension in preeclampsia patients within 5 years postpartum.

In order to help clinical doctors more accurately determine the risk of hypertension, we have constructed a nomogram. Based on this, clinical doctors can calculate the comprehensive risk score of patients by assigning values according to the significant influencing factors we have screened, and quickly assess the possibility of patients developing hypertension after childbirth. And our nomogram shows good discrimination and calibration, which can provide some reference for clinical decision-making.

This study also has certain limitations. As a retrospective study with a small sample size and limited factors included, the generalizability and applicability of the results are

restricted. We have only identified factors influencing the progression of preeclampsia to hypertension but have not conducted specific mechanistic investigations to explore the underlying biological mechanisms. Future studies should include more influencing factors and conduct larger-scale randomized controlled trials to further validate our conclusions, as well as mechanistic studies to better elucidate the biological basis.

## 5. Conclusion

The incidence of placental abruption, oligohydramnios, umbilical artery pulsatility index, UA, PLT, and ALT in preeclampsia patients who progress to hypertension are significantly higher than those in preeclampsia patients who do not progress to hypertension. Placental ischemia and persistent vascular damage postpartum may be important mechanisms for the progression of hypertension. The AST index one week postpartum is closely related to the progression of hypertension. The nomogram has good performance in predicting the risk of developing hypertension. However, due to the nature of this retrospective study, the conclusions should be cautiously validated in future prospective studies to eliminate potential biases and further confirm their clinical applicability. This study provides a predictive basis for the occurrence of postpartum hypertension in preeclampsia patients, which is helpful for clinical doctors to identify high-risk populations early.

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## Figure Legend

**Figure 1** (A) Nomogram model in the training set. (B) Nomogram model in the test set.

**Figure 2** (A) Calibration curve and ROC curve of nomogram model in training set (B) Calibration curve and ROC curve of nomogram model in test set.

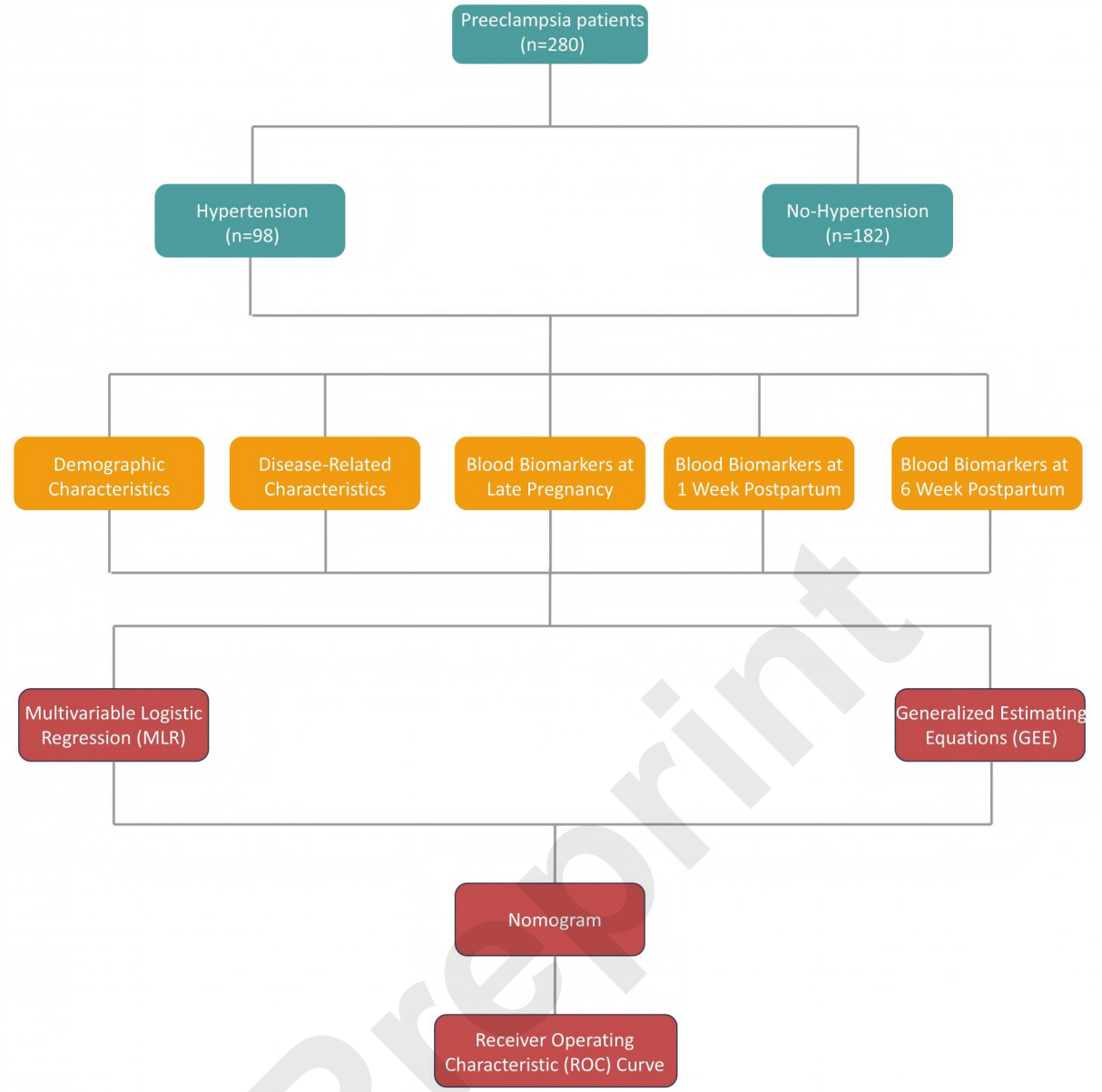

Preeclampsia patients (n=280)
Hypertension (n=98)
No-Hypertension (n=182)
Demographic Characteristics
Disease-Related Characteristics
Blood Biomarkers at Late Pregnancy
Blood Biomarkers at 1 Week Postpartum
Blood Biomarkers at 6 Week Postpartum
Multivariable Logistic Regression (MLR)
Generalized Estimating Equations (GEE)
Nomogram
Receiver Operating Characteristic (ROC) Curve

**Table. 1 Differences in Demographic and Disease-Related Characteristics Between Preeclampsia Patients Who Developed Hypertension and Those Who Did Not**

| | All Patients (n=280) | No - Hypertension (n=182) | Hypertension (n=98) | P-value |
|---|---|---|---|---|
| **Age** | 28 (20-36) | 28 (20-36) | 28 (20-35) | 0.682 |
| **Pre-pregnancy BMI** | 29.4 (22.7-35.4) | 28.7 (22.7-35.4) | 30.4 (22.8-35.4) | 0.047 |
| **Postpartum BMI** | 30.4 (24.6-35.8) | 29.4 (24.6-35.8) | 31.4 (24.7-35.8) | 0.005 |
| **Subtypes of Preeclampsia** | | | | 0.013 |
| Early-onset Preeclampsia, EOPE | 61 (21.79%) | 31 (17.03%) | 30 (30.61%) | |
| Late-onset Preeclampsia, LOPE | 219 (78.21%) | 151 (82.97%) | 68 (69.39%) | |
| **Severity of illness** | | | | 0.001 |
| Mild Preeclampsia | 201 (71.79%) | 143 (78.57%) | 58 (59.18%) | |
| Severe Preeclampsia | 79 (28.21%) | 39 (21.43%) | 40 (40.82%) | |
| **Diabetes** | | | | 0.091 |
| Yes | 34 (12.14%) | 27 (14.84%) | 7 (7.14%) | |
| No | 246 (87.86%) | 155 (85.16%) | 91 (92.86%) | |
| **Family history of cardiovascular disease** | | | | 0.446 |
| Yes | 57 (20.36%) | 40 (21.98%) | 17 (17.35%) | |
| No | 223 (79.64%) | 142 (78.02%) | 81 (82.65%) | |
| **Eclampsia** | | | | 0.584 |
| Yes | 3 (1.07%) | 1 (0.55%) | 2 (2.04%) | |
| No | 277 (98.93%) | 181 (99.45%) | 96 (97.96%) | |
| **Fetal Growth Restriction** | | | | 0.021 |

| | | | | |
|---|---|---|---|---|
| Yes | 70 (25%) | 37 (20.33%) | 33 (33.67%) | |
| No | 210 (75%) | 145 (79.67%) | 65 (66.33%) | |
| **Placental Abruption** | | | | 0.001 |
| Yes | 21 (7.5%) | 6 (3.3%) | 15 (15.31%) | |
| No | 259 (92.5%) | 176 (96.7%) | 83 (84.69%) | |
| **HELLP Syndrome** | | | | 0.234 |
| Yes | 2 (0.71%) | 0 (0%) | 2 (2.04%) | |
| No | 278 (99.29%) | 182 (100%) | 96 (97.96%) | |
| **Acute Pulmonary Edema** | | | | 0.098 |
| Yes | 5 (1.79%) | 1 (0.55%) | 4 (4.08%) | |
| No | 275 (98.21%) | 181 (99.45%) | 94 (95.92%) | |
| **Cesarean section** | | | | 0.849 |
| Yes | 165 (58.93%) | 106 (58.24%) | 59 (60.2%) | |
| No | 115 (41.07%) | 76 (41.76%) | 39 (39.8%) | |
| **Preterm Birth** | | | | 0.001 |
| Yes | 48 (17.14%) | 21 (11.54%) | 27 (27.55%) | |
| No | 232 (82.86%) | 161 (88.46%) | 71 (72.45%) | |
| **Oligohydramnios** | | | | 0.001 |
| Yes | 42 (15%) | 17 (9.34%) | 25 (25.51%) | |
| No | 238 (85%) | 165 (90.66%) | 73 (74.49%) | |
| **Edinburgh Postnatal Depression Scale, EPDS** | 10 (4-16) | 9 (4-16) | 11 (4-16) | 0.011 |

| | | | | |
|---|---|---|---|---|
| **Generalized Anxiety Disorder-7, GAD-7** | 10 (3-18) | 10 (3-18) | 12 (3-18) | 0.020 |
| **Uterine Artery Pulsatility Index, UtA-PI** | 1.8 (1.2-2.5) | 1.8 (1.2-2.5) | 1.9 (1.3-2.5) | 0.006 |
| **Umbilical Artery Pulsatility Index, UA-PI** | 1.9 (1.4-2.3) | 1.9 (1.4-2.3) | 1.9 (1.4-2.3) | 0.026 |

**Table. 2 Differences in Blood Biomarkers at Late Pregnancy, 1 Week Postpartum, and 6 Weeks Postpartum Between Preeclampsia Patients Who Developed Hypertension and Those Who Did Not**

| | All Patients (n=280) | No - Hypertension (n=182) | Hypertension (n=98) | P-value |
|---|---|---|---|---|
| **Platelet, PLT (×10^9/L)** | | | | |
| Late pregnancy | 135 (89-178) | 137 (89-178) | 128 (89-177) | 0.011 |
| 1 week postpartum | 183 (125-256) | 188 (126-256) | 170 (125-255) | 0.025 |
| 6 weeks postpartum | 220 (141-308) | 230 (141-308) | 201 (142-303) | 0.008 |
| **Aspartate aminotransferase, AST (U/L)** | | | | |
| Late pregnancy | 65.6 (43.8-88.9) | 64.6 (44.9-88.8) | 66.4 (43.8-88.9) | 0.654 |
| 1 week postpartum | 46.8 (38.1-55.2) | 46.0 (38.1-55.0) | 48.6 (38.3-55.2) | 0.005 |
| 6 weeks postpartum | 34.5 (23.9-46.3) | 34.1 (23.9-46.1) | 36.3 (23.9-46.3) | 0.027 |
| **Alanine aminotransferase, ALT (U/L)** | | | | |
| Late pregnancy | 68.4 (49.3-90.4) | 66.3 (49.3-90.1) | 72.2 (49.3-90.4) | 0.016 |
| 1 week postpartum | 45.0 (32.4-57.3) | 43.6 (32.4-57.2) | 46.9 (32.4-57.3) | 0.030 |
| 6 weeks postpartum | 36.3 (24.6-48.4) | 34.1 (24.6-48.4) | 38.6 (24.7-48.4) | 0.002 |
| **24-hour urine protein, 24-hour UP (mg/24 hours)** | | | | |
| Late pregnancy | 643.6 (360.1-963.5) | 634.4 (360.1-963.5) | 710.4 (361.6-945.7) | 0.015 |
| 1 week postpartum | 335.1 (241.1-427.6) | 325.5 (241.6-427.6) | 352.1 (241.1-426.7) | 0.038 |
| 6 weeks postpartum | 237.3 (161.9-306.6) | 229.2 (161.9-306.6) | 245.7 (164.9-305.0) | 0.032 |
| **Uric Acid, UA (mg/dL)** | | | | |
| Late pregnancy | 6.3 (5.5-7.0) | 6.2 (5.5-7.0) | 6.4 (5.5-7.0) | 0.013 |
| 1 week postpartum | 5.4 (4.8-6.1) | 5.4 (4.8-6.1) | 5.5 (4.8-6.1) | 0.021 |

| | | | | |
|---|---|---|---|---|
| 6 weeks postpartum | 4.3 (3.3-5.2) | 4.2 (3.3-5.2) | 4.4 (3.4-5.2) | 0.008 |
| **C-Reactive Protein, CRP (mg/L)** | | | | |
| Late pregnancy | 21.1 (15.0-28.0) | 20.5 (15.0-28.0) | 22.1 (15.2-28.0) | 0.019 |
| 1 week postpartum | 9.0 (5.5-12.6) | 8.7 (5.5-12.6) | 9.8 (5.6-12.6) | 0.012 |
| 6 weeks postpartum | 3.9 (2.2-5.7) | 3.7 (2.2-5.6) | 4.2 (2.2-5.7) | 0.026 |

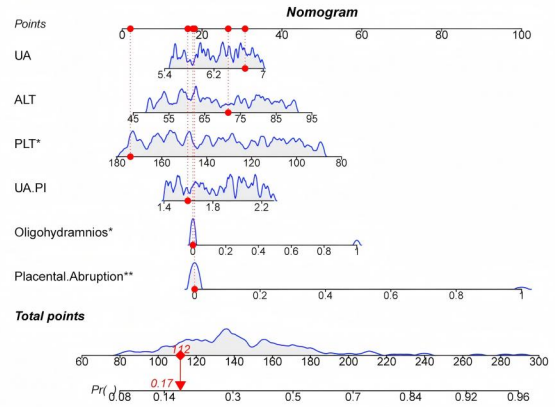
**Table. 3 Multivariate Logistic Regression to Identify Independent Risk Factors for Progression to Hypertension**

| Term | Estimate | Std error | statistic | p value | OR | CI_lower | CI_upper |
|---|---|---|---|---|---|---|---|
| **PRE-BMI** | 0.011 | 0.007 | 1.655 | 0.099 | 1.011 | 0.998 | 1.025 |
| **PRO-BMI** | 0.019 | 0.008 | 2.424 | 0.016 | 1.019 | 1.004 | 1.035 |
| **Subtypes of Preeclampsia** | -0.144 | 0.060 | -2.412 | 0.017 | 0.866 | 0.770 | 0.973 |
| **Severity of illness** | 0.166 | 0.056 | 2.955 | 0.003 | 1.180 | 1.057 | 1.317 |
| **Fetal Growth Restriction** | 0.112 | 0.057 | 1.951 | 0.052 | 1.119 | 1.000 | 1.252 |
| **Placental Abruption** | 0.363 | 0.094 | 3.865 | 0.000 | 1.438 | 1.196 | 1.728 |
| **Preterm Birth** | 0.182 | 0.067 | 2.722 | 0.007 | 1.200 | 1.052 | 1.368 |
| **Oligohydramnios** | 0.227 | 0.071 | 3.198 | 0.002 | 1.255 | 1.092 | 1.442 |
| **EPDS** | 0.019 | 0.007 | 2.700 | 0.007 | 1.019 | 1.005 | 1.033 |
| **GAD 7** | 0.016 | 0.006 | 2.587 | 0.010 | 1.016 | 1.004 | 1.028 |
| **UtA-PI** | 0.206 | 0.067 | 3.087 | 0.002 | 1.229 | 1.078 | 1.401 |
| **UA-PI** | 0.214 | 0.098 | 2.192 | 0.029 | 1.239 | 1.023 | 1.500 |

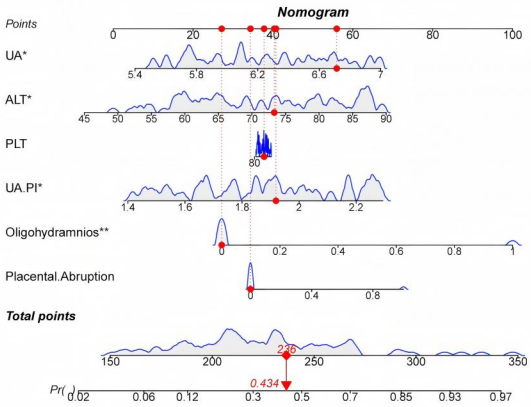
**Table. 4 Screening for Risk Factors of Progression to Hypertension Based on Generalized Estimating Equations (GEE)**

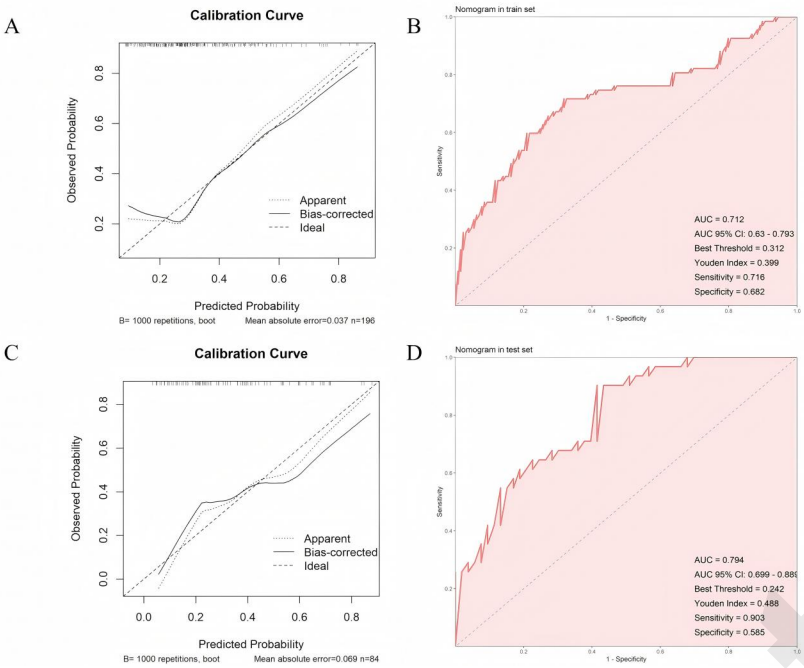
| Term | Estimate | Std error | Wald | P value |
|---|---|---|---|---|
| **PLT** | -0.008 | 0.002 | 15.205 | 0.000 |
| **AST** | 0.016 | 0.009 | 3.435 | 0.064 |
| **ALT** | 0.034 | 0.009 | 14.911 | 0.000 |
| **urine protein** | 0.002 | 0.001 | 8.063 | 0.005 |
| **UA** | 0.671 | 0.169 | 15.749 | 0.000 |
| **CRP** | 0.110 | 0.031 | 12.461 | 0.000 |
| **TimeT2** | 4.194 | 0.651 | 41.475 | 0.000 |
| **TimeT3** | 6.517 | 0.933 | 48.829 | 0.000 |
| | | | | |
| **term** | **Estimate** | **Std error** | **Wald** | **P value** |
| **PLT** | -0.013 | 0.005 | 5.551 | 0.018 |
| **TimeT2** | -2.321 | 3.755 | 0.382 | 0.536 |
| **TimeT3** | 0.212 | 3.166 | 0.004 | 0.947 |
| **AST** | 0.004 | 0.010 | 0.156 | 0.693 |
| **ALT** | 0.022 | 0.012 | 3.687 | 0.055 |
| **urine protein** | 0.002 | 0.001 | 4.905 | 0.027 |
| **UA** | 0.681 | 0.320 | 4.518 | 0.034 |
| **CRP** | 0.088 | 0.036 | 6.006 | 0.014 |
| **PLT*TimeT2** | 0.005 | 0.007 | 0.474 | 0.491 |
| **PLT*TimeT3** | 0.005 | 0.006 | 0.746 | 0.388 |
| **TimeT2*AST** | 0.060 | 0.030 | 4.101 | 0.043 |
| **TimeT3*AST** | 0.030 | 0.023 | 1.623 | 0.203 |
| **TimeT2*ALT** | 0.008 | 0.022 | 0.127 | 0.722 |
| **TimeT3*ALT** | 0.040 | 0.023 | 2.956 | 0.086 |
| **TimeT2*urine protein** | 0.003 | 0.003 | 1.036 | 0.309 |
| **TimeT3*urine protein** | 0.005 | 0.003 | 2.213 | 0.137 |
| **TimeT2*UA** | 0.071 | 0.491 | 0.021 | 0.885 |
| **TimeT3*UA** | -0.064 | 0.405 | 0.025 | 0.874 |
| **TimeT2*CRP** | 0.048 | 0.075 | 0.418 | 0.518 |
| **TimeT3*CRP** | 0.226 | 0.135 | 2.814 | 0.093 |

A


Nomogram
Points
UA
ALT
PLT*
UA.PI
Oligohydramnios*
Placental.Abruption**
Total points
Pr( )

B


Nomogram
Points
UA*
ALT*
PLT
UA.PI*
Oligohydramnios**
Placental.Abruption
Total points
Pr( )


A
Calibration Curve
Observed Probability
0.2
0.4
0.6
0.8
Apparent
Bias-corrected
Ideal
Predicted Probability
B= 1000 repetitions, boot
Mean absolute error=0.037 n=196
B
Nomogram in train set
Sensitivity
1 - Specificity
AUC = 0.712
AUC 95% CI: 0.63 - 0.793
Best Threshold = 0.312
Youden Index = 0.399
Sensitivity = 0.716
Specificity = 0.682
C
Calibration Curve
Observed Probability
0.0
0.2
0.4
0.6
0.8
Apparent
Bias-corrected
Ideal
Predicted Probability
B= 1000 repetitions, boot
Mean absolute error=0.069 n=84
D
Nomogram in test set
Sensitivity
1 - Specificity
AUC = 0.794
AUC 95% CI: 0.699 - 0.88
Best Threshold = 0.242
Youden Index = 0.488
Sensitivity = 0.903
Specificity = 0.585