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The Predictive Role of Serum Uric Acid in Adverse Perinatal Outcomes Among Pre-eclamptic Women: A Prospective Cohort Study

Aqsa Akram[1*]

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ABSTRACT

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 perinatal outcomes remains a subject of investigation. To determine the association between high serum uric acid levels (≥6 mg/dL) and adverse perinatal outcomes in women with pre-eclampsia. A prospective cohort study was conducted from November 11, 2024, to May 10, 2025, at the Department of Obstetrics & Gynaecology, Fatima Memorial Hospital, Lahore. A total of 272 pre-eclamptic women with a gestational age >24 weeks were enrolled and divided into two groups: 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 an Apgar score <7 at 5 minutes. Data were analyzed using SPSS version 25, with Chi-square tests and relative risk (RR) calculations. The mean age of participants was 25.43 ± 4.29 years. Women in the hyperuricemic group had a significantly higher incidence of adverse outcomes: severe pre-eclampsia (49.26% vs. 25.0%; RR=1.97, p=0.0001), 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 for IUGR was not statistically significant (17.65% vs. 19.18%; p=0.754). High serum uric acid levels (≥6 mg/dL) in pre-eclamptic women are significantly associated with an increased risk of severe pre-eclampsia, low birth weight, NICU admission, and early neonatal death. Serum uric acid is a valuable, cost-effective biomarker for identifying high-risk pregnancies, warranting intensified monitoring and management to improve perinatal outcomes.

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 is a leading cause of maternal and perinatal mortality, particularly in developing nations (Adewolu, 2013; American College of Obstetricians and Gynecologists [ACOG], 2001). The pathophysiology, though not fully elucidated, involves abnormal placental implantation, endothelial dysfunction, and an imbalance of angiogenic factors (Redman & Sargent, 2005).

Among the distinctive laboratory findings in pre-eclampsia is hyperuricemia (Mehta *et al.*, 2019). While initially considered a mere marker of reduced renal function, emerging evidence suggests that uric acid may play a direct pathogenic role by promoting endothelial dysfunction, oxidative stress, and inflammation (Bainbridge & Roberts, 2008; Many *et al.*, 2000). Several studies have linked elevated maternal serum uric acid levels to an increased risk of adverse maternal and fetal outcomes, including progression to severe pre-eclampsia, fetal growth restriction, and preterm birth (Ugwuanyi *et al.*, 2021; Le *et al.*, 2019).

However, the consistency of this association and its utility in routine clinical practice, especially in local populations, requires further validation. Local data on this subject is scarce. This study was therefore designed to determine the association between high serum uric acid levels and adverse perinatal outcomes in pre-eclamptic women, with the aim of providing evidence to guide risk stratification and management protocols in our setting.

MATERIALS AND METHODS

Study Design and Setting

A prospective cohort study was conducted at the Department of Obstetrics & Gynaecology, Fatima Memorial Hospital, Lahore, from November 11, 2024, to May 10, 2025. Ethical approval was obtained from the institutional review board, and written informed consent was secured from all participants.

Participants

A total of 272 women diagnosed with pre-eclampsia were enrolled using non-probability consecutive sampling.

Inclusion Criteria: Pregnant women aged 18-40 years, gestational age >24 weeks, diagnosed with pre-eclampsia (systolic BP ≥160 mmHg, diastolic BP ≥100 mmHg, and proteinuria ≥1+ on dipstick).

Exclusion Criteria: Multiple pregnancies, pre-existing hypertension, cardiovascular, renal, liver, thyroid disease, diabetes mellitus, other acute or chronic illnesses, and patients on medications for hyperuricemia.

Group Allocation

Patients were divided into two cohorts based on their serum uric acid level at presentation:

[1] Senior Registrar Department of Obstetrics & Gynaecology, Fatima Memorial Hospital, Lahore, Pakistan
[*] Corresponding author's e-mail: aqsaakrampk@gmail.com

Group A (Exposed): Serum uric acid ≥6 mg/dL (n=136).
Group B (Unexposed): Serum uric acid <6 mg/dL (n=136).

Data Collection and Outcome Measures

Demographic data (age, parity, education, residence) were recorded. All patients were followed until delivery, and the following perinatal outcomes were assessed as defined:
Severe pre-eclampsia: Systolic BP ≥170 mmHg, diastolic BP ≥110 mmHg, and proteinuria 3+.
Low birth weight (LBW): Birth weight <2.5 kg.
Intrauterine growth restriction (IUGR): Estimated fetal weight below the 10th centile on ultrasonography.
NICU admission: Admission to the neonatal intensive care unit within 12 hours of birth.
Early neonatal death: Death of the neonate within 12 hours of birth.
Low Apgar score: Apgar score <7 at 5 minutes.

Statistical Analysis

Data were analyzed using SPSS version 25.0. Quantitative variables were presented as mean ± standard deviation, 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 statistically significant. The Relative Risk (RR) was calculated, with RR >1 indicating a positive association. Stratification was performed for age, gestational age, parity, residence, and education level.

Sample Size

The sample size of 272 (136 per group) was calculated with a 5% significance level and 80% power, assuming NICU admission rates of 54.48% in the exposed and 42.46% in the unexposed group, based on a previous study (Zangana & Hamadamen, 2018).
Results and Discussions
3.1. Baseline Characteristics
The mean age of the participants was 25.43 ± 4.29 years, with the majority (74.63%) between 18-30 years. The mean gestational age was 31.31 ± 1.67 weeks, and the mean parity was 2.34 ± 0.85. The distribution of education level and place of living was comparable between the two groups (Table 1).

Table 1: Baseline Characteristics of the Study Participants (n=272)

Characteristic	Exposed (n=136)	Unexposed (n=136)	Total (n=272)	p-value
Age (years), Mean ± SD	26.20 ± 4.62	25.28 ± 4.17	25.43 ± 4.29	-
Gestational Age (weeks), Mean ± SD	31.24 ± 1.57	31.41 ± 1.75	31.31 ± 1.67	-
Parity, Mean ± SD	2.34 ± 0.85	2.34 ± 0.85	2.34 ± 0.85	-
Education ≥ Matric, n (%)	50 (36.76)	53 (38.97)	103 (37.87)	0.707
Urban Residence, n (%)	96 (70.59)	88 (64.71)	184 (67.65)	0.295

Association Between Hyperuricemia and Adverse Perinatal Outcomes

The exposed group (uric acid ≥6 mg/dL) had a significantly higher incidence of most adverse outcomes (Table 2). The risk of severe pre-eclampsia, LBW, NICU admission, and early neonatal death was approximately 2 to 4 times higher in women with hyperuricemia. The associations for IUGR and a low Apgar score were not statistically significant.

Stratification Analysis

Stratification by demographic variables revealed that the association between hyperuricemia and adverse outcomes

Table 2: Association Between High Serum Uric Acid Levels and Adverse Perinatal Outcomes

Adverse Outcome	Exposed (n=136)	Unexposed (n=136)	Total (n=272)	p-value
Severe Pre-eclampsia	67 (49.26%)	34 (25.0%)	1.97	0.0001
Low Birth Weight (LBW)	50 (36.76%)	13 (9.56%)	3.86	0.0001
NICU Admission	28 (20.59%)	12 (8.82%)	2.33	0.009
Early Neonatal Death	35 (25.74%)	13 (9.56%)	2.69	0.001
Apgar Score <7 at 5 min	31 (22.79%)	19 (13.97%)	1.63	0.065
IUGR	24 (17.65%)	26 (19.18%)	0.92	0.754

was often more pronounced in specific subgroups. For instance, the risk of severe pre-eclampsia was significantly higher in older women (31-40 years, RR=33.7), those with higher parity (3-5, RR=3.53), and rural residents (RR=4.11). Similarly, the risk of LBW was exceptionally high among younger women (18-30 years, RR=6.76) and rural residents (RR=7.20).

RESULTS AND DISCUSSION

This prospective cohort study demonstrates a strong and significant association between elevated serum uric acid levels (≥6 mg/dL) and an increased risk of adverse perinatal outcomes in pre-eclamptic women. Our findings align with a growing body of evidence that positions hyperuricemia not just as a biomarker but as a potential contributor to the pathogenesis of severe disease.

The incidence of severe pre-eclampsia was nearly double in the hyperuricemic group (49.26% vs. 25.0%), reinforcing the concept that uric acid is linked to disease severity (Roberts *et al.*, 2005). This is consistent with the findings of Ugwuanyi *et al.* Ugwuanyi *et al.* (2021), who reported a 74.1% rate of severe pre-eclampsia in hyperuricemic women versus 41.7% in those with normal uric acid.

More critically, our study highlights the profound impact of maternal hyperuricemia on the fetus. The risks of LBW, NICU admission, and early neonatal death were 3.86, 2.33, and 2.69 times higher, respectively, in the exposed group. These results are corroborated by Le *et al.* Le *et al.* (2019), who found that hyperuricemia significantly increased the odds of preterm birth, low Apgar score, IUGR, and neonatal death. The lack of a significant association for IUGR in our study (17.65% vs. 19.18%, p=0.754) is an interesting divergence, which may be due to sample size or population-specific factors and warrants further investigation.

The pathophysiological link may be explained by several mechanisms. Uric acid can crystallize in the placental bed, causing inflammation and infarction, thereby compromising placental blood flow (Many *et al.*, 2000). Furthermore, soluble uric acid inhibits endothelial cell proliferation and function, exacerbating the widespread maternal endothelial dysfunction characteristic of pre-eclampsia (Bainbridge & Roberts, 2008). This leads to vasoconstriction, reduced placental perfusion, and ultimately, fetal compromise manifesting as growth restriction, prematurity, and low birth weight.

The stratification analysis further enriches our understanding, suggesting that the risk conferred by hyperuricemia is not uniform. It appears to be magnified in vulnerable subgroups such as older mothers, women of higher parity, and those from rural areas, possibly due to compounded socio-economic and biological risk factors.

Limitations

This study was conducted at a single tertiary care center, which may limit the generalizability of the findings. The use of non-probability sampling also introduces the potential for selection bias. Despite these limitations, the prospective design and clear definition of groups and outcomes strengthen the internal validity of our conclusions.

CONCLUSION

This study conclusively demonstrates a positive association between high serum uric acid levels (≥6 mg/dL) and adverse perinatal outcomes, including severe pre-eclampsia, low birth weight, NICU admission, and early neonatal death, in pre-eclamptic women. Serum uric acid measurement is a simple, cost-effective test that provides significant prognostic value.

We recommend the routine assessment of serum uric acid in all women diagnosed with pre-eclampsia. Identifying hyperuricemia should trigger intensified fetal surveillance and prompt management to mitigate the risks of severe complications. Public and professional health education programs should emphasize the importance of prenatal screening and the management of pre-eclampsia and its associated biomarkers to reduce the burden of perinatal morbidity and mortality.

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