

Serum uric acid-to-creatinine ratio and preeclampsia: a retrospective cross-sectional analysis with machine learning discrimination using the MIMIC-IV database

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Abstract

Objective

Preeclampsia continues to be a primary cause of health complications and death for expectant mothers and their unborn children. Early identification of pregnant women at risk, followed by timely preventive interventions, carries clear clinical value. We examined whether the serum uric acid to creatinine ratio (UA/Cr) measured at admission is associated with preeclampsia and whether it adds discriminative value when used in machine learning (ML) models.

Methods

We conducted a retrospective cross-sectional study using the MIMIC-IV database, identifying 4,756 pregnant women with gestational age ≥ 20 weeks; 4,247 were excluded for missing data, leaving 509 for analysis (78 preeclampsia cases, 431 controls). Preeclampsia was identified by ICD-9/10 codes. UA/Cr (uric acid mg/dL $\div$ creatinine mg/dL, first admission-day value) entered logistic regression as both a continuous variable and a quartile variable (Q1 as reference), with two adjustment sets: Model 1 adjusted for age, and Model 2 for age, language, and red blood cell count. Restricted cubic splines characterized nonlinearity, and subgroup analyses tested robustness. Six machine learning algorithms—random forest, XGBoost, LightGBM, CatBoost, AdaBoost, and TabPFN—were trained on the training set ($n = 355$) and validated on the validation set ($n = 154$). Features were selected by univariate screening, variance inflation factor (VIF) diagnostics, and LASSO. Univariate analysis for screening, VIF diagnostics, and LASSO were utilized to choose features.

Result

UA/Cr rose with preeclampsia risk and the dose–response curve was approximately linear (nonlinearity $P = 0.911$): each 1-unit increment was associated with an OR of 1.184 (95% CI 1.061–1.320, $P = 0.002$). The highest quartile carried an OR of 2.758 versus the lowest quartile (95% CI 1.318–6.128, $P = 0.009$; trend $P = 0.020$). AUCs in the validation set ranged from 0.655 to 0.761 (LightGBM the highest), with UA/Cr ranking second in feature importance. The four top-performing models did not differ significantly from one another.

Conclusion

In this MIMIC-IV cohort of hospitalized pregnant women, a higher admission UA/Cr was associated with preeclampsia, and an ML model built from routine admission data achieved moderate concurrent discrimination. Because of the cross-sectional design, the analysis does not support prospective

prediction. Prospective and external validation, alongside head-to-head comparison with absolute uric acid, is required before any clinical use in risk stratification.

Key Message

Elevated admission serum UA/Cr is independently linked with preeclampsia in hospitalized pregnant women and serves as a valuable feature for moderate-performance machine learning discrimination models.

1. INTRODUCTION

Preeclampsia is a major subtype of gestational hypertension disorder (HDP) and is one of the leading causes of maternal and perinatal mortality worldwide^[1]. It originates from abnormal placental development at the maternal-fetal interface, eventually leading to extensive endothelial dysfunction and organ damage, and ultimately causing multi-system diseases^[2]. The underlying mechanism of preeclampsia involves heightened systemic vascular resistance, elevated afterload, diminished vascular volume, and decreased cardiac output^[3]. After extensive investigation over many years, the fundamental mechanisms driving preeclampsia remain only partially understood. With the global demographic changes and delayed childbearing, its prevalence has continued to rise, posing a global health challenge^[4]. With the continuous demographic changes and delayed childbearing worldwide, the burden of hypertensive complications among elderly pregnant women is becoming increasingly prominent, while effective biomarkers for the early prediction and assessment of preeclampsia remain limited^[5].

Serum uric acid results from the breakdown of purine^[6]. Over a hundred years back, Slemons and his group initially detected a notable rise in uric acid concentrations among expectant mothers experiencing preeclampsia^[7]. Later, there were related reports that hyperuricemia could serve as a clinical marker and potential trigger for preeclampsia^[8]. In recent years, an increasing amount of evidence has indicated that uric acid is involved in multiple pathological pathways related to hypertension and kidney injury, many of which highly overlap with preeclampsia^[9–11]. Experimental studies have shown that elevated uric acid levels can lead to endothelial dysfunction, oxidative stress and mitochondrial damage^[12]. In preeclampsia, serum hyperuricemia can exacerbate vascular endothelial injury, disrupt spiral artery remodeling, and promote superficial trophoblast invasion, thereby leading to poor placental blood perfusion and hypoxia, affecting placental function and fetal growth and development^[13]. This pathophysiological process is a key driving mechanism for the occurrence of maternal diseases and fetal complications (such as intrauterine growth restriction). Since hyperuricemia can result from impaired uric acid excretion by the kidneys or excessive production mediated by xanthine oxidase, the serum uric acid/creatinine ratio (UA/Cr) has more clinical guiding significance than applying the serum uric acid value alone, as the UA/Cr value can not only reflect renal function but also better reflect the endogenous uric acid load^{[14][15]}. At present, a large number of studies have shown that preeclampsia is a maternal vascular disease characterized by endothelial dysfunction, impaired angiogenesis and

increased long-term cardiovascular risk^[16–18]. The reactive oxygen species produced by hyperuricemia secondary to elevated xanthine oxidase activity are closely related to endothelial and vascular damage^[19]. This mechanism is highly consistent with the onset, progression and severity of preeclampsia^[20]. At present, there is a growing interest in maternal biomarkers, but research on the ratio of uric acid to creatinine and preeclampsia remains limited. This study explored the predictive indicators of the UA/Cr ratio in different risk stratifications of preeclampsia.

2. MATERIAL AND METHODS

Research design and data sources

We used a retrospective cross-sectional design with data from the Critical Care Medical Information Market IV (MIMIC-IV, version 3.1, 2008–2022), an openly available electronic health record dataset covering inpatients at a tertiary academic medical center^[21]. All records are de-identified and access is credentialed, so the requirement for informed consent does not apply. The reporting is conducted in accordance with the STROBE guidelines for observational research, specifically tailored for cross-sectional study designs^[22]. The ML component follows the TRIPOD + AI statement on internal validation.

Study Population

We identified pregnant women with gestational age ≥ 20 weeks in the MIMIC-IV database using the ICD-10-CM Z3A20–Z3A42 and Z3A49 codes (N = 4,756), with each woman contributing one index hospitalization. Gestational age was taken directly from the ICD-10-CM Z3A code, so hospitalizations recorded only under ICD-9, or lacking the Z3A code, were excluded. After excluding 4,247 records with missing analytical variables (complete-case analysis), the final sample contained 509 women (78 preeclampsia cases, 431 controls). The selection flow is shown in Fig. 1.

Diagnostic Criteria for Preeclampsia

The study included women diagnosed with preeclampsia in the case group and those without the condition as the control group. Preeclampsia was identified through discharge diagnosis codes: ICD-9-CM 6424x, 6425x, 6427x and ICD-10-CM O11x, O14x. These codes implement the clinical criteria issued by the American College of Obstetricians and Gynecologists (ACOG)^[23] and the International Society for the Study of Hypertension in Pregnancy (ISSHP)^[24], with administrative coding used as a proxy for those clinical standards. All laboratory values are the first recorded on the day of admission.

Calculation of the ratio of serum uric acid to creatinine (UA/Cr)

The UA/Cr ratio was determined by dividing the concentration of uric acid in the blood (mg/dL) by the level of creatinine in the blood (mg/dL). The ratio is dimensionless and has been previously evaluated in pregnant populations^[25]. We analyzed UA/Cr both as a continuous variable (per 1-unit increase) and across interquartile groups (Q1–Q4). Quartile cut-offs were derived from the cohort distribution, with Q1

(≤ 6.67) as the reference (cut-offs: 6.67–7.83, 7.83–9.33, ≥ 9.33). The team recorded a median UA/Cr level of 7.83 (IQR 6.67–9.33).

Covariates

Baseline covariates were age (years), race (Asian, Black, Hispanic, other, white), marital status (married, other, single/divorced), language (English, other), and the first-day-of-admission values of white blood cell count (WBC), red blood cell count (RBC), hemoglobin, hematocrit, platelet count, red cell distribution width (RDW), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). Two logistic regression models were formulated: The first model was adjusted exclusively for age; Model 2 was calibrated considering age, language, and RBC as covariates, which showed significance with $P < 0.05$ in univariate analysis but did not enter the final ML feature set. The covariate set is therefore data-driven, and we refer to Model 2 as the “best-adjusted” rather than a fully adjusted model.

Statistical Analysis

Continuous variables with a normal distribution are presented as the average $\pm$ standard deviation. Alternatively presented as the midpoint (interquartile range). Count values and percentage metrics are utilized to describe categorical variables efficiently. For group comparisons involving continuous data, the Wilcoxon rank-sum test was utilized, whereas Pearson's chi-square test was applied for the analysis of categorical data. The UA/Cr–preeclampsia association was assessed with binary logistic regression. We report odds ratios (ORs) and 95% confidence intervals (CIs) for the continuous exposure and for each quartile versus Q1, along with P-for-trend (quartiles modeled as an ordinal term).

Dose–response was evaluated with restricted cubic splines (RCS). The number of knots (3–5) was chosen by minimizing the Akaike information criterion (AIC), and knot positions defaulted to the rms::rcs quantile convention (10th, 50th, 90th percentiles for three knots). We report both overall P and nonlinearity P.

The ML models were developed on a training set stratified by outcome (seed = 62) ($n = 355$, 69.7%); the remaining 154 cases (30.3%) formed the validation set. All feature screening and parameter tuning were performed within the training set only. Candidate features were first filtered by univariate logistic regression ($P < 0.1$) and then analyzed for collinearity with the variance inflation factor (VIF), using a threshold of greater than 5 (refer to Table S2). Hematocrit was flagged here because it was nearly collinear with hemoglobin ($r \approx 0.956$) (Refer to Table S3). LASSO (10-fold cross-validation) was then applied to the full candidate pool (including hematocrit) after univariate screening, yielding the final four-variable feature set: UA/Cr, ALT, marital status, and hematocrit. VIF assessment functioned as an initial diagnostic measure. The final feature set reflects the LASSO selection. The effectiveness of the model was assessed using metrics such as AUC, precision, recall, specificity, F1 score, Cohen's kappa, and the Matthews correlation coefficient. The assessment of calibration utilized log-loss metrics alongside calibration graphs. Assessment of clinical relevance using decision curve evaluation. discrimination stability through DeLong tests; and incremental value through category-free NRI and IDI. The LightGBM

model was analyzed with SHapley Additive exPlanations (SHAP). Two-sided statistical evaluations were conducted, setting the threshold for significance identification at an alpha value of 0.05. All evaluations were performed using R programming (version 4.3.x).

3. RESULTS

Cohort and baseline characteristics

Of 4,756 pregnant women with a gestational age ≥ 20 weeks identified in MIMIC-IV, 4,247 were excluded because of missing analytical or baseline variables. The analytic sample therefore comprised 509 women, including 78 preeclampsia cases (15.3%) and 431 controls (84.7%) (Fig. 1).

Baseline characteristics are summarized in Table 1. versus controls, women with preeclampsia had a higher UA/Cr (median 8.54 [IQR 7.00–10.00] vs. 7.80 [6.57–9.00], $P = 0.004$), higher alanine aminotransferase (ALT; 14.00 [11.00–21.00] vs. 12.00 [10.00–16.00] IU/L, $P < 0.001$), higher aspartate aminotransferase (AST; 22.00 [17.00–26.00] vs. 20.00 [16.00–24.00] IU/L, $P = 0.044$), and a higher proportion of non-English speakers (15.4% vs. 6.3%, $P = 0.011$). They had lower red blood cell count (RBC; 3.89 ± 0.39 vs. $4.04 \pm 0.46 \times 10^6/\mu\text{L}$, $P = 0.002$), hemoglobin (11.33 ± 1.23 vs. 11.72 ± 1.35 g/dL, $P = 0.012$), hematocrit (34.32 ± 3.23 vs. $35.45 \pm 3.64\%$, $P = 0.006$), and white blood cell count (WBC; 9.95 [8.00–12.50] vs. 11.00 [9.10–13.40] $\times 10^3/\mu\text{L}$, $P = 0.023$). Age, race, marital status, platelet count, and red cell distribution width (RDW) did not differ significantly between groups (all $P > 0.05$).

Association between UA/CR and Preeclampsia

A comprehensive overview of the results from the logistic regression analysis in Table 2. UA/Cr was positively associated with preeclampsia across all models. In the fully adjusted Model 2, each 1-unit increase in UA/Cr was linked to an 18.4% higher odds of preeclampsia (OR 1.184, 95% CI 1.061–1.320, $P = 0.002$).

In the quartile analysis, the strongest association appeared in the Q4-vs-Q1 comparison (Model 2: OR 2.758, 95% CI 1.318–6.128, $P = 0.009$), whereas Q2 (OR 1.975, 95% CI 0.913–4.483, $P = 0.091$) and Q3 (OR 1.593, 95% CI 0.722–3.657, $P = 0.256$) did not reach significance. Preeclampsia incidence across quartiles was 8.9%, 16.7%, 13.7%, and 21.9%, respectively. The small dip at Q3 is consistent with sampling fluctuation, given only 78 events. P-for-trend was significant in all models (Model 2: P-for-trend = 0.020). Covariate adjustment produced only modest attenuation: the Q4-vs-Q1 OR shifted from 2.876 to 2.758, and the corresponding P-value from 0.006 to 0.009.

Dose-response relationship between UA/CR and preeclampsia

Restricted cubic spline (RCS) regression with three knots characterized the dose–response of UA/Cr with preeclampsia. Knot count (range 3–5) was selected by the AIC, with knots placed at the 10th, 50th, and 90th percentiles of the UA/Cr distribution following the rms package defaults. RCS analyses showed an approximately linear, positive association between UA/Cr and preeclampsia in all models (Fig. 2). The

overall association was significant in Model 2 (P-overall = 0.001), with no significant nonlinearity (P-nonlinear = 0.911). The cohort median UA/Cr (7.83) was set as the reference (OR = 1.0). The crude model and Model 1 produced the same pattern: a significant overall association with no significant nonlinearity.

Machine learning discrimination performance

Of the 509 patients with complete records, 355 (69.7%) were assigned to the training set and 154 (30.3%) to the internal validation set; 54 (15.2%) and 24 (15.6%) in each set developed preeclampsia. Baseline characteristics—including demographics and routine laboratory values—were well balanced between the two sets (all $P > 0.05$; Supplementary Table S1), supporting exchangeability between training and validation. We trained six ML algorithms (AdaBoost, CatBoost, XGBoost, LightGBM, random forest (RF), and TabPFN) on the same predictor set and compared their discrimination, calibration, and reclassification.

In the training set (Table 3, Fig. 4A), all six models reached an AUC above 0.65. RF performed best (AUC = 0.931), followed by CatBoost (AUC = 0.867); the remaining four models showed moderate discrimination (AUC 0.671 for XGBoost to 0.747 for TabPFN). RF also led on accuracy (0.848), sensitivity (0.889), specificity (0.841), F1 (0.640), kappa (0.553), and MCC (0.590).

In the internal validation set (Table 4, Fig. 4B), discriminative performance dropped for most models. LightGBM achieved the highest AUC (0.761), followed by TabPFN (0.748), AdaBoost (0.740), CatBoost (0.733), XGBoost (0.679), and RF (0.655). The largest training-to-validation drop occurred for RF ($\Delta\text{AUC} = 0.276$), with CatBoost showing a similarly large decline (AUC 0.867 to 0.733, $\Delta\text{AUC} = 0.134$)—both consistent with overfitting. LightGBM, TabPFN, and AdaBoost, by contrast, were essentially stable between sets (LightGBM 0.729 to 0.761; TabPFN 0.747 to 0.748; AdaBoost 0.744 to 0.740), suggesting reasonable generalizability. On the classification metrics, TabPFN had the highest validation sensitivity (0.833), followed by AdaBoost and CatBoost (both 0.750) and LightGBM (0.708); XGBoost achieved the highest specificity (0.777) at the cost of the lowest sensitivity (0.458). MCCs in the validation set ranged from 0.185 to 0.303.

Log-loss values are reported in Supplementary Table S5. RF had the lowest training log-loss (0.303) but a much higher validation log-loss (0.457), echoing the overfitting signal from AUC. AdaBoost (0.386) and LightGBM (0.389) achieved the lowest validation log-loss with negligible train–validation gaps (AdaBoost 0.374 to 0.386; LightGBM 0.391 to 0.389); CatBoost (0.460) and XGBoost (0.458) gave the worst probabilistic fit on the validation set. Calibration curves (Fig. 4C, D) showed acceptable agreement between predicted risks and observed event frequencies in the training set, while larger deviations appeared in the validation set, especially for the high-optimism models (RF and CatBoost).

Pairwise DeLong tests in the validation set are reported in Supplementary Table S6. The AUCs of AdaBoost, TabPFN, CatBoost, and LightGBM were all significantly higher than that of RF (AdaBoost vs RF: $\Delta\text{AUC} = 0.085$, $Z = 2.007$, $P = 0.045$; TabPFN vs RF: $\Delta\text{AUC} = 0.093$, $Z = 2.253$, $P = 0.024$; CatBoost vs RF: $\Delta\text{AUC} = 0.078$, $Z = 2.869$, $P = 0.004$; LightGBM vs RF: $\Delta\text{AUC} = 0.106$, $Z = 2.641$, $P = 0.008$). LightGBM

also significantly outperformed XGBoost ($\Delta\text{AUC} = 0.082$, $Z = 2.523$, $P = 0.012$). All other pairwise comparisons—including those among the gradient-boosting variants (AdaBoost, CatBoost, XGBoost, and LightGBM) and TabPFN—did not reach significance (all $P > 0.05$).

The category-free (continuous) NRI and IDI results are presented in Supplementary Table S7. AdaBoost showed a significant NRI gain over TabPFN (NRI = 0.601, 95% CI: 0.200–1.002, $P = 0.003$) and LightGBM (NRI = 0.539, 95% CI: 0.113–0.964, $P = 0.013$). The IDI of AdaBoost was significantly positive versus TabPFN (IDI = 0.053, 95% CI: 0.019–0.088, $P = 0.002$), CatBoost (IDI = 0.049, 95% CI: 0.013–0.085, $P = 0.008$), XGBoost (IDI = 0.069, 95% CI: 0.029–0.109, $P < 0.001$), and LightGBM (IDI = 0.028, 95% CI: 0.004–0.051, $P = 0.021$), with a borderline improvement over RF (IDI = 0.040, 95% CI: –0.0002–0.080, $P = 0.051$). Among the remaining pairs, CatBoost had a significantly higher IDI than XGBoost (IDI = 0.020, 95% CI: 0.002–0.038, $P = 0.032$), whereas TabPFN had significantly lower NRI and IDI than LightGBM (NRI = –0.356, $P = 0.009$; IDI = –0.026, $P = 0.002$).

Decision curve analysis (Fig. 4G, H) showed that across the clinically relevant threshold range (approximately 10%–60%), most models delivered higher net benefit than treat-all or treat-none strategies in both sets, with the advantage most pronounced and stable for the low-optimism models (AdaBoost, TabPFN, and LightGBM). Taken together, no single model dominated across discrimination, train–validation stability, calibration, and reclassification gain. LightGBM achieved the highest validated discrimination, while AdaBoost combined a stable AUC, the lowest validation log-loss, a favorable sensitivity profile, and significant NRI/IDI gains over competing models—giving it the most balanced overall performance for preeclampsia discrimination in this cohort.

SHapley Additive exPlanations (SHAP) analysis was performed on the LightGBM model within the training set to interpret feature contributions to preeclampsia risk (Fig. 5). By mean absolute SHAP value, hematocrit ranked first (0.506), followed by UA/Cr (0.482), alanine aminotransferase (ALT, 0.429), and marital status. This descriptive ranking reflects the average magnitude of feature influence within LightGBM and does not by itself constitute formal evidence for incremental predictive value.

The SHAP bee-swarm plot visualized the distribution of SHAP values for each feature (Fig. 5B). The SHAP waterfall plot illustrated per-feature contributions to predicted risk for a representative case (Fig. 5C). SHAP dependence plots characterized the marginal association between feature magnitude and model output: higher UA/Cr and ALT corresponded to higher SHAP values (greater predicted preeclampsia risk), whereas higher hematocrit corresponded to lower SHAP values (reduced risk) (Fig. 5D–G).

Subgroup analyses were performed for the Q4-vs-Q1 comparison under Model 2, using quartile cut-offs derived from the cohort distribution (Fig. 6). Point estimates for odds ratios exceeded 1 in most strata. Statistical significance was reached only within the Hispanic subgroup (OR 9.78, 95% CI 1.12–85.63, $P = 0.039$; $n = 49$), with a significant multiplicative interaction by race (P -interaction = 0.026). The Asian subgroup estimate could not be calculated because of sparse outcome events ($n = 31$). Age group (P -

interaction = 0.441), marital status (P-interaction = 0.697), and language (P-interaction = 0.632) showed no significant interactions.

4. DISCUSSION

This study examined the association between the admission-day serum uric acid to creatinine ratio (UA/Cr) and preeclampsia, and evaluated how routine admission laboratory values—including this ratio—contribute to machine learning discrimination of the disease.

Comparison with previous studies and the positioning of this research

Most prior work used absolute uric acid as the exposure, with substantial heterogeneity in reported effect sizes. The overall prediction accuracy was only moderate—not sufficient to independently support clinical decisions^[26]. Dividing by creatinine partly corrects for glomerular filtration, theoretically capturing endogenous uric acid load and xanthine oxidase activity more cleanly, and reducing exposure misclassification from inter-individual variation in renal function^[27]. The roughly linear dose–response observed here is consistent with that expectation.

In terms of discrimination, early- and mid-pregnancy models based on angiogenic markers such as PlGF and sFlt-1 can achieve AUCs above 0.9 for preterm preeclampsia^[28], well above what we report. The two settings are not comparable, however: the former is prospective prediction, while ours is concurrent discrimination on the day of admission. Our models rely only on routine laboratory tests, which are low-cost and widely accessible. The model should therefore be positioned as a low-cost first-line screening tool for hospitalized pregnant women rather than as a prospective prediction model.

Our subgroup analysis found no significant interaction between UA/Cr and age in preeclampsia, which contradicts the conclusion of Zhang et al^[29]. Zhang et al. reported that higher early-pregnancy SUA/sCr was associated with an increased risk in advanced-age women (≥ 35 years). The discrepancy is most plausibly explained by population composition: our cohort included multiple ethnic groups, whereas Zhang et al. focused on a Chinese population.

Biological Rationality and Mechanism Exploration

We observed a positive association between SUA/sCr and preeclampsia, plausibly because uric acid generated via xanthine oxidase drives reactive oxygen species production. Hyperuricemia is closely linked to oxidative stress and endothelial dysfunction^{[30][31]}. Animal experiments suggest that experimentally raising uric acid during pregnancy can trigger preeclampsia-like features, implying an active rather than incidental role for uric acid in disease onset^[32]. Hyperuricemia may impair trophoblast invasion and spiral artery remodeling, compromising placental perfusion and triggering the sFlt-1/PlGF imbalance that precedes maternal endothelial damage^[33]. In established preeclampsia, however, glomerular endothelial damage reduces uric acid clearance, raising serum levels and creating a feedback

loop of “injury–retention–re-injury” that the cross-sectional design cannot disentangle^[34]. The elevated ratio may therefore reflect either a pathogenic contributor or a marker of renal involvement, and the present data support only the association and concurrent discrimination—not temporal causality.

Analysis of the Discriminative Efficiency of Machine Learning

The six algorithms achieved broadly similar discrimination, with no significant pairwise difference among the top four—suggesting that the structural advantages of gradient boosting and TabPFN are hard to demonstrate in this low-dimensional, small-sample setting. Their generalization stability, however, varied: TabPFN’s discrimination barely declined between training and validation sets, while that of random forest declined sharply, consistent with the inherent regularization effect of TabPFN’s pretraining. Sensitivity and specificity trade off; at deployment, the model and threshold should be chosen based on the relative clinical cost of missed versus false-positive cases. The optimal cut-off here was derived from the training set, and under sparse validation events its absolute performance estimate is unstable—recalibration is required before external use. The SHAP ranking is a descriptive marginal contribution and does not by itself demonstrate incremental predictive value; we therefore claim incremental value only when the Δ AUC direction matches the NRI/IDI direction. Decision curve analysis concentrated net benefit in the low-to-moderate threshold range, with the benefit approaching the reference strategies as the threshold rises—consistent with a low-prevalence outcome and moderate discrimination. Models of this kind are useful as low-threshold first-line screening to identify candidates for further testing (e.g., angiogenic markers) or for shortening the monitoring interval, rather than as direct guides to treatment.

Differences among Different Populations and hypothesized Generative Discoveries

In the stratified analysis, only the highest-quartile estimate among Hispanics was significant, with confidence intervals spanning nearly two orders of magnitude—a sign of unstable estimation under sparse events. Although the racial interaction was statistically significant, the parallel stratification has not been corrected for multiple comparisons, and chance cannot be excluded. If the effect is real, it may reflect differences in baseline renal function, dietary purine load, or access to care; It can also stem from inaccuracies in the recorded racial information in official documentation. We therefore treat this interaction as a hypothesis-generating signal that requires confirmation in a more diverse external cohort.

Advantages and Limitations

The innovation of this study is to use renal-function-corrected SUA/sCr as the exposure and confirm, through continuous, quartile, and RCS analyses, an approximately linear dose–response relationship with preeclampsia—providing a basis for threshold setting and biological gradient. In the same design, we integrated conventional epidemiological analysis with six machine learning algorithms and built a four-domain evaluation (“discrimination–calibration–clinical utility–interpretability”) with a transparent, reproducible workflow. We drew a clear line between concurrent discrimination and prospective

prediction, anchored the low-threshold screening positioning via decision curve analysis, and used Δ AUC–NRI/IDI consistency as the incremental-value criterion—an explicit acknowledgement of the inference limits imposed by small samples. Because the model relies only on routine laboratory tests, it is straightforward to deploy in low-resource settings.

Constraints arise from the cross-sectional nature of the design, as it fails to determine causation or the sequence of events over time. The outcome relied on administrative coding. The absence of gestational-week coding for many records caused systematic exclusion. 89.3% of candidates were excluded because of missing laboratory tests, and the resulting selection bias is hard to quantify. Only 78 events were available, limiting certainty. Focused, localized sampling restricts broader applicability. Key risk elements such as gestational period, body mass index, number of pregnancies, and long-term hypertension were not taken into account, resulting in remaining confounding factors. We did not perform head-to-head comparisons with absolute uric acid or with established prediction models, and the exploratory subgroup analyses were not corrected for multiple comparisons. True external validation has not yet been done.

5. CONCLUSION

An increase in SUA/sCr is independently and positively associated with preeclampsia, and the relationship is approximately linear. Machine learning models built from routine laboratory tests achieve moderate concurrent discrimination, with net benefits concentrated in the low-to-medium threshold range that suits screening and risk stratification. SUA/sCr may serve as a low-cost, readily accessible adjunct for risk stratification. Given the limitations above, however, our results do not support prospective prediction. Before any clinical incorporation, prospective multicenter studies, head-to-head comparisons against existing indicators, and external validation are still required.

Declarations

Author Contributions: Conceptualization, AMethodology, Software, Formal Analysis, Visualization, Resources, Data Curation, Writing and Original Draft, Writing, Zixin Pi; Review & Editing, Supervision and Validation, Yangyang Xie.

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Ethical Statement: Ethical approval was not required because all data were obtained from public transcriptome databases.

Conflicts of Interest: We declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Orcid:

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Tables

Tables 1 to 4 are available in the supplementary files section.

Figures

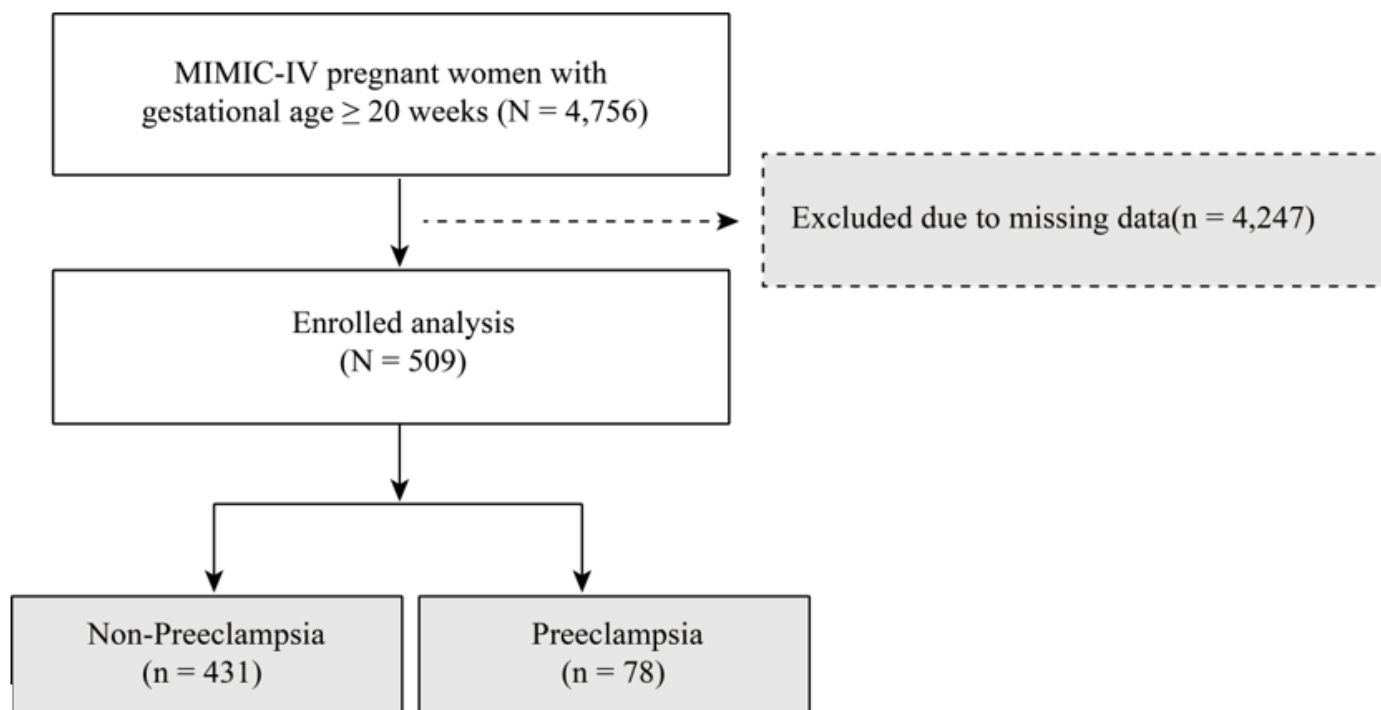


Figure 1. Flowchart of the sample selection from the MIMIC-IV

Figure 1

Flowchart of the sample selection from the MIMIC-IV

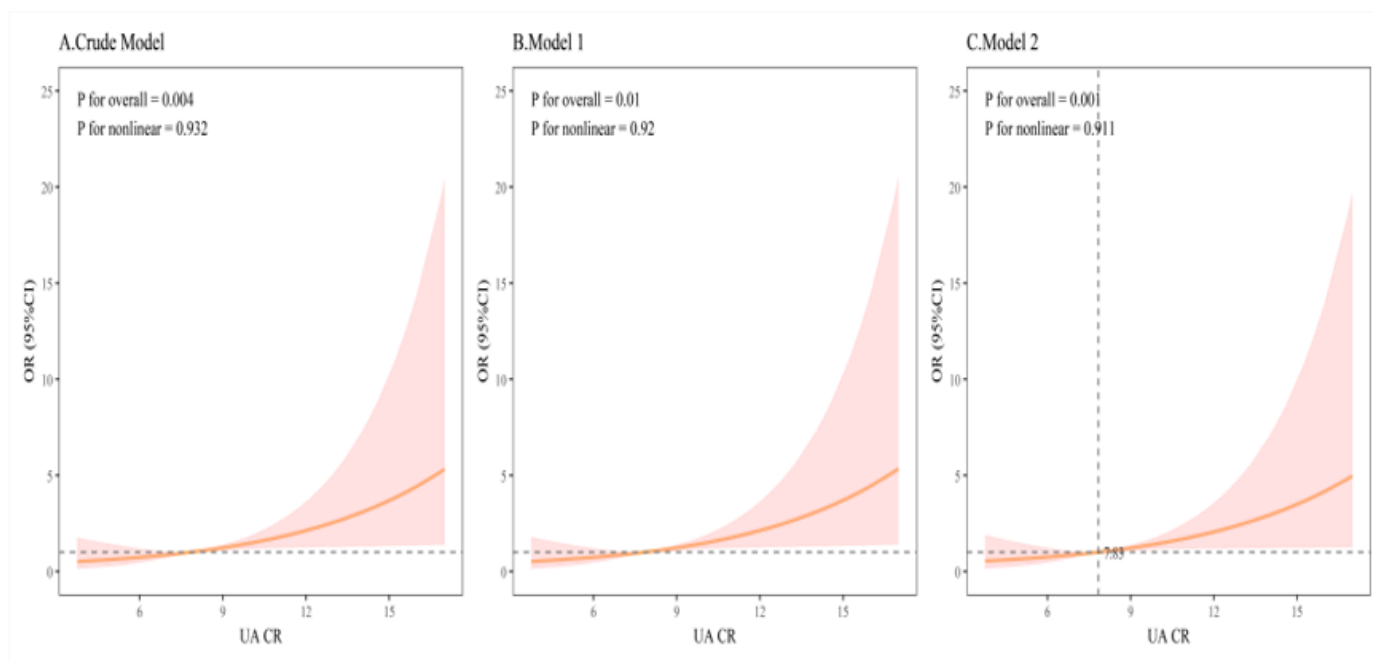


Figure 2

RCS plot between UA CR and Case

Spearman correlation of ML features

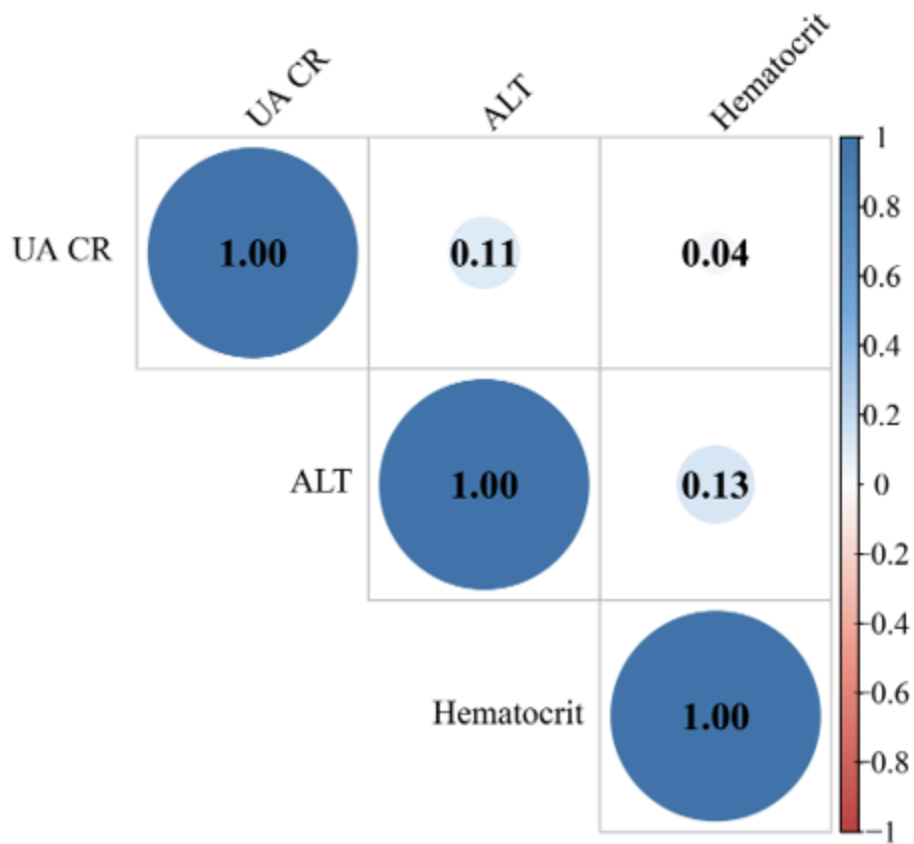


Figure 3. Correlation Heatmap

Figure 3

Correlation Heatmap

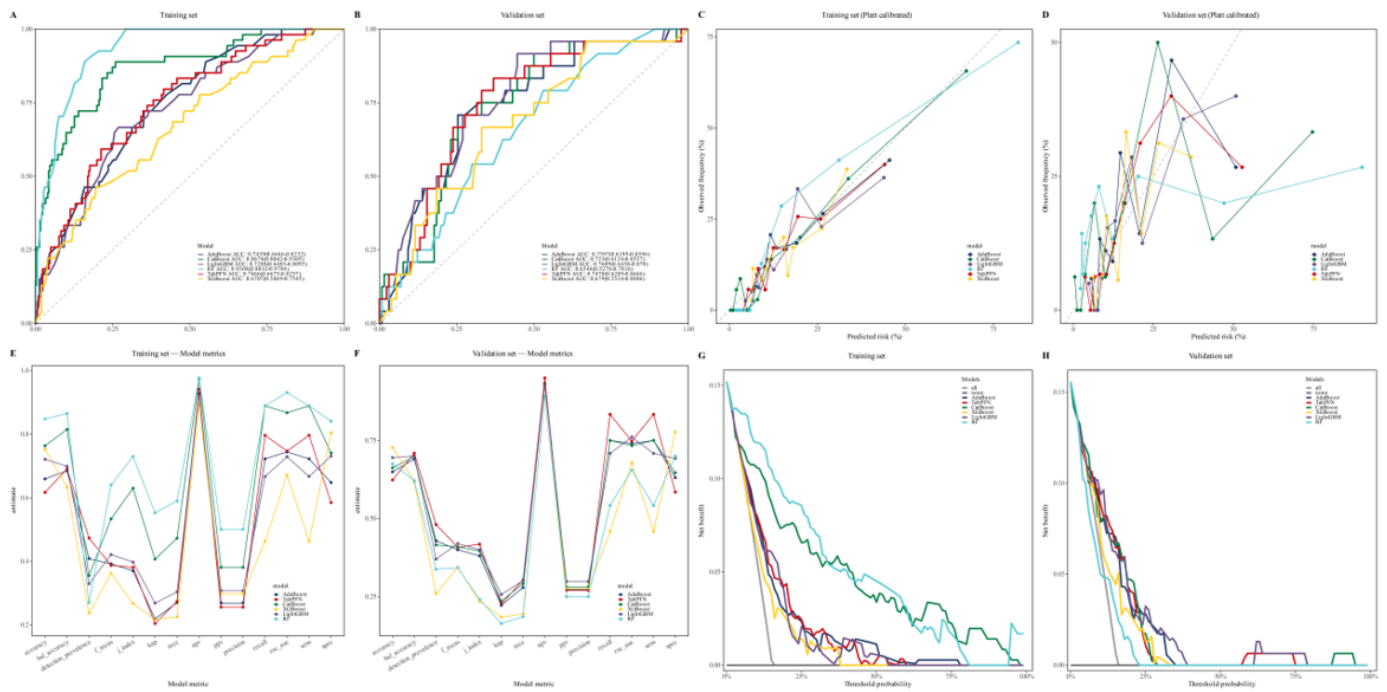


Figure 4

ML performance

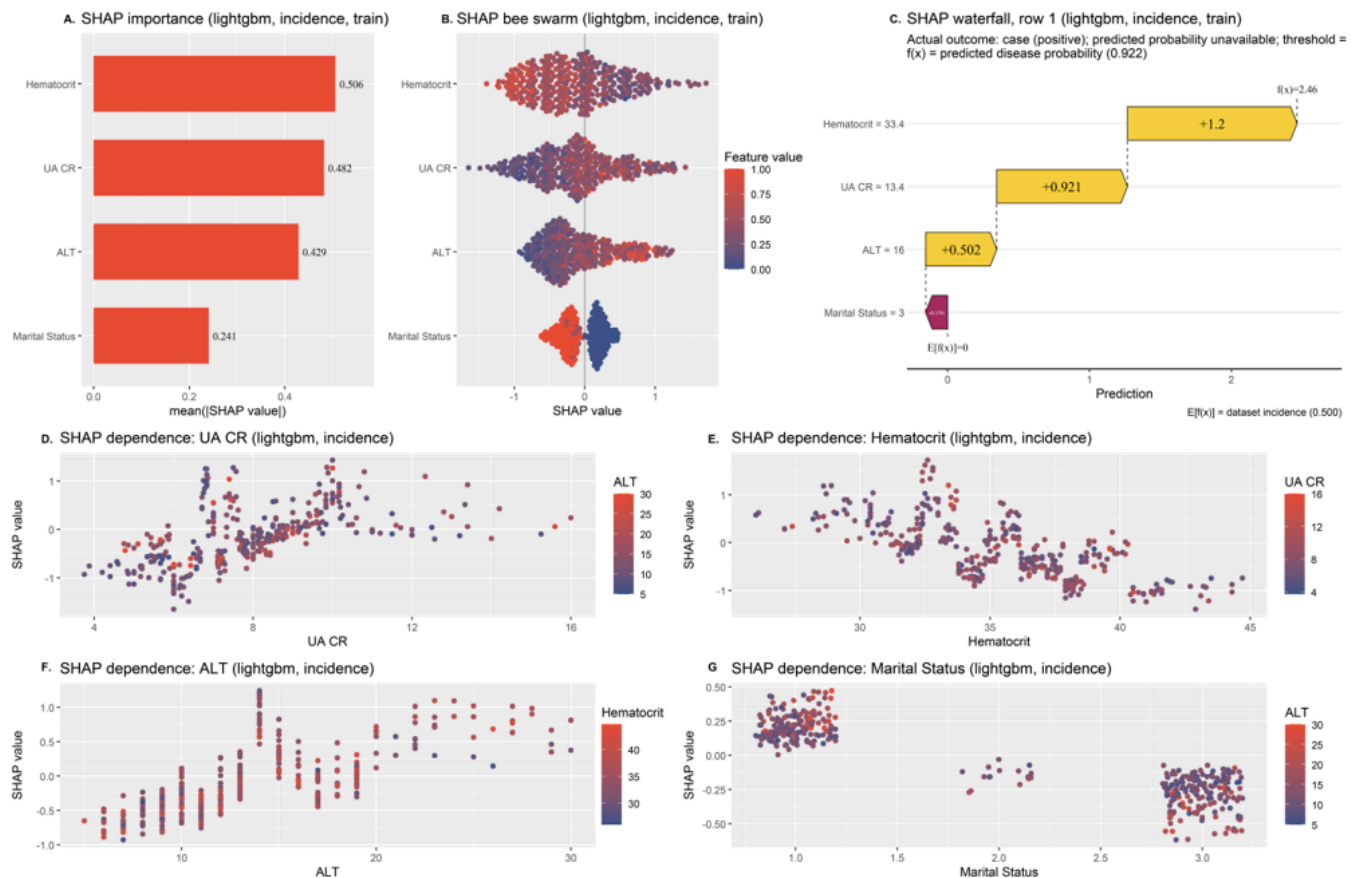


Figure 5

SHAP

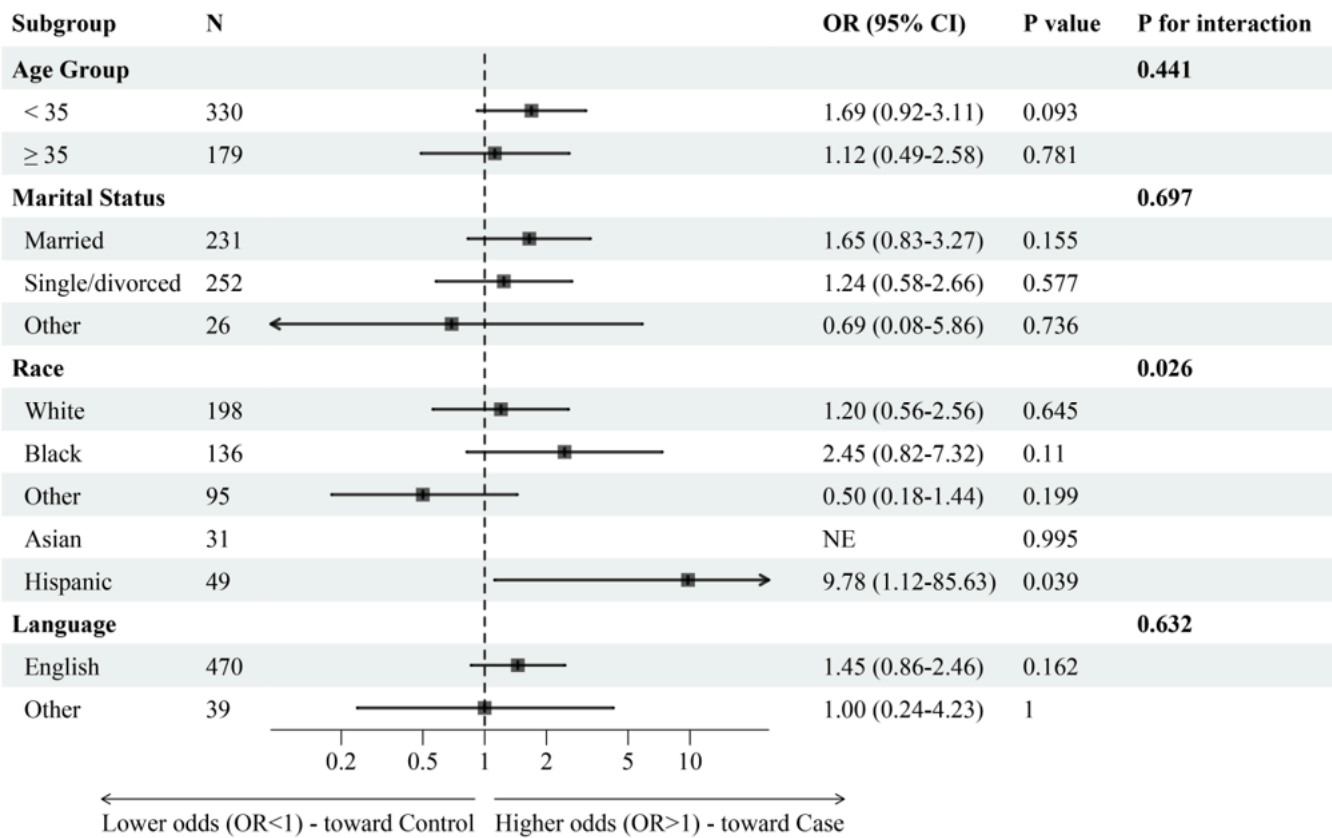


Figure 6

Subgroup Forest analyses of UA CR

Supplementary Files

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