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ISSN: 2573-9506

Review Article

International Journal of Women's Health Care

The Role of Hyperuricemia as a Predictor of Adverse Perinatal Outcomes in Pre-eclamptic Women

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Submitted: 2025, Dec 01; **Accepted**: 2025, Dec 30 **Published**: 2026, Jan 16

Citation: Akram, A. (2026). The Role of Hyperuricemia as a Predictor of Adverse Perinatal Outcomes in Pre-eclamptic Women. *Int J Women's Health Care, 11*(1), 01-03.

Abstract

Background: *Pre-eclampsia is a major cause of maternal and perinatal morbidity and mortality. Hyperuricemia is a common finding in pre-eclampsia, but its role as a predictor of adverse outcomes remains a subject of investigation.*

Objective: *To determine the association between elevated serum uric acid levels and adverse perinatal outcomes in women with pre-eclampsia.*

Methods: *A prospective cohort study was conducted from Nov 13, 2024, to April 22, 2025. A total of 272 pre-eclamptic women with a gestational age >24 weeks were enrolled and divided into two cohorts: the exposed group (serum uric acid ≥6 mg/dL, n=136) and the unexposed group (serum uric acid <6 mg/dL, n=136). The primary outcomes measured were severe pre-eclampsia, low birth weight (LBW), intrauterine growth restriction (IUGR), early neonatal death, NICU admission, and a 5-minute Apgar score <7. Data were analyzed using SPSS version 25, with Chi-square tests and relative risk (RR) calculations.*

Results: *Women with hyperuricemia had significantly higher rates of adverse outcomes. Severe pre-eclampsia occurred in 49.26% of the exposed group vs. 25.0% in the unexposed group (RR=1.97, p=0.0001). Similarly, the exposed group had higher incidences of LBW (36.76% vs. 9.56%; RR=3.86, p=0.0001), NICU admission (20.59% vs. 8.82%; RR=2.33, p=0.009), and early neonatal death (25.74% vs. 9.56%; RR=2.69, p=0.001). The association with IUGR and low Apgar score was not statistically significant.*

Conclusion: *Hyperuricemia (serum uric acid ≥6 mg/dL) in pre-eclamptic women is strongly associated with an increased risk of severe maternal disease and several adverse perinatal outcomes, including low birth weight, NICU admission, and early neonatal death. Serum uric acid measurement is a valuable, low-cost prognostic marker that can help identify high-risk pregnancies for more intensive management.*

Keywords: Pre-eclampsia, Hyperuricemia, Perinatal Outcome, Low Birth Weight, Cohort Study.

1. Introduction

Pre-eclampsia, a multisystem disorder characterized by new-onset hypertension and proteinuria after 20 weeks of gestation, complicates 2-8% of pregnancies globally and remains a leading cause of maternal and fetal morbidity and mortality [1]. The pathophysiology involves endothelial dysfunction, abnormal placentation, and an imbalance of angiogenic factors, leading to systemic complications [2].

Among the characteristic laboratory findings in pre-eclampsia is hyperuricemia [3]. While historically used as a diagnostic marker, its role was later overshadowed by proteinuria. However, a growing body of evidence suggests that elevated serum uric acid is not merely an epiphenomenon but may contribute to the pathogenesis of pre-eclampsia by promoting endothelial dysfunction, oxidative stress, and inflammation [4,5].

Several studies have linked hyperuricemia to worse pregnancy outcomes, including progression to severe pre-eclampsia, fetal growth restriction, and preterm birth [6,7]. However, local data in this context is scarce. This study aimed to determine the association between high serum uric acid levels and adverse perinatal outcomes in a cohort of pre-eclamptic women in a tertiary care setting in Pakistan.

2. Methods

2.1 Study Design and Setting

A prospective cohort study was conducted in the Department of Obstetrics & Gynecology at Fatima Memorial Hospital, Lahore, over six months from Nov 03, 2024, to April 22, 2025. Ethical approval was obtained from the institutional review board, and written informed consent was secured from all participants.

2.2 Participants

A total of 272 pre-eclamptic women were enrolled using non-probability consecutive sampling. The sample size was calculated as 136 per group with 80% power and a 5% significance level, based on previous literature [8].

2.3 Inclusion Criteria:

Pregnant women >24 weeks gestation diagnosed with pre-eclampsia (SBP ≥160 mmHg, DBP ≥110 mmHg, and proteinuria ≥1+ on dipstick).
Age 18-40 years.

2.4 Exclusion Criteria:

Multiple pregnancies.
Pre-existing hypertension, diabetes, renal, liver, thyroid, or cardiovascular disease.
Patients on medications for hyperuricemia.

3. Groups and Variables

Participants were stratified into two cohorts:
3.1 Exposed Group: Serum uric acid levels ≥6 mg/dL (n=136).
3.2 Unexposed Group: Serum uric acid levels <6 mg/dL (n=136).
3.3 Primary Outcomes: The adverse perinatal outcomes assessed were:

1. Severe pre-eclampsia (SBP ≥170 mmHg, DBP ≥110 mmHg, proteinuria 3+)
2. Low birth weight (LBW) (<2.5 kg)
3. Intrauterine growth restriction (IUGR) (EFW <10th percentile)
4. NICU admission within 12 hours of birth
5. Early neonatal death (within 12 hours of birth)
6. Apgar score <7 at 5 minutes

3.4 Data Collection and Analysis

Demographic and clinical data were recorded on a structured proforma. Patients were followed until delivery to record the final outcomes. Statistical analysis was performed using SPSS v25.0. Quantitative variables were expressed as mean ± SD, and qualitative variables as frequencies and percentages. The Chi-square test was used to compare outcomes between groups, with a p-value ≤0.05 considered significant. Relative Risk (RR) was calculated to measure the association.

4. Results

4.1 Baseline Characteristics

The mean age of participants was 25.43 ± 4.29 years, with no significant difference between the exposed (26.20 ± 4.62) and unexposed (25.28 ± 4.17) groups. The majority (74.63%) were aged 18-30. Mean gestational age was comparable between groups (Exposed: 31.24 ± 1.57 weeks; Unexposed: 31.41 ± 1.75 weeks). Parity, education level, and place of living were also similarly distributed (Tables I-V).

4.2 Association between Hyperuricemia and Adverse Outcomes

The exposed group (uric acid ≥6 mg/dL) had a significantly higher incidence of most adverse outcomes (Table VI).
Severe Pre-eclampsia: 49.26% vs. 25.0% (RR=1.97, p=0.0001)
Low Birth Weight: 36.76% vs. 9.56% (RR=3.86, p=0.0001)
NICU Admission: 20.59% vs. 8.82% (RR=2.33, p=0.009)
Early Neonatal Death: 25.74% vs. 9.56% (RR=2.69, p=0.001)
The differences in the rates of IUGR (17.65% vs. 19.18%, p=0.754) and Apgar score <7 at 5 minutes (22.79% vs. 13.97%, p=0.065) were not statistically significant.
Stratified Analysis

Stratification by age, gestational age, parity, residence, and education level revealed that the association between hyperuricemia and adverse outcomes like severe pre-eclampsia, LBW, and early neonatal death remained significant across many subgroups, particularly among younger women (18-30 years), those with lower gestational age (24-32 weeks), and women from rural areas (Tables VII-XII).

5. Discussion

This prospective cohort study demonstrates a strong and significant association between maternal hyperuricemia (≥6 mg/dL) and an increased risk of adverse perinatal outcomes in pre-eclamptic women. Our findings align with existing literature that positions uric acid as more than a bystander in pre-eclampsia.

The nearly two-fold increased risk of progressing to severe pre-eclampsia in the hyperuricemic group underscores the role of uric acid in disease severity. Uric acid can crystallize in the renal tubules, exacerbating renal dysfunction and hypertension, and can directly induce endothelial inflammation and oxidative stress [5,9].

The most pronounced association was with low birth weight, with the hyperuricemic group having a 3.86 times higher risk. This is consistent with studies by Ryu et al. and Le et al., who found similar strong correlations. This likely reflects worsened placental perfusion and function due to the underlying maternal endothelial pathology, which is exacerbated by high uric acid levels [6,7].

Furthermore, the significantly higher rates of NICU admission and early neonatal death in the exposed group highlight the critical impact of the maternal condition on neonatal wellbeing. These outcomes are often consequences of iatrogenic preterm delivery for maternal indications or profound placental insufficiency.

It is noteworthy that IUGR was not significantly different between the groups. This suggests that while hyperuricemia is a marker of severe maternal disease, the specific pathway to symmetrical fetal growth restriction may be multifactorial and not solely dependent on uric acid levels.

Our stratified analysis further enriches these findings, indicating that the risks associated with hyperuricemia are potentiated in specific demographic groups, such as younger women and those from rural backgrounds, possibly due to disparities in healthcare access or nutritional status.

6. Strengths and Limitations

A key strength of this study is its prospective cohort design, which allows for a temporal sequence between exposure and outcome. The well-defined groups and comprehensive follow-up add to the validity of the results. A limitation includes the single-center setting, which may affect generalizability. Furthermore, the study was not blinded to the uric acid status of the patients.

7. Conclusion

This study concludes that serum uric acid level is a significant and easily measurable prognostic indicator in pre-eclampsia. Hyperuricemia (≥6 mg/dL) is positively associated with a higher risk of the disease progressing to a severe form and with adverse perinatal outcomes, including low birth weight, NICU admission, and early neonatal death. We recommend the routine assessment of serum uric acid in all pre-eclamptic women to stratify risk and guide more intensive monitoring and timely intervention, thereby improving perinatal outcomes. Public health initiatives should focus on educating healthcare providers about the prognostic value of this simple test.

Funding Statement

This study received no external funding. The work was supported solely by departmental and institutional resources of the Fatima Memorial Hospital.

Conflict of Interest Disclosure

The author declare no conflicts of interest regarding the publication of this article.

Ethics Approval Statement

This study was approved by the Institutional Review Board of Fatima Memorial Hospital.

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