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A Retrospective Study to Compare Serum Uric Acid Levels in Women with Preeclampsia and Pregnancy-Induced Hypertension and Normotensive Pregnant Women

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Abstract

Background: This study aimed to compare serum uric acid (sUA) levels in 59 women with preeclampsia (PE), 61 women with pregnancy-induced hypertension (PIH), and 80 normotensive pregnant women at 24–34 weeks of gestation.

Methods and Results: This case-control study included 200 pregnant women at the Obstetrics and Gynecology Clinic, University Clinical Center of Kosovo. Groups comprised 59 PE patients, 61 PIH patients, and 80 normotensive controls. SUA levels were measured and analyzed for statistical significance. Preeclampsia was diagnosed based on criteria of the International Society for the Study of Hypertension in Pregnancy, which include hypertension onset after 20 weeks of gestation and significant proteinuria. Pregnancy-induced hypertension was identified as hypertension after 20 weeks of gestation without proteinuria. Serum uric acid levels were quantified using enzymatic methods with validated laboratory equipment.

Significant differences in serum uric acid levels were found among groups *(P*=0.0000). PE patients had the highest sUA levels (326.1±64.3 µmol/L) compared to PIH (263.3±60.3 µmol/L; *P*=0.0000) and normotensive women (232.6±44.3 µmol/L; *P*=0.0000). Sensitivity and specificity for PE detection were 96.6% and 48.8%, respectively, with ROC analysis confirming predictive value (AUC:0.857)

Conclusion: Elevated sUA levels are strongly associated with preeclampsia and demonstrate high sensitivity for detecting it. This finding highlights the potential of sUA as a valuable biomarker for early identification and management of preeclampsia, enabling timely interventions to improve maternal and fetal outcomes.(**International Journal of Biomedicine. 2025;15(1):129-134.**)

Keywords: preeclampsia • hypertension • pregnancy • uric acid

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Abbreviations

DBP, diastolic blood pressure; **PIH**, pregnancy-induced hypertension; **PE**, preeclampsia; **SBP**, systolic blood pressure, **sUA**, serum uric acid.

Introduction

Preeclampsia is one of the leading contributors to maternal mortality and is frequently associated with fetal complications that contribute significantly to perinatal morbidity and mortality.[1] In preeclampsia, the condition's precursors can manifest before clinical signs and symptoms become evident,[2] making early detection and prompt treatment critical for positive pregnancy outcomes for both the mother and the child. Identifying precursors of preeclampsia will help detect cases quickly and reduce the negative consequences of the condition during pregnancy.

Much research has been conducted, and many predictive tests for preeclampsia have been explored. However,

preeclampsia is not a completely preventable disease. Routine and specialized biochemical investigations remain the main methods for assessing the risk of preeclampsia in pregnant women and their subsequent management.

Serum uric acid (sUA) levels gradually increase to levels similar to those observed in non-pregnant women at full-term gestation (4–6 mg/dL).[1] Higher levels of sUA correlate with notable rates of morbidity and mortality in both mothers and fetuses.[3,4] However, the cause of hyperuricemia and its specific role in the pathogenesis of preeclampsia remain unclear.[2] Research has shown that elevated sUA levels are a clinical feature of preeclampsia, often preceded by hypertension and proteinuria.[3]

There are several assumptions about the association of sUA with preeclampsia. Hyperuricemia is primarily attributed to impaired renal function.[4] Renal dysfunction is commonly observed in women with preeclampsia.[5,6] Throughout pregnancy, sUA levels usually decrease by 25–35%.[6,7] In women who develop preeclampsia, the sUA level is elevated even at 10 weeks of gestation.[7] Elevated sUA levels often occur before the onset of clinical symptoms of preeclampsia, such as a decrease in glomerular filtration rate.[7] However, an increase in sUA tends to occur before any reduction in plasma volume.[8]

This study aimed to compare sUA levels in women with preeclampsia (PE), women with pregnancy-induced hypertension (PIH), and normotensive women at 24–34 weeks of gestation.

Materials and Methods

A retrospective case-control study was conducted at the Obstetrics and Gynecology Clinic of the University Clinical Center of Kosovo.

This case-control study included 200 pregnant women at the Obstetrics and Gynecology Clinic, University Clinical Center of Kosovo. Groups comprised 59 PE patients (Group 1), 61 PIH patients (Group 2), and 80 normotensive pregnant women (Group 3). Preeclampsia was diagnosed based on criteria of the International Society for the Study of Hypertension in Pregnancy, which include hypertension onset after 20 weeks of gestation and significant proteinuria. PIH was identified as hypertension after 20 weeks of gestation without proteinuria.

Comprehensive Clinical Evaluations included collection of medical history, risk factors for preeclampsia, and comorbid conditions. Physical examination included monitoring blood pressure and identifying clinical signs of hypertensive disorders.

Laboratory Tests

Serum uric acid levels were quantified using enzymatic methods with validated laboratory equipment. Proteinuria was assessed using dipstick testing and 24-hour urinary protein measurements.

Diagnostic Criteria for PE (ISSHP 2021)

Hypertension (SBP≥140 mmHg and/or DBP≥90 mmHg, measured on two occasions at least four hours apart after 20 weeks of gestation).

Proteinuria (≥300 mg per 24-hour urine collection, protein-to-creatinine ratio ≥30 mg/mmol, or dipstick ≥2+).

Alternatively, preeclampsia could be diagnosed in the absence of proteinuria if maternal organ dysfunction was evident, including renal insufficiency, hepatic dysfunction, neurological complications, or hematological abnormalities.

Diagnostic criteria for PIH

PIH was identified as hypertension after 20 weeks of gestation without proteinuria or maternal organ dysfunction.

Statistical analysis was performed using the statistical software package SPSS version 20.0 (SPSS Inc, Armonk, NY: IBM Corp). Baseline characteristics were summarized as frequencies and percentages for categorical variables and mean±standard deviation (SD) for continuous variables.

Multiple comparisons were performed with one-way ANOVA and a Post Hoc Tukey HSD test. The frequencies of categorical variables were compared using the chi-square test.

Receiver operating characteristic (ROC) curves were used to evaluate the performance of diagnostic tests. Sensitivity (true positive rate) and specificity (true negative rate) were calculated at various thresholds. The area under the curve (AUC) was used to quantify overall diagnostic accuracy. All values of $P<0.05$ were considered significant.

Ethical Statement

Ethical approval was obtained from the Medical Faculty of the University of Prishtine Ethics Committee (Approval No: 4689). The study adhered to ethical principles outlined in the Declaration of Helsinki, and all participants provided written informed consent before inclusion.

Results

The mean sUA values for all groups fell within the normal physiological range of 155.0–430.0 µmol/L. Significant differences in mean sUA levels were observed across the groups (P=0.0000). PE patients demonstrated the highest sUA levels (326.1±64.3 µmol/L), followed by PIH patients (263.3±60.3 µmol/L) and normotensive controls (232.6±44.3 µmol/L) (Figure 1).

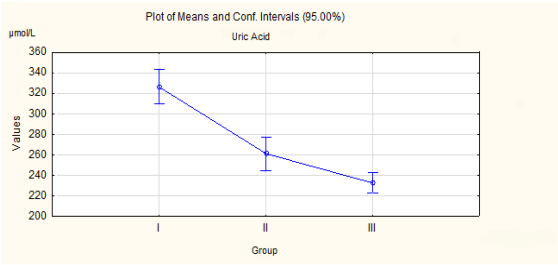

Fig. 1. *Serum uric acid levels in the study groups.*

A one-way ANOVA revealed significant differences in sUA levels among the three groups (P=0.0000). Post hoc Tukey HSD tests further demonstrated pairwise differences: PE group vs. PIH group (P=0.0000), PE group vs. the

normotensive group (P=0.0000), and PIH group vs. the normotensive group (P=0.0040) (Table 1).

Table 1.

One-way ANOVA and Tukey HSD for pairwise comparisons.

Parameter	Group 1 (n=59)	Group 2 (n=61)	Group 3 (n=80)	One-way ANOVA, Tukey HSD
sUA, µmol/L	326.1±64.3	263.3±60.3	232.6 ± 44.3	F=48.2509, P=0.0000 P_{1-2}=0.0000, P_{1-3}=0.0000 P_{2-3}=0.0040

Additionally, Table 2 summarizes the distribution of sUA levels across the three groups, categorized as below, within, or above the normal range. Only in the PE and PIH groups did we identify a small percentage of patients (3.4% and 1.6%, respectively) with sUA levels above normal (155.0–430.0 µmol/L).

Table 2.

Percentage of uric acid levels categorized as below, within, and above the normal range (155.0–430.0 µmol/L) across the study groups.

Normotensive group	Count	Percent
155.0-430.0	78	97.5
<155	2	2.5
>430	0	
PIH group		
155.0-430.0	59	96.7
<155	1	1.6
>430	1	1.6
PE group		
155.0-430.0	56	94.9
<155	1	1.7
>430	2	3.4

A Receiver Operating Characteristic (ROC) analysis confirmed sUA's utility as a biomarker for preeclampsia. The sensitivity was 96.6%, and the specificity was 48.8%, with an area under the curve (AUC) of 0.857 (P=0.000) (Figure 2).

Among patients initially diagnosed with PIH, 27.9% progressed to PE during delivery (Table 3). This progression highlights the importance of close monitoring of hypertensive pregnancies. Additionally, 7.5% of normotensive patients at the study's onset developed hypertensive disorders during pregnancy, with 4 cases progressing to PIH and 2 to PE.

This study reinforces the utility of sUA levels as a significant biomarker for preeclampsia, a condition associated with maternal and fetal morbidity. Elevated sUA levels often precede the onset of hypertension and proteinuria, supporting its role as an early predictive marker. Given the complex pathophysiology of preeclampsia, sUA measurements can complement existing diagnostic frameworks to enable timely interventions.

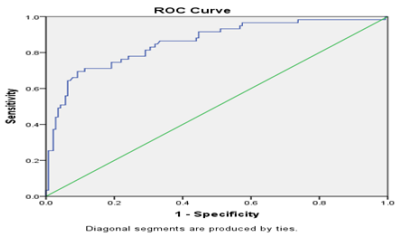

Fig. 2. *ROC curve for sUA levels as a predictor of PE.*

Table 3.

The number of patients with initial diagnosis at admission compared to diagnosis at delivery.

Diagnosis at admission				Diagnosis at delivery			
	n	severity	n		n	severity	n
Normotensive women	80			Normotensive women	74		
				PIH women	4		
				PE women	2	Mild	1
						Severe	1
PIH women	61			PIH women	44		
				PE women	17	Mild	15
						Severe	2
PE women	59	Mild	48	PE women	59	Mild	13
		Ssevere	11			Severe	46

Discussion

This study highlights the potential of sUA levels as a diagnostic marker for preeclampsia. Significant differences in sUA levels were observed among the three patient groups: preeclampsia (PE), pregnancy-induced hypertension (PIH), and normotensive pregnancies.

Patients with preeclampsia exhibited the highest mean sUA levels (326.1±64.3 µmol/L), followed by those with PIH (263.3±60.3 µmol/L) and normotensive women (232.6±44.3 µmol/L). These findings suggest that elevated sUA levels may serve as an early biomarker for preeclampsia, aiding in its timely identification and management.

In the PE group, 94.9% of the patients had sUA levels within the normal range, while 3.4% had levels above 430

μmol/L. In the PIH group, 96.7% of the patients had sUA levels within the normal range, while 1.6% had levels above 430 μmol/L.

Several previous studies revealed findings [10-13] similar to ours. However, some research has indicated that sUA is not a reliable predictor of preeclampsia.[9,14-18]

The ROC curve analysis underscored the clinical utility of sUA levels in diagnosing preeclampsia. So, the ROC curve analysis demonstrated uric acid's high predictive sensitivity (96.6%) for diagnosing preeclampsia, with a specificity of 48.8%. These results suggest that while elevated sUA levels can effectively identify patients at risk of preeclampsia, there remains a significant number of false positive results, emphasizing the importance of additional diagnostic criteria. The area under the curve (AUC) was 0.857 (P=0.000), reinforcing its value as a diagnostic tool. While these results demonstrate high sensitivity, the moderate specificity suggests that sUA should be part of a comprehensive diagnostic framework rather than a standalone marker.

The findings of this study align with previous research highlighting the association between elevated sUA levels and preeclampsia. For example, Roberts et al.[19] demonstrated the link between hyperuricemia and adverse maternal and fetal outcomes in cases of gestational hypertension and preeclampsia. Similarly, Johnson et al.[20] established the role of uric acid in endothelial dysfunction, a hallmark of preeclampsia. Kang et al. emphasized its utility as an early indicator of renal impairment in preeclampsia.[21]

Recent studies continue to support these observations. Nakagawa et al.[22] noted that elevated sUA levels precede the clinical onset of preeclampsia, highlighting its role as an early biomarker. A study by de Mendonça ELSS et al.[23] indicated that hyperuricemia (sUA ≥6 mg/dL) in PE women was a factor associated with cesarean delivery (P=0.030), prematurity (P=0.001), low birth weight (P<0.001) and small for gestational age (P=0.020).

A study by Bellomo et al.[24] screened 206 primiparas with a singleton pregnancy who were referred for recent onset of hypertension and followed the women until 1 month after delivery and recorded pregnancy outcome. ROC analysis showed that sUA, at a 309-μmol/L cutoff, predicted the development of preeclampsia (AUC: 0.955), with 87.7% sensitivity and 93.3% specificity, and the delivery of small-for-gestational-age infants (AUC: 0.784) with 83.7% sensitivity and 71.7% specificity.

A meta-meta-analysis performed by Bellos et al.[25] found that preeclampsia was associated with significantly elevated sUA levels during the 1st (mean difference [MD]: 0.21 mg/dL, 95% confidence intervals [CI]: 0.06-0.35) trimester, 2nd (MD: 1.41 mg/dL, 95% CI: 0.78-2.05) trimester, and 3rd (MD: 2.26 mg/dL, 95% CI: 2.12-2.40) trimester. The authors suggested that sUA levels can be used to predict disease severity and pregnancy complications. At the same time, in a study by Mohamed et al.,[26] sUA showed insignificant statistical elevation in women with severe PE compared with mild PE (P=0.27).

Corominas et al.[27] found that uric acid levels in preeclamptic pregnant women increased by at least 1.5 times after the 20th week of gestation, with no changes in uremia or creatininemia, showing the absence of renal compromise. The authors proposed that a Uric acid ratio (UAr) greater than 1.5 may be related to preeclampsia. In a subsequent study, Corominas et al.,[28] reported that UAr at a cut-off point ≥1.5 had a very low positive predictive value, but a high negative predictive value of 99.5% for preeclampsia.

The results of the presented studies confirm the clinical significance of uric acid monitoring in pregnant women. Serum uric acid should be evaluated in pregnancies with hypertensive disorders.

Clinical Implications

The study's findings have significant implications for clinical practice. Monitoring sUA levels in pregnant women, especially those with hypertensive disorders, could enhance the early detection of preeclampsia. Early identification of elevated sUA levels may prompt timely interventions, reducing the risk of adverse outcomes for both mothers and fetuses. Moreover, combining uric acid with other biomarkers or clinical parameters could improve diagnostic accuracy and enable more comprehensive risk assessments.

Conclusion

Elevated serum uric acid levels are significantly associated with preeclampsia, underscoring their potential as a predictive biomarker. Statistical analysis demonstrates that serum uric acid levels have a sensitivity of 96.6% and a specificity of 48.8%, with a diagnostic accuracy of 85.7% (P=0.000). These findings highlight the clinical utility of monitoring serum uric acid levels to facilitate early detection and management of preeclampsia.

In summary, serum uric acid levels serve as a reliable biomarker for preeclampsia, offering a cost-effective and accessible tool to aid in the early diagnosis and effective management of this significant obstetric complication. Future research should aim to integrate serum uric acid monitoring into comprehensive screening protocols to optimize patient care further.

Study Limitations

While this study provides valuable insights into the predictive role of serum uric acid levels in preeclampsia, several limitations must be acknowledged to contextualize its findings.

Variability in Measurement Timing: One significant limitation is the variability in gestational ages at which serum uric acid levels were measured. Uric acid levels naturally fluctuate throughout pregnancy, potentially influencing the results. Future studies should standardize the timing of measurements to ensure more consistent and comparable data.

Maternal Comorbidities: The study did not comprehensively evaluate maternal comorbidities such as diabetes, chronic hypertension, or renal disease. These conditions are known to affect serum uric acid levels and may

act as confounding factors. Including a detailed assessment of these comorbidities in future research would enhance the robustness of the findings and allow for more accurate stratification of patients.

Medication History: Another limitation is the lack of detailed information on participants' medication histories. The use of antihypertensive drugs, diuretics, or other treatments may alter serum uric acidlevels and confound the results. Future studies should control medication use to exclude possible effects on serum uric acid levels in hypertensive disorders during pregnancy.

Competing Interests

The authors declare that they have no competing interests.

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