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Predictive value of serum uric acid levels for adverse perinatal outcomes in preeclampsia

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Abstract

Preeclampsia is a multisystem disorder associated with pregnancy and is a common cause of perinatal morbidity. The aim of this study was to determine whether elevated serum uric acid levels, alone or in combination with other laboratory factors could predict preeclampsia in women with adverse perinatal outcomes.

We conducted a prospective observational study of women who were admitted to Soonchunhyang University Cheonan Hospital from January 2016 to December 2016. Demographic, clinical and laboratory data were collected for each pregnancy at the time of delivery. Women were grouped according to status (preeclampsia or normotensive), and a logistic regression analysis was used to determine the relationship between serum uric acid levels and adverse outcomes.

The mean age of the study participants was 31.3 ± 5.0 years. In patients with preeclampsia, serum uric acid level was associated with the severity of preeclampsia, including blood pressure ($R = 0.321$, $P = .014$), serum creatinine levels ($R = 0.505$, $P < .001$), and proteinuria ($P = .014$), as well as adverse fetal outcomes, including preterm labor ($P = .027$) and low birth weight delivery ($P = .001$). The optimal maternal serum uric acid threshold that predicted low birth weight at delivery was 6.35 mg/dL (sensitivity, 0.58; specificity, 0.95). The multivariable logistic regression model that was used to predict low birth weight at delivery displayed an area under the receiver-operating characteristic curve of 0.902 (95% confidence interval, 0.817–0.986).

In women with preeclampsia, maternal serum uric acid level is an important parameter for predicting low birth weight. Additionally, the combination of uric acid, hemoglobin, and bilirubin levels appear to be optimal for predicting low birth weight in women with preeclampsia.

Abbreviations: AIC = Akaike information criterion, ALT = alanine transaminase, aPTT = activated partial thromboplastin time, AST = aspartate transaminase, AUC = area under the ROC curve, BIC = Bayesian information criterion, BMI = body mass index, BP = blood pressure, BW = birth weight, CI = confidence interval, GA = gestational age, LBW = low birth weight, PT = prothrombin time, ROC = receiver-operating characteristic, SGA = small for gestational age.

Keywords: low birth weight infants, prediction, preeclampsia, uric acid

1. Introduction

Preeclampsia is a pregnancy-induced syndrome defined by sudden onset hypertension (≥140 systolic/90 diastolic mm Hg) and proteinuria (>300 mg/24 h) after 20 weeks of gestation. The incidence of preeclampsia is estimated to be between 2% and 8% of all pregnancies.[1] Preeclampsia remains one of the most severe causes of maternal and perinatal morbidity and mortality. Preeclampsia is a multiple organ disorder characterized by severe cardiopulmonary, renal, hepatic, and neurologic complications. The fetus is also affected, and adverse perinatal outcomes include fetal growth restriction, preterm birth, and intrauterine death. Although termination of pregnancy is the definitive treatment for preeclampsia, many pregnant women can be managed expectantly with maternal blood pressure monitoring, fetal monitoring, and seizure prophylaxis. Therefore, it is important to predict preeclampsia and its complications to avoid mortality and morbidity of both the mother and the baby.

Increased uric acid concentration is one of the most pronounced clinical findings in preeclampsia. Hyperuricemia in preeclamptic women is primarily due to a reduction in glomerular filtration rate due to endothelial dysfunction.[2,3] Several studies have reported elevated uric acid concentrations to be positively correlated with adverse maternal and fetal outcomes.[4,5] However, others propose that an increased uric acid level is a poor predictor of maternal and fetal outcomes.[6,7] The purpose of this study was to determine whether maternal serum uric acid concentration, alone or combination with other biomarkers, can predict maternal or perinatal outcomes in women with preeclampsia.

Editor: Daryle Wane.

AR and NJC contributed equally to this work.

The authors have obtained a signed consent form from the patients which will be filed as part of the records. The protocol for the research project had been approved by a suitably constituted Soonchunhyang University Cheonan Hospital Ethics Committee of the institution (eIRB) (IRB no: 2015-04-019).

This work was supported by the Soonchunhyang University Research Fund (200180007). The authors have no conflicts of interest to disclose.

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Medicine (2019) 98:18(e15462)

Received: 5 December 2018 / Received in final form: 8 February 2019 / Accepted: 5 April 2019

http://dx.doi.org/10.1097/MD.0000000000015462

2. Materials and methods

2.1. Study population

Our patient population included all pregnant patients with singleton pregnancies admitted for delivery at Soonchunhyang University Cheonan Hospital between June 2015 and February 2016. A total of 65 women with preeclampsia and 75 women with normal pregnancies were recruited. Patients with a history of preexisting medical disorders such as type II diabetes mellitus, chronic hypertension, renal disease, liver disease, as well as any cardiovascular, thyroid, or other endocrinologic disorders were excluded from the study. Preeclampsia was diagnosed based on the "ACOG Task Force on Hypertension in Pregnancy 2013"[8] as follows: women known to be normotensive who developed a systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg on 2 occasions at least 4 hours apart after the 20th week of gestation and proteinuria ≥300 mg/24 h urine collection or a protein/creatinine ratio ≥0.3. In the absence of proteinuria, preeclampsia was diagnosed as hypertension with new-onset thrombocytopenia, elevated liver transaminase levels, renal insufficiency, pulmonary edema, and/or now-onset cerebral or visual disturbances.

Demographic information, clinical and laboratory data at the time of delivery, and the outcomes for mothers and babies were collected prospectively. After admission, a medical and family history was taken for all patients to ensure that they fulfilled the inclusion criteria. Additionally, for every patient, a physical examination was performed and recorded. For all patients, the blood pressure was carefully recorded at the time of admission and after 2 hours of rest with the woman in a sitting position. Concurrently, using all aseptic precautions, 5 mL of venous blood was drawn for measurement of serum uric acid levels. The normal values used for reference in the 3rd trimester range between 3.1 and 6.3 mg/dL.[9] For urinary protein analysis, 10 mL midstream urine was collected. Urine protein was measured with a dipstick and graded as Trace to 4+. The guidelines of the National Clinical Chemistry Laboratory Standards were followed for collection, handling, and transportation of samples to the laboratory.[10] Serum uric acid concentrations were measured within 24 hours of enrollment, and the highest level was recorded.

2.2. Statistical analysis

Categorical variables were expressed as counts (percentage), normally distributed continuous variables as mean ± standard deviation, and nonnormally distributed continuous variables as medians (interquartile ranges). For continuous variables, differences between 2 groups were analyzed by a Student *t* test. Categorical variables were analyzed using the Pearson Chi-squared test or Fisher exact test, as appropriate. Pearson correlation coefficient was used to test the correlation between individual continuous variables. For multiple comparisons, a pairwise *t* test with a Bonferroni correction was performed.

To select parameters for our prediction model, univariate logistic regression analyses were performed, and covariates whose *P* value was <.1 were selected for further analysis. All of the subset logistic regression models were constructed using the selected parameters along with age and body mass index. The model was the model that minimized Akaike information criterion and the Bayesian information criterion or maximized prediction accuracy as determined by a repeated 10-fold cross-validation method and a bootstrap validation method was designated as the best model. Additionally, the best model was validated by receiver-operating characteristic (ROC) curve analysis. The optimal thresholds were determined by selecting the data point that maximized the sum of sensitivity and specificity. Nonlinear associations were examined by using restricted cubic splines to relax linearity assumptions for continuous variables.

Statistical analyses were performed using R version 3.4.0 (The R Foundation for Statistical Computing, Vienna, Austria). A *P* value <.05 was considered statistically significant and 2-tailed tests were performed for all hypothesis tests.

2.3. Ethics statement

The study was approved by the Soonchunhyang University Cheonan Hospital Institutional Review Board (IRB), and all patients provided written informed consent.

3. Results

3.1. Baseline characteristics

A total of 140 participants were enrolled in this study; 75 were women with normal pregnancies and 65 were patients with preeclampsia. The baseline characteristics of participants with normal pregnancies and preeclampsia are presented in Table 1. In comparing patients with preeclampsia to those experiencing a normal pregnancy, we observed higher body mass indices and blood pressure, and more frequent adverse outcomes such as cesarean section, low birth weight, preterm delivery, and small for gestational age births. Furthermore, in patients with preeclampsia, the blood levels of hemoglobin, urea nitrogen, creatinine, alanine transaminase, uric acid, triglycerides, and total cholesterol were all significantly higher, and prothrombin time was lower (Table 1).

3.2. Serum uric acid level reflects the severity of preeclampsia

In patients with preeclampsia, serum uric acid levels had a positive correlation with systolic blood pressure ($R = 0.321$, $P = .014$), serum creatinine levels ($R = 0.505$, $P < .001$), and proteinuria ($P = .014$), but not with platelet count ($R = -0.103$, $P = .449$) (Fig. 1). Among patients with full-term labor and normal birth weight delivery, serum uric acid levels were significantly higher in those who experienced preterm labor (full-term, 5.1 ± 1.3; preterm, 6.2 ± 1.7; $P = .027$) and low birth weight delivery (normal birth weight, 4.8 ± 1.1; low birth weight, 6.5 ± 1.6; $P = .001$), respectively (Fig. 2).

3.3. Cut-off values of serum uric acid for predicting low birth weight delivery

The optimal maternal serum uric acid threshold concentration for predicting low birth weight delivery was 6.35 mg/dL (sensitivity, 0.58; specificity, 0.95) (Fig. 3A). The restricted cubic spline model revealed that when uric acid levels were below 6.35 mg/dL, the odds ratios for low birth weight delivery did not change significantly, but when uric acid levels were above 6.35 mg/dL, the odds ratios increased as uric acid levels increased (Fig. 3B). This value was also effective for predicting adverse fetal outcomes, including preterm labor (sensitivity, 0.46; specificity,

Table 1

Baseline characteristics of participants with normal pregnancy and preeclampsia.

	Normotensive (n = 75)	Preeclampsia (n = 65)	*P* value
Age, yrs	31.0 ± 5.1	31.7 ± 5.0	.379
BMI, kg/m^2	20.5 (19.3–23.8)	22.7 (20.6–26.2)	.002
Systolic BP, mm Hg	120 (110–120)	150 (140–160)	<.001
Diastolic BP, mm Hg	70 (70–80)	100 (90–100)	<.001
GA at delivery, wks	37.7 (36.1–38.9)	35.9 (33.9–37.4)	<.001
Birth weight, g	2920 (2435–3220)	2280 (1560–2880)	<.001
Hemoglobin, g/dL	11.5 ± 1.3	12.7 ± 1.6	<.001
Platelet count, $\times 10^3/\mu$L	217.1 ± 58.6	204.8 ± 62.1	.233
Albumin, g/dL	3.5 (3.2–3.7)	3.4 (3.1–3.6)	.468
Glucose, mg/dL	85 (75–92)	83 (77–96)	.431
Urea nitrogen, mg/dL	7.3 (6.0–8.7)	9.8 (7.9–13.2)	<.001
Creatinine, mg/dL	0.5 (0.4–0.5)	0.6 (0.5–0.7)	<.001
Total bilirubin, mg/dL	0.3 (0.2–0.4)	0.3 (0.2–0.4)	.253
AST, IU/L	17 (13–21)	22 (15–29)	.064
ALT, IU/L	9 (7–12)	13 (9–23)	.027
Uric acid, mg/dL	3.9 (3.1–4.6)	5.8 (4.7–6.6)	<.001
Triglycerides, mg/dL	236.5 (174.3–325.3)	344.0 (253.5–436.3)	<.001
Total cholesterol, mg/dL	252.5 (221.3–277.8)	268.5 (237.3–336.8)	.007
Phosphorus, mg/dL	3.6 (3.1–4.0)	3.7 (3.2–4.1)	.139
Calcium, mg/dL	8.8 (8.5–9.3)	8.8 (8.3–9.2)	.220
PT, s	10.8 (10.4–11.2)	10.4 (10.0–10.8)	.005
aPTT, s	28.2 (27.2–29.5)	27.8 (26.3–30.1)	.649
Cesarean section	41 (54.7)	55 (84.6)	<.001
Stillbirth	1 (1.3)	2 (3.1)	.597
Low birth weight	23 (30.7)	40 (61.5)	<.001
Small for GA	12 (16.0)	28 (43.1)	.001
Preterm labor	24 (32.0)	45 (69.2)	<.001

Data are presented as mean ± standard deviation, median (interquartile range), or count (%) as appropriate. *P* values are calculated by Pearson Chi-squared test or Fisher exact test for categorical variables, and by Student *t* test for continuous variables.

ALT = alanine transaminase, aPTT = activated partial thromboplastin time, AST = aspartate transaminase, BMI = body mass index, BP = blood pressure, GA = gestational age, PT = prothrombin time.

0.82) and small for gestational age births (sensitivity, 0.52; specificity, 0.73) (Fig. 4).

3.4. Risk prediction model for low birth weight delivery in preeclampsia

Of the 65 preeclamptic patients, 40 (61.5%) delivered low birth weight newborns. In univariate logistic regressions performed to select parameters for predictive modeling, hemoglobin, blood urea nitrogen, serum creatinine, serum total bilirubin, serum uric acid levels, prothrombin time, and urine dipstick protein levels were significantly associated with low birth weight delivery (Table 2). The prediction model constructed via multivariate logistic regression using hemoglobin, serum total bilirubin, and serum uric acid levels was the best fitted model considering Akaike information criterion, Bayesian information criterion, and bootstrap validation (Table 3). The point estimates of the variables and the equation of the model are presented in Table 4.

3.5. Validation of the prediction model

Figure 4 displays the ROC curves of the best fitted model and univariate models. The validation analysis revealed that the area under the ROC curve (AUC) of the final model (AUC 0.902; 95% confidence interval [CI], 0.817–0.986) was significantly higher than those of the univariate models, whose explanatory variables were uric acid (AUC 0.808; 95% CI, 0.700–0.916; $P = .049$), hemoglobin (AUC 0.709; 95% CI, 0.573–0.845; $P = .006$), or total bilirubin (AUC 0.660; 95% CI, 0.527–0.793; $P < .001$) levels (Fig. 5). In the internal validation of the model using repeated a 10-fold cross-validation method and a bootstrap validation method, the prediction accuracies were 79.3% and 78.7%, respectively (Table 3).

4. Discussion

In the present study, maternal hyperuricemia measured near delivery was found to be associated with adverse fetal outcomes, especially low birth weight. It was found that maternal serum hyperuricemia was significantly associated with preeclampsia progression and poor perinatal outcomes, such as low birth weight. Many previous studies have identified a relationship between hyperuricemia and adverse maternal and perinatal outcomes in women with preeclampsia.[7,11] In a large cohort study, it was found that women with preeclampsia had an increased risk for adverse fetal outcomes (OR 1.8; 95% CI, 1.5–2.1).[12]

Uric acid is the end product of purine metabolism and is synthesized by the enzyme xanthine oxidase. The etiology of hyperuricemia in preeclampsia is associated with oxidative stress and renal function impairment as a result of placental ischemia and reduced maternal glomerular filtration rate.[13] One probable mechanism is that the placenta may be affected by uric acid production associated with the levels and activity of xanthine oxidase/dehydrogenase.[14] Hyperuricemia is a result of various different mechanisms. What mechanism will blood pressure rise with hyperuricemia? Mazzali et al[15]

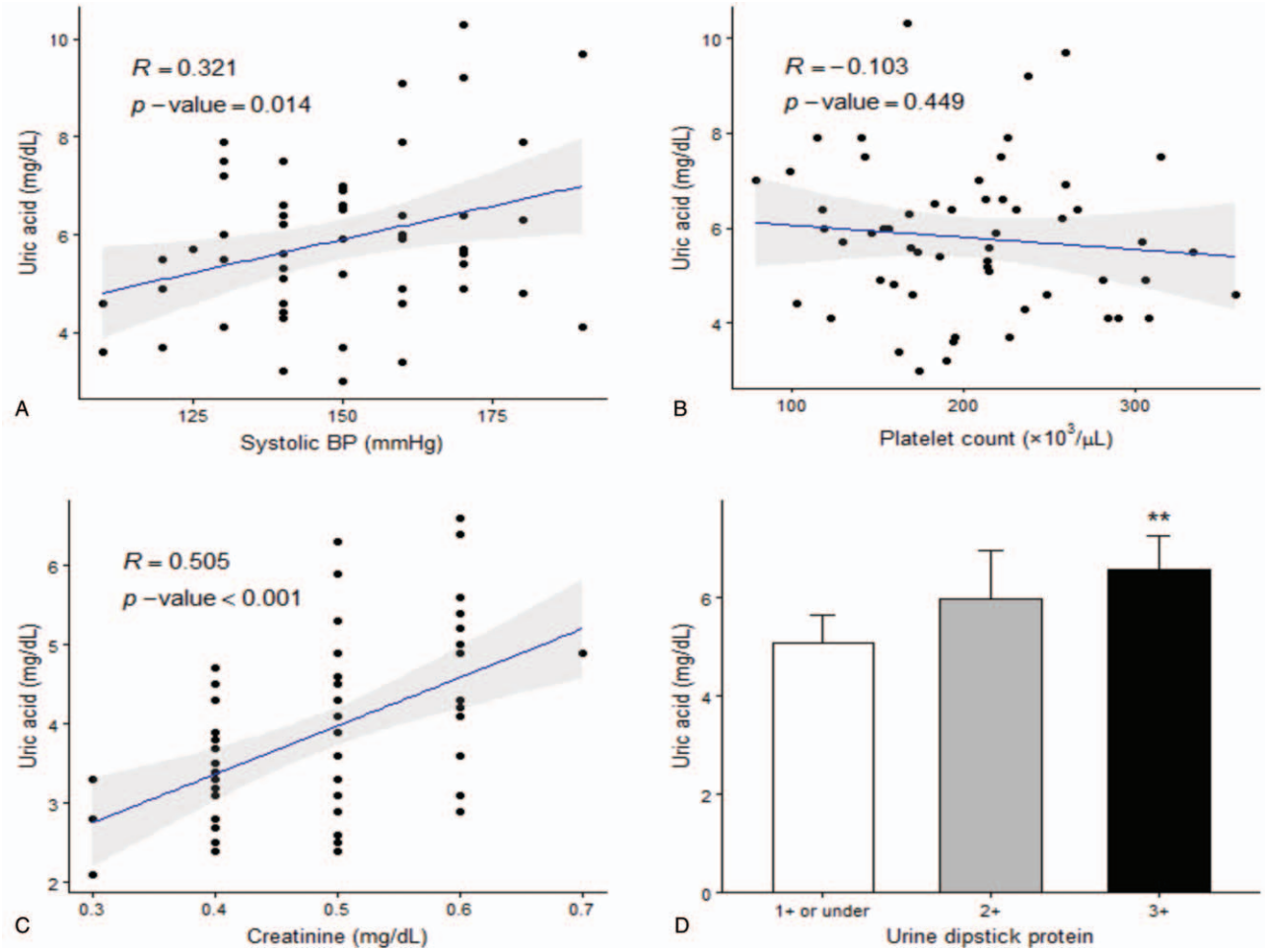

Figure 1. Associations of serum uric acid level with severity markers of preeclampsia. Severity markers of preeclampsia are composed of (A) systolic blood pressure, (B) platelet count, (C) serum creatinine, and (D) urine dipstick protein. $^{**}P < .01$ compared with urine dipstick protein 1+ or under.

demonstrated an elevation in serum uric acid followed by an increase in blood pressure via a crystal-independent mechanism in rat models. Reduction of serum uric acid was associated with a decrease in blood pressure through the regulation of renin angiotensin and nitric oxide system.[16] Hypertension was developed by uric acid-mediated renal vasoconstriction resulting from a reduction in endothelial levels of nitric oxide, with activation of renin-angiotensin system. We demonstrated that

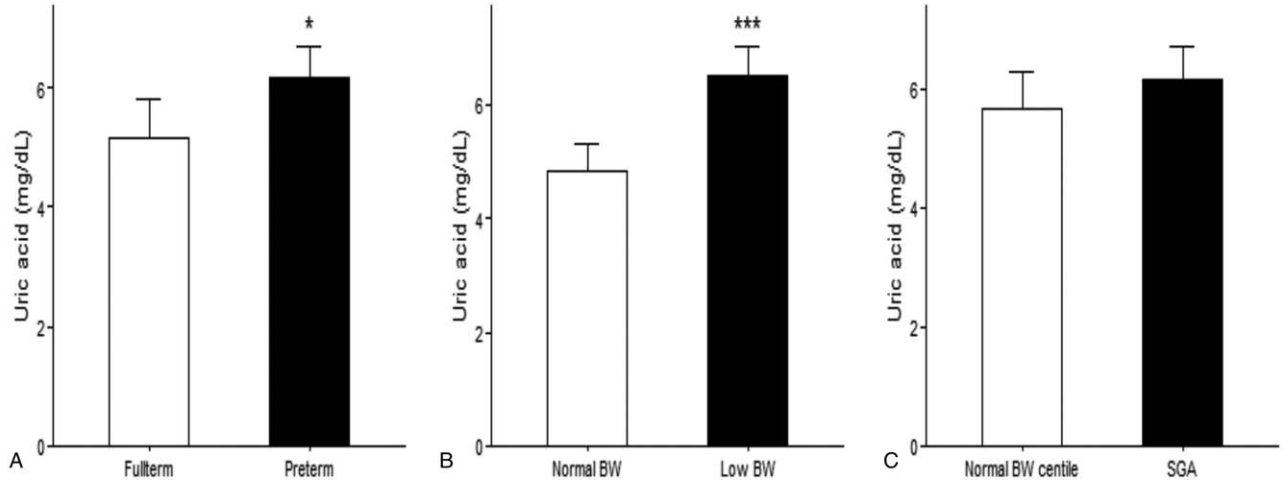

Figure 2. Associations of serum uric acid level with adverse fetal outcomes in preeclampsia. Adverse fetal outcomes are composed of (A) preterm birth, (B) low birth weight delivery, and (C) small for gestational age. BW = birth weight, SGA = small for gestational age. $^{*}P < .05$; $^{***}P < .001$.

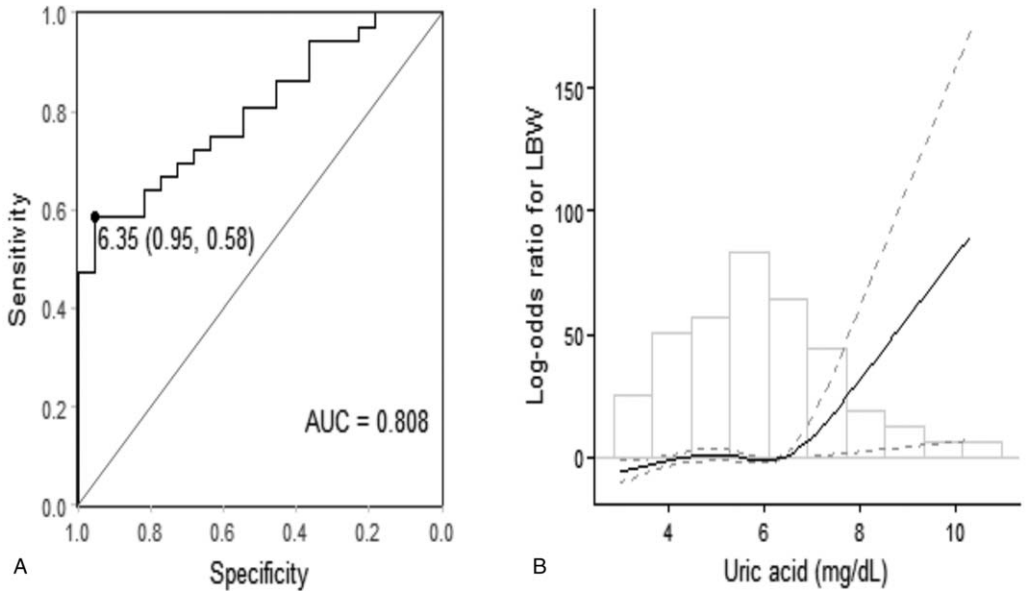

Figure 3. Analyses for selecting the best cut-off values of uric acid for predicting low birth weight delivery. (A) Receiver-operating characteristic (ROC) analysis for predicting low birth weight delivery using maternal serum uric acid level. Best cut-off values were presented as black circles and certain values (with specificity and sensitivity). (B) Log-odds ratios (and 95% confidence interval) for low birth weight delivery associated with serum uric acid. Nonlinear relationships between the predictors and log-odds ratio of low birth weight delivery were assessed by restricted cubic spline regressions. AUC = area under the ROC curve, LBW = low birth weight.

maternal renal function is an important factor influencing hyperuricemia, but we did not further investigate this relationship in our study.

In a recent meta-analysis, the description of various uric acid threshold values suggested that uric acid concentration is clinically useful in predicting adverse outcomes of preeclampsia.[4] Our study suggests that the best threshold concentration of maternal uric acid for predicting a low birth weight delivery is 6.35 mg/dL (sensitivity, 0.58; specificity, 0.95). This is supported by a similar study, which reported that maternal hyperuricemia was associated with low birth weight. They found that uric acid concentrations >5.9 mg/dL were associated with adverse perinatal outcomes.[12] A prospective clinical observational study in India, they found that mean serum uric acid concentration to predict significant adverse fetal outcome was 6.37 mg/dL. This value almost coincides with our value of 6.35 mg/dL.[17] Hemoglobin levels >13 g/dL suggest the presence of hemoconcentration in severe preeclampsia.[18]

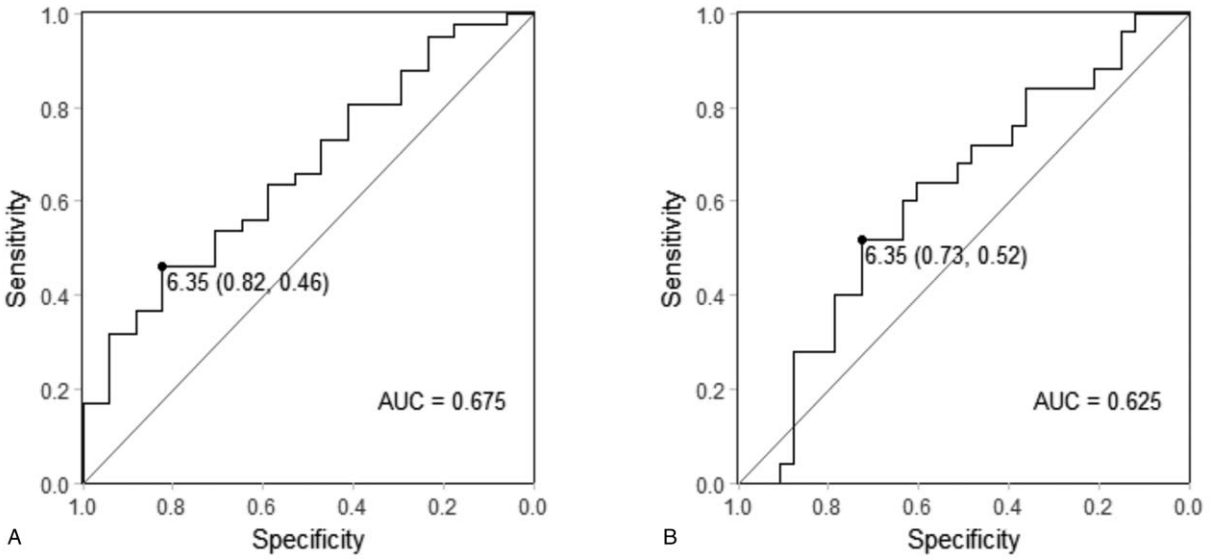

Figure 4. Receiver-operating characteristic (ROC) analyses for predicting adverse fetal outcomes using maternal serum uric acid level. ROC curves are shown according to the outcomes: a. Preterm birth and b. small for gestational age. Best cut-off values were presented as black circles and certain values (with specificity and sensitivity). AUC = area under the ROC curve.

Table 2

Univariable logistic regression models for variable selection.

	OR	95% CI	*P* value
Age, yrs	0.94	0.84–1.04	.230
BMI, kg/m^2	0.97	0.89–1.06	.507
Systolic BP, mm Hg	1.01	0.98–1.04	.505
Diastolic BP, mm Hg	1.00	0.96–1.04	.930
Hemoglobin, g/dL	1.78	1.25–2.72	.003
Platelet count, $\times 10^3/\mu L$	1.00	0.99–1.01	.930
Albumin, g/dL	0.56	0.14–2.03	.383
Glucose, mg/dL	1.00	0.97–1.02	.891
Urea nitrogen, mg/dL	1.29	1.10–1.56	.004
Creatinine, mg/dL	1.88	1.22–3.26	.011
Total bilirubin, mg/dL	0.02	0.00–0.49	.024
AST, IU/L	1.00	0.98–1.00	.390
ALT, IU/L	1.00	0.99–1.01	.554
Uric acid, mg/dL	2.60	1.58–4.88	.001
Triglycerides, mg/dL	1.00	1.00–1.00	.362
Total cholesterol, mg/dL	1.01	1.00–1.01	.135
Phosphorus, mg/dL	1.23	0.67–2.73	.545
Calcium, mg/dL	0.68	0.31–1.34	.283
PT, s	0.42	0.18–0.82	.020
aPTT, s	1.04	0.96–1.20	.466
Dipstick protein*	3.33	1.17–10.29	.029

Univariable logistic regressions which set low birth weight delivery as dependent variable were performed for variable selection for predictive modeling.

ALT = alanine transaminase, aPTT = activated partial thromboplastin time, AST = aspartate transaminase, BMI = body mass index, BP = blood pressure, CI = confidence interval, OR = odds ratio, PT = prothrombin time.

* Dipstick protein was grouped as below 3+ and 3+.

Low levels of bilirubin were associated with poor maternal and fetal outcomes in women diagnosed with preeclampsia.[19] There are no studies on the relationship between uric acid, hemoglobin, bilirubin, and low birth weight in preeclampsia. The results of this study showed that the higher the uric acid and hemoglobin level and the lower the bilirubin level, the higher the probability of giving birth to the low birth weight infant. More research is needed on threshold values of hemoglobin and bilirubin in the future, which is why this study is valuable.

Although we identified an association between elevated concentrations of maternal serum uric acid and preeclampsia, the predictive value of hyperuricemia alone is limited by a relatively low AUC value. In this study, maternal serum uric acid was shown to be valuable for predicting preeclampsia (AUC = 0.808). However, a number of combined laboratory factors are also useful for providing a clinically meaningful prediction of preeclampsia (AUC = 0.902). Therefore, we propose that screening for preeclampsia could begin with this model, which can predict preeclampsia progression and adverse outcomes. Furthermore, this combined model may be more easily applicable in patients with a high risk of preeclampsia.

There are limitations to this study. First, the sample size was relatively small. Although the results suggest that the combined model improves prediction of preeclampsia, larger prospective studies are needed to confirm these findings. Second, the study population was recruited from a single hospital and further studies are needed to evaluate this proposed model in other high-risk pregnant women. Third, all members of our study population were referred to an obstetric specialist during their pregnancy, which may exclude women with less severe clinical findings. For most women, only laboratory values obtained near delivery were available, and we could not determine the temporal relationship between uric acid changes and diagnosis of hypertension or progression of preeclampsia.

In this study, serum uric acid level was not adjusted according to gestational age. It is important to adjust uric acid concentration for gestational age, because uric acid concentrations vary with physiologic changes during pregnancy. Using a uric acid *Z* score to account for gestation-related changes, a previous study demonstrated that hyperuricemia is associated with both maternal and fetal adverse outcomes.[20] Unfortunately, the use of a *Z* scores has low clinical utility because it requires calculation.

Table 4

Best fitted multivariable logistic regression model predicting low birth weight delivery.

Estimates of the multivariable logistic regression model

	Estimate	Standard error	*Z* value	*P* value
(Intercept)	–12.020	3.904	–3.078	.0021
Uric acid	1.095	0.355	3.081	.0021
Total bilirubin	–8.060	3.190	–2.526	.0115
Hemoglobin	0.705	0.280	2.516	.0119

Equation based on the model

Predicted probability (*P*) of low birth weight delivery in patients with preeclampsia is expressed as follows:

$$P = \frac{e^{X\beta}}{1+e^{X\beta}},$$

where $X\beta$ is presented as follows:

$$X\beta = -12.02 + 1.095\cdot(\text{Uric acid}) - 8.06\cdot(\text{Total bilirubin}) + 0.705\cdot(\text{Hemoglobin})$$

Table 3

Assessing the performance of prediction models for low birth weight delivery.

Variables included	AIC	BIC	Cross validation*	Bootstrap validation*
Hemoglobin, total bilirubin, uric acid	51.75	59.99	79.3	78.7
BMI, hemoglobin, total bilirubin, uric acid	52.23	62.53	79.6	78.2
Hemoglobin, total bilirubin, uric acid, total cholesterol	52.38	62.68	77.9	78.1
Age, hemoglobin, total bilirubin, uric acid	52.55	62.85	76.9	76.8
Hemoglobin, urea nitrogen, total bilirubin, uric acid	52.76	63.06	79.6	77.3
Hemoglobin, creatinine, total bilirubin, uric acid	52.88	63.18	77.6	76.9
Systolic BP, hemoglobin, total bilirubin, uric acid	52.89	63.18	76.2	75.8
Diastolic BP, hemoglobin, total bilirubin, uric acid	52.93	63.23	76.7	76.7
Hemoglobin, total bilirubin, uric acid, prothrombin time	53.06	63.28	78.1	76.7
Hemoglobin, total bilirubin, uric acid, dipstick protein	53.23	63.45	79.1	76.5

Top 10 fitted multivariable logistic regression models are presented based on AIC.

AIC = Akaike information criterion, BIC = Bayesian information criterion, BP = blood pressure.

* The predicting abilities obtained by repeated 10-fold cross validation method and bootstrap validation method were presented as accuracy of prediction (%).

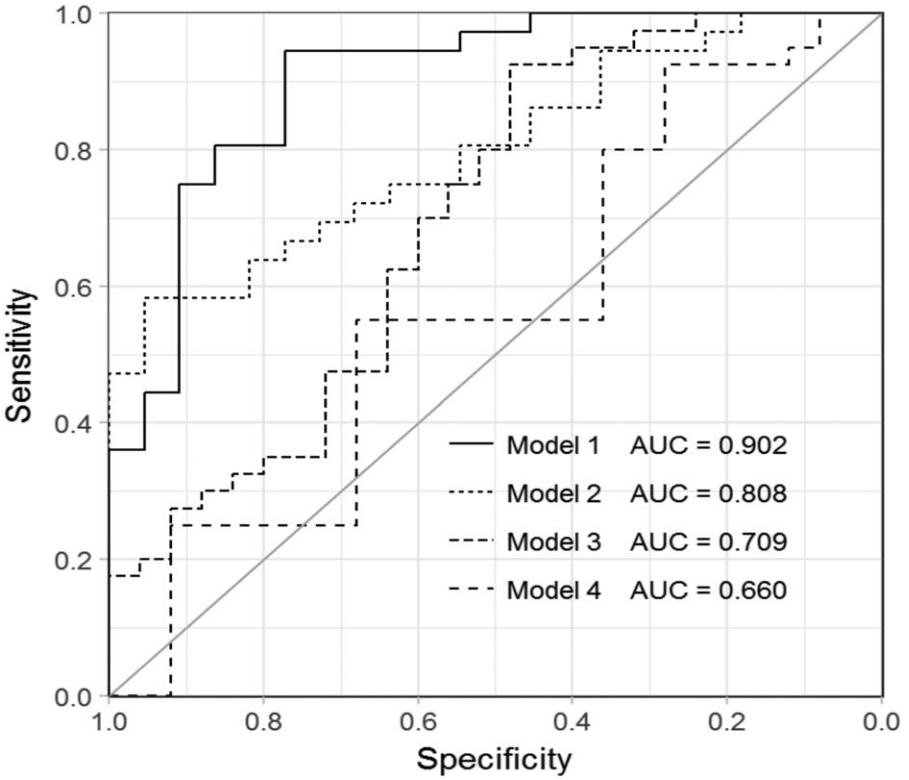

Figure 5. Receiver-operating characteristic (ROC) analyses for models predicting low birth weight delivery. Model 1, best fitted multivariable logistic regression model based on uric acid, hemoglobin, and total bilirubin level; Model 2, univariable logistic regression model based on uric acid level; Model 3, univariable logistic regression model based on hemoglobin level; Model 4, univariable logistic regression model based on total bilirubin level. AUC = area under the ROC curve.

However, our combined prediction model effectively predicts preeclampsia without the need to correct for gestational age.

Uric acid concentration is not necessarily considered a criterion for diagnosing preeclampsia or used in management decisions regarding hypertensive women in clinics. If clinicians were aware of uric acid levels, it may have affected the timing of delivery for some women as well as fetal growth.[21]

In addition, further studies are needed to determine the precise role of uric acid in the development and deterioration of preeclampsia, and future studies will help to identify changes to the microenvironment of the placenta in preeclamptic mothers.

5. Conclusion

The principal findings of this study are that maternal serum uric acid is the important key parameter in predicting low birth weight in women with preeclampsia, and according to the logistic regression analysis, a combination of uric acid, hemoglobin, and bilirubin levels was the best predictor of preeclampsia.

Acknowledgment

The authors are grateful to Soonchunhyang University Cheonan Hospital for its assistance and encouragement.

Author contributions

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EY analyzed and interpreted the patient data regarding the preeclampsia. AL collected the samples and got the consent. YS was a major contributor in writing and revising the manuscript. All authors read and approved the final manuscript.

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Writing – review & editing: Yun Sook Kim, Eun Young Lee.

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