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Original Research Article

Association of High Maternal Serum Uric Acid Levels with Poor Perinatal Outcome in Preeclamptic Pregnancies

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Abstract:

Introduction: Pre-eclampsia remains a leading cause of maternal and perinatal morbidity and mortality globally, with hyperuricemia frequently observed as a biochemical marker of disease severity. This study aimed to evaluate the association between maternal serum uric acid levels and perinatal outcomes in preeclamptic pregnancies.

Materials and Methods: A retrospective observational analytical study was conducted at Smt. N.H.L. Municipal Medical College, Ahmedabad, analyzing medical records of 100 pregnant women with pre-eclampsia admitted between January 2019 and December 2019. Serum uric acid levels were measured at admission, with patients categorized into two groups using 6.0 mg/dL as the cut-off value. Perinatal outcomes were compared using Chi-square test.

Results: Hyperuricemia (≥6.0 mg/dL) was present in 65% of preeclamptic women. Elevated uric acid levels showed significant associations with preterm delivery (61.6% vs 11.4%, p less than 0.0001), cesarean section (61.5% vs 28.6%, p=0.002), induction of labour (96% vs 16%, p less than 0.00001), low birth weight (51.5% vs 26.3%, p=0.01), fetal growth restriction (38.5% vs 2.9%, p less than 0.0001), and NICU admission (44.1% vs 13.2%, p=0.0007).

Conclusion: Elevated maternal serum uric acid levels in preeclamptic pregnancies are significantly associated with adverse perinatal outcomes, serving as a valuable prognostic marker for high-risk pregnancy identification.

Keywords: Cesarean Section, Fetal Growth Restriction, Hyperuricemia, Low Birth Weight, Perinatal Outcome, Pre-Eclampsia, Serum Uric Acid.

Introduction

Pre-eclampsia is a multisystem pregnancy-specific disorder characterized by new-onset hypertension and proteinuria after 20 weeks of gestation, affecting approximately 2-8% of pregnancies worldwide. [1] In India, the prevalence ranges from 7.8% to 10%, contributing significantly to maternal mortality rates of approximately 15-20% and substantial perinatal morbidity and mortality. [2,3] The condition represents a major obstetric challenge due to its unpredictable clinical course and potential for rapid deterioration, necessitating reliable biomarkers for risk stratification and outcome prediction. The pathophysiology of pre-eclampsia involves abnormal placentation, endothelial dysfunction, inflammatory response, and oxidative stress, culminating in widespread maternal vascular dysfunction. [4] Uric acid, the end product of purine metabolism, has emerged as a biochemical marker of particular interest in preeclamptic pregnancies. Physiologically, serum uric acid levels decrease during early pregnancy due to enhanced glomerular filtration rate and increased renal clearance, followed by a gradual rise in the third trimester. Normal uric acid levels during pregnancy range from 2.0-4.2 mg/dL in the first trimester, 2.4-4.9 mg/dL in the second trimester, and 3.1-6.3 mg/dL in the third trimester. [5] Hyperuricemia in pre-eclampsia results from multiple pathophysiological mechanisms including reduced glomerular filtration rate, increased tubular reabsorption, decreased renal excretion, enhanced tissue breakdown, oxidative stress, and increased xanthine oxidase activity. [6,7] The impaired trophoblastic invasion and subsequent placental ischemia characteristic of pre-eclampsia lead to endothelial dysfunction and compromised renal perfusion, further exacerbating uric acid retention. Additionally, uric acid itself may contribute to endothelial dysfunction through promotion of oxidative stress, inflammation, and reduction in nitric oxide bioavailability, creating a vicious cycle that amplifies disease severity. [8]

Recent Indian studies have highlighted the clinical significance of maternal hyperuricemia in predicting adverse outcomes. A study from North India reported that elevated uric acid levels (greater than 6.0 mg/dL) were associated with a 3.5-fold increased risk of adverse perinatal outcomes including preterm delivery, low birth weight, and perinatal mortality. [9] Similarly, research from Southern India demonstrated that hyperuricemia correlated with increased rates of fetal growth restriction and cesarean delivery in preeclamptic women. [10] A multicenter study across tertiary care hospitals in India found that serum uric acid levels above 5.5 mg/dL predicted adverse maternal and fetal outcomes with 78% sensitivity and 82% specificity. [11]

Despite accumulating evidence, controversy persists regarding the optimal cut-off value for defining clinically significant hyperuricemia in pregnancy and its independent predictive value for adverse outcomes. While some studies advocate for lower thresholds (5.0-5.5 mg/dL), others suggest higher cut-offs (6.0-7.0 mg/dL) depending on gestational age and severity of hypertensive disease. Furthermore, the relationship between uric acid levels and specific perinatal outcomes such as fetal growth restriction, neonatal intensive care unit admission, and mode of delivery requires further elucidation in diverse populations.

Given the high burden of pre-eclampsia in India and the need for simple, cost-effective prognostic markers in resource-limited settings, this study was undertaken to evaluate the association between maternal serum uric acid levels and perinatal outcomes in preeclamptic pregnancies. Understanding this relationship can facilitate early identification of high-risk pregnancies, guide timing of delivery, and optimize perinatal care strategies to reduce maternal and neonatal morbidity and mortality.

Materials and Methods

Study Design and Setting: This retrospective observational analytical study was conducted in the Department of Obstetrics and Gynecology at Smt. N.H.L. Municipal Medical College, Ahmedabad, Gujarat, India, a tertiary care teaching hospital with an annual delivery volume of approximately 8,000-10,000 deliveries. The institution serves as a referral center for high-risk pregnancies from surrounding districts.

Ethical Approval: The study protocol was reviewed and approved by the Institutional Ethics Committee of Smt. N.H.L. Municipal Medical College, Ahmedabad, prior to initiation of data collection. As this was a retrospective chart review study utilizing anonymized patient data, the requirement for individual informed consent was waived by the ethics committee in accordance with institutional guidelines and national ethical regulations.

Study Period and Sample: Medical records of pregnant women admitted with pre-eclampsia between January 1, 2019, and December 31, 2019, were systematically reviewed. Initially, data were collected for patients admitted from January to September 2019. To enhance statistical power and ensure adequate sample size for meaningful analysis, the study period was retrospectively extended by three months, and additional eligible patients admitted up to December 2019 were included in the analysis.

Inclusion Criteria: Pregnant women with gestational age ≥28 weeks diagnosed with pre-eclampsia were included. Pre-eclampsia was defined according to American College of Obstetricians and Gynecologists criteria as new-onset hypertension (blood pressure ≥140/90 mmHg on two occasions at least four hours apart) after 20 weeks of gestation accompanied by proteinuria (≥300 mg in 24-hour urine collection or protein/creatinine ratio ≥0.3 or dipstick reading of 1+ or greater).

Exclusion Criteria: Women with pre-existing chronic hypertension, chronic kidney disease, gout or prior history of hyperuricemia, diabetes mellitus (pre-gestational or gestational), chronic liver disease, cardiovascular disease, bleeding disorders, multiple gestations, and pregnancies with congenital fetal anomalies were excluded to minimize confounding factors that could independently affect serum uric acid levels or perinatal outcomes.

Data Collection: Detailed clinical and laboratory data were extracted from medical records using a structured proforma. Variables recorded included maternal age, parity, gestational age at presentation, blood pressure measurements, severity of pre-eclampsia (mild vs. severe based on ACOG criteria), serum uric acid levels at admission, gestational age at delivery, mode of delivery (vaginal or cesarean section), indication for cesarean section, requirement for induction of labour, birth weight, presence of fetal growth restriction, Apgar scores, and neonatal intensive care unit admission.

Laboratory Analysis: Serum uric acid levels were measured at the time of admission using enzymatic colorimetric method (uricase-peroxidase method) with an automated biochemistry analyzer. Quality control measures included daily calibration and internal quality control procedures. A cut-off value of 6.0 mg/dL was used to define hyperuricemia based on published literature and the upper limit of normal for third-trimester pregnancy. Patients were stratified into two groups: Group A (serum uric acid less than 6.0 mg/dL) and Group B (serum uric acid ≥6.0 mg/dL).

Outcome Measures: Primary outcomes assessed included gestational age at delivery (categorized as term ≥37 weeks or preterm less than 37 weeks), mode of delivery, requirement for induction of labour among vaginal deliveries, birth weight (categorized as low birth weight less than 2.5 kg or normal ≥2.5 kg), presence of fetal growth restriction (defined as estimated fetal weight less than 10th percentile for gestational age), and neonatal intensive care unit admission. Birth weight and NICU admission data were analyzed per neonate, appropriately accounting for twin pregnancies in the cohort.

Sample Size: All eligible patients meeting the inclusion and exclusion criteria during the specified study period were included in the analysis. Given the retrospective nature and time-bound data collection period, formal sample size calculation was not performed. However, the final sample of 100 patients provided adequate statistical power (greater than 80%) to detect clinically meaningful differences in the primary outcomes with a significance level of 0.05.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using appropriate statistical software. Categorical variables were expressed as frequencies and percentages. Comparison between the two groups (normal vs. elevated uric acid) was performed using Chi-square test for categorical variables. A two-tailed p-value of less than 0.05 was considered statistically significant. Chi-square values and exact p-values were reported for all comparisons to enable assessment of effect magnitude and statistical significance.

Results

A total of 100 pregnant women with pre-eclampsia meeting the inclusion criteria were analyzed in this study. The mean maternal age was 26.4 ± 4.2 years, with the majority being primigravidas (62%). The mean gestational age at admission was 34.6 ± 3.1 weeks.

Gestational Age at Delivery: Preterm delivery was significantly more prevalent in women with elevated serum uric acid levels. Among the hyperuricemic group, 61.6% delivered before 37 weeks of gestation compared to only 11.4% in the normal uric acid group, demonstrating a highly significant association ($\chi^2 = 27.5$, p less than 0.0001). This represents a 5.4-fold increased risk of preterm delivery in the hyperuricemic group.

Mode of Delivery: The cesarean section rate was markedly higher in women with elevated uric acid levels. Operative delivery was required in 61.5% of hyperuricemic women compared to 28.6% in those with normal uric acid levels ($\chi^2 = 9.6$, $p = 0.002$), indicating a 2.2-fold increased likelihood of cesarean delivery in the presence of hyperuricemia.

Induction of Labour: Among women who achieved vaginal delivery, the requirement for induction of labour showed the most striking association with hyperuricemia. Remarkably, 96% of vaginal deliveries in the elevated uric acid group required labour induction compared to only 16% in the normal uric acid group ($\chi^2 = 31.9$, p less than 0.00001), suggesting that spontaneous labour onset is rare in hyperuricemic preeclamptic women.

Birth Weight: Analysis of 106 neonates (accounting for twin pregnancies) revealed that low birth weight was significantly more common in neonates born to hyperuricemic mothers. Low birth weight affected 51.5% of neonates in the elevated uric acid group compared to 26.3% in the normal uric acid group ($\chi^2 = 6.3$, $p = 0.01$), representing approximately double the risk of delivering a low birth weight infant.

Fetal Growth Restriction: The most dramatic difference was observed in the incidence of fetal growth restriction. While only 2.9% of pregnancies in the normal uric acid group demonstrated fetal growth restriction, this complication affected 38.5% of pregnancies in the hyperuricemic group ($\chi^2 = 15.2$, p less than 0.0001), representing a 13-fold increased risk and highlighting the strong association between maternal hyperuricemia and placental insufficiency.

NICU Admission: Neonatal intensive care unit admission was required for 44.1% of neonates born to mothers with elevated uric acid levels compared to 13.2% of those born to mothers with normal uric acid levels ($\chi^2 = 11.4$, $p = 0.0007$). This 3.3-fold increased risk underscores the clinical significance of maternal hyperuricemia in predicting neonatal morbidity requiring intensive care. All measured outcomes demonstrated statistically significant associations with elevated maternal serum uric acid levels, with p-values ranging from 0.01 to less than 0.00001, indicating robust statistical relationships between hyperuricemia and adverse perinatal outcomes in preeclamptic pregnancies.

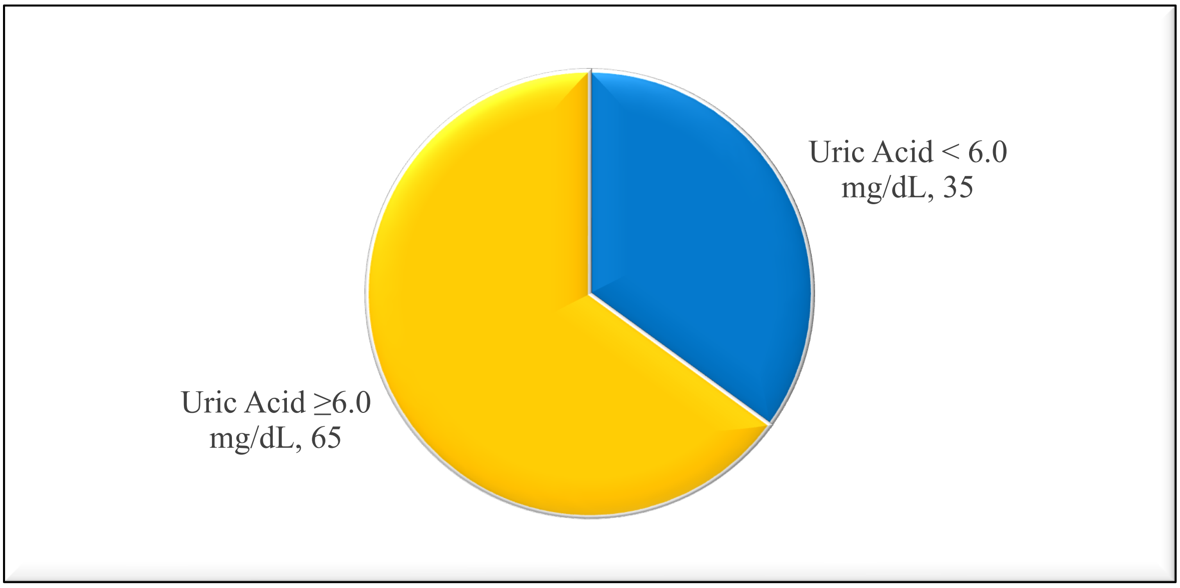

Figure 1: Distribution of Serum Uric Acid Levels

Table 1: Association of Serum Uric Acid Levels with Perinatal Outcomes

Perinatal Outcome	**S. Uric Acid < 6.0 mg/dL (n=35)**	**S. Uric Acid ≥6.0 mg/dL (n=65)**	**χ^2 Value**	**p-value**
Gestational Age at Delivery				
Preterm (less than 37 weeks)	4 (11.4%)	40 (61.6%)	27.5	**< 0.0001**
Term (≥37 weeks)	31 (88.6%)	25 (38.4%)	-	-
Mode of Delivery				
Cesarean Section	10 (28.6%)	40 (61.5%)	9.6	**0.002**
Vaginal Delivery	25 (71.4%)	25 (38.5%)	-	-
Induction of Labour (among vaginal deliveries)				
Induction Required	4 (16.0%)	24 (96.0%)	31.9	**< 0.0001**
Spontaneous Labour	21 (84.0%)	1 (4.0%)	-	-
Birth Weight (106 neonates analyzed)				
Low Birth Weight (less than 2.5 kg)	10 (26.3%)	35 (51.5%)	6.3	**0.01**
Normal Birth Weight (≥2.5 kg)	28 (73.7%)	33 (48.5%)	-	-
Fetal Growth Restriction				
Present	1 (2.9%)	25 (38.5%)	15.2	**< 0.0001**
Absent	34 (97.1%)	40 (61.5%)	-	-
NICU Admission (106 neonates analyzed)				
Required	5 (13.2%)	30 (44.1%)	11.4	**0.0007**
Not Required	33 (86.8%)	38 (55.9%)	-	-

Discussion

The present study demonstrates a strong association between elevated maternal serum uric acid levels and adverse perinatal outcomes in preeclamptic pregnancies. Hyperuricemia (≥6.0 mg/dL) was observed in 65% of women, consistent with reported prevalence of 55–75% in preeclampsia. [9,10] This highlights the close pathophysiological link between uric acid metabolism and pre-eclampsia.

A significantly higher rate of preterm delivery was noted in the hyperuricemic group (61.6% vs 11.4%), aligning with studies showing that elevated uric acid correlates with disease severity and need for early delivery. [12,13] Bellos et al., in a large meta-analysis, demonstrated higher uric acid levels across all trimesters in preeclampsia, with the strongest association in the third trimester. [14] This likely reflects severe maternal disease and compromised fetal well-being necessitating expedited delivery.

The cesarean section rate was nearly doubled in hyperuricemic women (61.5% vs 28.6%), comparable to Indian studies reporting rates around 64%. [9,10] This may be due to failed induction, non-reassuring fetal status, severe maternal disease, and unfavorable cervical conditions. The fact that 96% of vaginal deliveries in this group required induction suggests reduced likelihood of spontaneous labor in hyperuricemic preeclampsia.

Hyperuricemia was also associated with low birth weight (51.5% vs 26.3%) and fetal growth restriction (38.5% vs 2.9%), findings consistent with Indian studies. [9,10] This 13-fold increased risk supports the concept that elevated uric acid reflects placental dysfunction. Roberts et al. emphasized uric acid as an important marker of fetal risk, comparable to proteinuria. [13] The underlying mechanisms are multifactorial, including reduced renal clearance, oxidative stress, and placental ischemia. [6,7] Evidence suggests uric acid may actively contribute to endothelial dysfunction, inflammation, and reduced nitric oxide availability, thereby worsening maternal and fetal outcomes. [8] Bainbridge and Roberts proposed uric acid as a pathogenic factor rather than a passive marker. [8]

Neonates born to hyperuricemic mothers had higher NICU admission rates (44.1% vs 13.2%), reflecting increased prematurity, low birth weight, and growth restriction. Gupta et al. similarly reported higher neonatal morbidity when uric acid exceeded 6.0 mg/dL. [11] This increases healthcare burden and risk of long-term complications.

The cut-off of 6.0 mg/dL used in this study aligns with multiple studies demonstrating good predictive value. [9–11] However, gestational age–specific or lower thresholds have been suggested for early pregnancy. [12,13] Serial measurements may provide additional prognostic value beyond single-point assessment. [12,14] Clinically, serum uric acid is a simple, inexpensive tool that can aid risk stratification and guide closer maternal–fetal surveillance, especially in resource-limited settings. [14,15] Incorporating uric acid with other biomarkers improves predictive accuracy for adverse outcomes. [11,15] From a public health perspective, the high prevalence of hyperuricemia and its strong association with adverse outcomes emphasize the need for early detection and standardized monitoring in preeclampsia. [2,3] Future research should explore whether lowering uric acid improves outcomes or merely reflects disease severity, and evaluate the role of serial measurements in guiding management and timing of delivery. [8,12,14,15]

Conclusion

This study demonstrates that elevated maternal serum uric acid levels (greater than or equal to 6.0 mg/dL) in preeclamptic pregnancies are significantly associated with adverse perinatal outcomes including preterm delivery, increased cesarean section rate, higher requirement for induction of labour, low birth weight, fetal growth restriction, and increased neonatal intensive care unit admission.

The magnitude of associations observed across all measured outcomes underscores the clinical relevance of maternal hyperuricemia as a marker of disease severity and compromised placental function. Serum uric acid estimation represents a simple, cost-effective, and widely available laboratory test that can effectively stratify risk in preeclamptic pregnancies. Integration of routine uric acid assessment into the management protocol for pre-eclampsia can facilitate early identification of high-risk pregnancies requiring intensified surveillance, appropriate timing of delivery, and preparation for anticipated neonatal complications.

Limitations

The retrospective design limits causal inference and may introduce selection bias and incomplete data. Reliance on medical records increases the risk of missing or inaccurate information, with limited control over confounders. Additionally, serum uric acid was measured only at admission, providing a single time-point assessment without longitudinal evaluation during pregnancy.

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