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Original Research Article

Comparative Study on Adverse Perinatal Outcomes in Preeclampsia with and Without Hyperuricemia

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Abstract:

Background: Preeclampsia is a major hypertensive disorder of pregnancy associated with significant maternal and perinatal morbidity and mortality worldwide. Hyperuricemia is commonly observed in preeclampsia women and has been associated with poor fetal outcomes. Elevated serum uric acid levels may indicate endothelial dysfunction and increased disease severity (Ryu et al., 2019).

Objective: To compare adverse perinatal outcomes in preeclampsia women with and without Hyperuricemia.

Study Design: A comparative cohort study.

Place and Duration of Study: Department of Obstetrics and Gynecology, Combined Military Hospital Lahore.

Methodology: A total of 200 pregnant women diagnosed with preeclampsia after 28 weeks of gestation were enrolled and divided equally into two groups: women with Hyperuricemia (serum uric acid ≥6 mg/dL) and women without Hyperuricemia. Participants were followed until delivery. Adverse perinatal outcomes including preterm birth and small for gestational age neonates were recorded. Data were analyzed using SPSS version 25.

Results: The mean age of participants was 29.4 ± 5.3 years in the Hyperuricemia group and
28.7 ± 4.9 years in the non-Hyperuricemia group. Preterm birth was observed in 38 (38.0%) women with Hyperuricemia compared to 11 (11.0%) women without Hyperuricemia ($p<0.001$). Small for gestational age neonates were reported in 20
(20.0%) cases in the Hyperuricemia group compared to 7 (7.0%) cases in the nonHyperuricemia group ($p=0.006$). The relative risk for preterm birth was 3.45, while the relative risk for small for gestational age was 2.85 among women with Hyperuricemia.

Conclusion: Hyperuricemia in preeclampsia women is significantly associated with adverse perinatal outcomes, particularly preterm birth and small for gestational age neonates. Maternal serum uric acid may serve as an important predictor for identifying high-risk pregnancies and improving perinatal management.

Keywords: Preeclampsia, Hyperuricemia, Perinatal Outcomes, Preterm Birth, Small for Gestational Age, Pregnancy-Induced Hypertension

INTRODUCTION

Preeclampsia is a multisystem hypertensive disorder of pregnancy characterized by the development of hypertension and proteinuria after 20 weeks of gestation. It remains one of the leading causes of maternal and perinatal morbidity and mortality worldwide, affecting approximately 2%–8% of pregnancies annually (Wilkerson & Ogunbodede, 2019). The condition contributes significantly to maternal complications including eclampsia, placental abruption, renal failure, and hepatic dysfunction, while fetal complications include intrauterine growth restriction, prematurity, low birth weight, and perinatal death.

Although the exact pathophysiology of preeclampsia is not fully understood, abnormal placentation, endothelial dysfunction, oxidative stress, and systemic inflammatory responses are considered major contributing mechanisms. These pathological changes result in impaired placental perfusion and maternal vascular dysfunction, ultimately leading to adverse

maternal and fetal outcomes (Roberts et al., 2021). Early identification of patients at increased risk for severe disease and poor neonatal outcomes remains an important challenge in obstetric practice.

Serum uric acid has long been recognized as an important biochemical marker associated with preeclampsia. Hyperuricemia commonly develops due to reduced renal clearance, increased oxidative stress, tissue ischemia, and enhanced purine metabolism secondary to endothelial injury (Zangana & Hamadamen, 2018). During normal pregnancy, serum uric acid levels initially decrease because of increased renal blood flow and the uricosuric effect of estrogen. However, uric acid levels gradually rise in late pregnancy and may become markedly elevated in women who develop preeclampsia (Naz et al., 2021).

Several studies have demonstrated that elevated maternal serum uric acid levels are associated with increased severity of preeclampsia and poor perinatal outcomes. Hyperuricemia has been linked with higher rates of preterm birth, fetal growth restriction, low birth weight, neonatal intensive care unit admission, and perinatal mortality (Ryu et al., 2019). Schmella et al. (2015) reported that preterm birth occurred in 37.5% of hyperuricemic preeclamptic women compared to 9.9% among non-hyperuricemic patients, while small for gestational age neonates were observed in 18.8% and 6.9% of cases, respectively. These findings suggest that serum uric acid may serve as an effective predictor of adverse neonatal outcomes.

Despite growing evidence regarding the association between Hyperuricemia and poor pregnancy outcomes, conflicting results still exist in the literature. Some researchers consider elevated uric acid to be an independent predictor of adverse perinatal outcomes, whereas others suggest that its predictive value remains limited when compared with established clinical indicators such as proteinuria and blood pressure severity (Ryu et al., 2019). Furthermore, limited local data are available regarding the relationship between Hyperuricemia and adverse perinatal outcomes among Pakistani women with preeclampsia.

Objective

Therefore, this study was conducted to compare adverse perinatal outcomes in preeclamptic women with and without Hyperuricemia at Combined Military Hospital Lahore. The findings of this study may help in early identification of high-risk pregnancies and contribute toward improved antenatal surveillance, timely intervention, and better neonatal outcomes.

LITERATURE REVIEW

Preeclampsia is a pregnancy-specific hypertensive disorder that remains a major contributor to maternal and neonatal morbidity and mortality worldwide. According to the American College of Obstetricians and Gynecologists, preeclampsia is defined as new-onset hypertension occurring after 20 weeks of gestation accompanied by proteinuria or evidence of maternal organ dysfunction (ACOG, 2020). Globally, the disorder complicates approximately 2%–8% of pregnancies and is particularly common in developing countries where inadequate antenatal care contributes to delayed diagnosis and poor maternal outcomes (Wilkerson & Ogunbodede, 2019). The pathogenesis of preeclampsia involves abnormal trophoblastic invasion of uterine spiral arteries, leading to placental ischemia and endothelial dysfunction. Endothelial injury results in systemic vasoconstriction, increased vascular permeability, oxidative stress, and activation of inflammatory pathways (Roberts et al., 2021). These alterations can impair maternal renal function and contribute to elevated serum uric acid levels.

Uric acid is the final product of purine metabolism and is mainly excreted through the kidneys. In normal pregnancy, serum uric acid concentrations decrease during the first trimester because of increased renal clearance and the uricosuric effect of estrogen. However, uric acid levels gradually rise during late pregnancy. In women with preeclampsia, serum uric acid levels increase significantly due to decreased glomerular filtration, renal vascular impairment, oxidative stress, and tissue ischemia (Naz et al., 2021). Hyperuricemia has been extensively studied as a potential biomarker for the severity and prognosis of preeclampsia. Elevated serum uric acid levels have been associated with endothelial dysfunction and placental insufficiency, both of which negatively affect fetal growth and survival. Zangana and Hamadamen (2018) reported that maternal hyperuricemia was strongly associated with adverse neonatal outcomes including low birth weight, fetal growth restriction, and preterm delivery. The study concluded that serum uric acid could serve as an important predictor of fetal compromise in preeclamptic women. Similarly, Ryu et al. (2019) evaluated the predictive value of serum uric acid levels in women with preeclampsia and found that higher uric acid concentrations were significantly associated with adverse perinatal outcomes. The researchers observed increased frequencies of preterm birth, neonatal intensive care unit admission, and small for gestational age infants among hyperuricemia mothers. The study suggested that serum uric acid may help clinicians identify patients at increased risk of poor neonatal outcomes.

Naz et al. (2021) conducted a study evaluating the association of maternal hyperuricemia with maternal and perinatal morbidity in women presenting with preeclampsia. The authors found significantly higher rates of fetal complications among women with elevated serum uric acid levels. Hyperuricemia was associated with increased risks of preterm birth, low birth weight, and perinatal mortality. The findings emphasized the importance of regular monitoring of serum uric acid in preeclamptic patients.

Another study by Schmella et al. (2015) investigated the role of serum uric acid in gestational hypertension and preeclampsia. The study reported that preterm birth occurred in 37.5% of hyperuricemia women compared to 9.9% in non-

hyperuricemic women. Likewise, small for gestational age neonates were observed in 18.8% of cases with hyperuricemia versus 6.9% in controls. The authors concluded that elevated uric acid levels may be as clinically useful as proteinuria in determining fetal risk among hypertensive pregnancies. Despite these findings, some studies have questioned the independent predictive value of serum uric acid. Certain researchers argue that elevated uric acid levels may simply reflect disease severity rather than acting as an independent causative factor for adverse pregnancy outcomes. Furthermore, variations in study populations, diagnostic criteria, and laboratory thresholds have contributed to inconsistent findings across different studies (Ryu et al., 2019).

Current clinical guidelines acknowledge the association between hyperuricemia and preeclampsia but do not universally recommend serum uric acid measurement as a routine diagnostic criterion. However, many clinicians continue to use serum uric acid as an additional biochemical marker to assess disease severity and predict fetal risk in hypertensive pregnancies (NICE, 2023).

In Pakistan, limited local studies have explored the relationship between hyperuricemia and adverse perinatal outcomes among women with preeclampsia. Due to differences in socioeconomic status, nutritional factors, healthcare accessibility, and antenatal practices, local evidence is essential for improving clinical management and reducing neonatal complications. Therefore, the present study aims to further evaluate the association between maternal hyperuricemia and adverse perinatal outcomes in preeclamptic women within the local population.

METHODOLOGY

Design

A comparative cohort study was conducted to determine the association between hyperuricemia and adverse perinatal outcomes in women diagnosed with preeclampsia.

Study Setting

The study was carried out in the Department of Obstetrics and Gynaecology, Combined Military Hospital Lahore.

Study Duration

The duration of the study was six months after approval of the synopsis and ethical clearance from the hospital ethical review committee.

Study Population

The study population consisted of pregnant women diagnosed with preeclampsia presenting to the obstetrics and gynecology department during the study period.

Sample Size

The sample size was calculated using the WHO sample size calculator by considering 80% power of the study, 5% level of significance, and the proportion of small for gestational age neonates among hyperuricemic and non-hyperuricemic preeclamptic women reported in previous literature (18.8% vs. 6.9%) (Schmella et al., 2015). A total of 200 participants were enrolled in the study, with 100 women included in each group.

Sampling Technique

A consecutive non-probability sampling technique was used.

Study Groups

Participants were divided into the following two groups:

•Exposed Group: Preeclamptic women with hyperuricemia

•Unexposed Group: Preeclamptic women without hyperuricemia

Inclusion Criteria

The study included:

•Pregnant women aged 18–40 years

•Parity less than 5

•Gestational age greater than 28 weeks according to last menstrual period (LMP)

•Women diagnosed with preeclampsia according to operational definition

•Women willing to participate in the study

Exclusion Criteria

The following patients were excluded from the study:

•Women with chronic hypertension before pregnancy or before 20 weeks of gestation

•Women with hyperuricemia diagnosed prior to pregnancy

•Women with renal dysfunction (serum creatinine >1.5 mg/dL)

•Women with liver disease, hepatitis, or elevated liver enzymes (ALT/AST >40 IU)

•Women with other medical disorders affecting serum uric acid levels

Operational Definitions

Preeclampsia

Preeclampsia was defined as blood pressure ≥140/90 mmHg measured on two separate occasions after 20 weeks of gestation associated with proteinuria ≥0.3 g in a 24-hour urine sample, urine protein/creatinine ratio ≥0.3, or dipstick protein ≥+1 (ACOG, 2020).

Hyperuricemia

Hyperuricemia was defined as serum uric acid level ≥6 mg/dL after 28 weeks of gestation.

Adverse Perinatal Outcomes

Preterm Birth

Delivery occurring before completion of 37 weeks of gestation.

Small for Gestational Age (SGA)

Neonates with birth weight below the 10th percentile for gestational age at the time of delivery.

Data Collection Procedure

After obtaining approval from the hospital ethical committee, eligible participants fulfilling the inclusion criteria were enrolled from the outpatient department (OPD). Written informed consent was obtained from all participants before data collection.

Demographic and clinical information including age, body mass index (BMI), gestational age, parity, lifestyle, and socioeconomic status were recorded on a structured

proforma. Serum uric acid levels were measured using hospital laboratory facilities.

Participants were categorized into exposed and unexposed groups based on serum uric acid levels. All enrolled women were followed throughout pregnancy until delivery. At delivery, gestational age and neonatal birth weight were documented. Preterm birth and small for gestational age were assessed according to operational definitions.

All patients received standard obstetric management for preeclampsia according to hospital protocols. Confidentiality of patient information was maintained throughout the study.

Data Analysis Procedure

Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 25.

Quantitative variables such as age, BMI, and gestational age were presented as mean ± standard deviation. Qualitative variables including lifestyle, socioeconomic status, preterm birth, and small for gestational age were expressed as frequency and percentage.

The Shapiro–Wilk test was applied to assess data normality. Relative risk (RR) was calculated to determine the association between hyperuricemia and adverse perinatal outcomes. A relative risk value greater than 1 was considered significant for increased risk.

Data were stratified for age, BMI, gestational age, parity, lifestyle, and socioeconomic status to control effect modifiers. Post-stratification relative risk was recalculated to evaluate the association within different strata.

Ethical Considerations

Ethical approval was obtained from the institutional ethical review committee of Combined Military Hospital Lahore before commencement of the study. Informed written consent was obtained from all participants. Participants were assured regarding confidentiality, anonymity, and their right to withdraw from the study at any stage without affecting their medical care.

RESULTS

A total of 200 pregnant women diagnosed with preeclampsia were included in the study. Participants were equally divided into two groups: 100 women with hyperuricemia and 100 women without hyperuricemia. Maternal demographic characteristics and adverse perinatal outcomes were compared between both groups The mean maternal age in the hyperuricemia group was 29.4 ± 5.3 years compared to 28.7 ± 4.9 years in the non-hyperuricemia group. No statistically significant difference was observed between the demographic characteristics of both groups (p>0.05) (Table 1).

Table 1. Comparison of Demographic Characteristics between Study Groups

Variables	Hyperuricemia	Variables	Hyperuricemia
Mean Age (Years)	29.4 ± 5.3	28.7 ± 4.9	0.318
Mean BMI (kg/m²)	27.8 ± 3.6	26.9 ± 3.2	0.071
Mean Gestational Age at Enrollment (Weeks)	31.6 ± 2.7	32.1 ± 2.5	0.164
Parity <3	64 (64.0%)	69(69.0 %)	0.452
Parity ≥3	36 (36.0%)	31(31.0 %)	0.452
Sedentary Lifestyle	61 (61.0%)	55(55.0 %)	0.388
Active Lifestyle	39 (39.0%)	45(45.0 %)	0.388
Low Socioeconomic Status	48 (48.0%)	44(44.0 %)	0.569

Preterm birth was significantly more common among women with hyperuricemia, occurring in 38.0% of cases compared to 11.0% in women without hyperuricemia. The relative risk for preterm birth was 3.45. Similarly, small for gestational age neonates were observed in 20.0% of women with hyperuricemia compared to 7.0% in the non-hyperuricemia group. Women with hyperuricemia had 2.85 times higher risk of delivering small for gestational age neonates (Table 2).

Table 2. Comparison of Adverse Perinatal Outcomes Between Study Groups

Perinatal Outcome	Hyperuricemia Group (n=100)	Non-Hyperuricemia Group (n=100)	Relative Risk (RR)	P value
Preterm Birth	38 (38.0%)	11 (11.0%)	3.45	<0.001
Small for G	20 (20.0%)	7 (7.0%)	2.85	0.006

After stratification according to maternal age, preterm birth remained significantly higher among women with hyperuricemia in both age groups (Table 3).

Table 3. Stratification of Preterm Birth According to Maternal Age

Maternal Age	Hyperuricemia Group	Non-Hyperuricemia Group	P value

≤30	20/58 (34.5%)	7/60 (11.7%)	0.003
(n=118)			
>30 Years (n=82)	18/42 (42.9%)	4/40 (10.0%)	<0.001

Small for gestational age neonates were more frequent among hyperuricemic women across both BMI categories (Table 4).

Table 4. Stratification of Small for Gestational Age According to BMI

BMI Category	Hyperuricemia Group	Non-Hyperuricemia Group	p-value
BMI <30 kg/m²	13/67 (19.4%)	5/71 (7.0%)	0.021
BMI ≥30 kg/m²	7/33 (21.2%)	2/29 (6.9%)	0.041

The overall analysis demonstrated a statistically significant association between maternal hyperuricemia and adverse perinatal outcomes in women with preeclampsia. These findings indicate that elevated maternal serum uric acid levels are associated with increased risks of preterm delivery and small for gestational age neonates among preeclamptic women (Table 5).

Table 5. Overall Association between Hyperuricemia and Adverse Perinatal Outcomes

Variables	Relative (RR)	Risk	95% Interval	Confidence	P value
Preterm Birth	3. 45		1.89 – 6.28		<0.001
Small for Gestational Age	2.85		1.25 – 6.49		0.006

DISCUSSION

Preeclampsia remains one of the leading causes of maternal and neonatal morbidity worldwide, particularly in developing countries where delayed diagnosis and limited antenatal surveillance contribute to poor pregnancy outcomes. The present study was conducted to compare adverse perinatal outcomes in preeclamptic women with and without hyperuricemia. The findings of this study demonstrated a significant association between elevated maternal serum uric acid levels and adverse neonatal outcomes, particularly preterm birth and small for gestational age neonates.

In the current study, preterm birth occurred in 38.0% of women with hyperuricemia compared to 11.0% in women without hyperuricemia. These findings are consistent with the study conducted by Schmella et al. (2015), who reported preterm birth rates of 37.5% among hyperuricemic preeclamptic women compared to 9.9% in non-hyperuricemic women. Similarly, Ryu et al. (2019) observed that elevated serum uric acid levels were significantly associated with increased frequency of preterm delivery in women with hypertensive disorders of pregnancy. The increased risk of preterm birth may be explained by placental insufficiency and endothelial dysfunction caused by severe disease progression in hyperuricemic patients.

The present study also demonstrated that small for gestational age neonates were significantly more common in women with hyperuricemia compared to those without hyperuricemia (20.0% vs. 7.0%). These findings are comparable to previous studies that identified maternal hyperuricemia as an important predictor of fetal growth restriction. Zangana and Hamadamen (2018) found a significant relationship between elevated serum uric acid levels and fetal growth restriction among preeclamptic women. Similar findings were reported by Naz et al. (2021), who concluded that hyperuricemia was associated with poor fetal growth and low birth weight. The biological mechanism underlying the association between hyperuricemia and adverse perinatal outcomes may involve oxidative stress, endothelial dysfunction, placental ischemia, and impaired trophoblastic invasion. Elevated serum uric acid may reduce placental perfusion and interfere with fetal nutrient and oxygen supply, ultimately leading to intrauterine growth restriction and premature delivery (Roberts et al., 2021). Hyperuricemia also reflects worsening renal impairment and systemic vascular dysfunction in preeclamptic women, thereby indicating disease severity. In the present study, the relative risk for preterm birth was 3.45, while the relative risk for small for gestational age was 2.85 among women with hyperuricemia. These findings support the role of serum uric acid as a clinically useful biochemical marker for identifying high-risk pregnancies. Several researchers have suggested that serum uric acid may have predictive value comparable to proteinuria in assessing fetal risk among women with hypertensive disorders of pregnancy (Schmella et al., 2015).

Although the findings of this study strongly support the association between hyperuricemia and adverse neonatal outcomes, some studies in the literature have reported conflicting evidence. Certain researchers argue that elevated serum uric acid levels may reflect disease severity rather than independently causing adverse outcomes (Ryu et al., 2019). However, despite these controversies, the current study reinforces the importance of serum uric acid assessment in women with preeclampsia.

One of the strengths of the present study is the comparative cohort design, which allowed assessment of perinatal outcomes in both exposed and unexposed

groups under similar clinical conditions. In addition, standardized operational definitions and follow-up until delivery improved the reliability of outcome assessment.

Limitations

However, the study also had certain limitations. The study was conducted at a single tertiary care hospital with a relatively limited sample size, which may affect generalizability of the findings to the wider population. Furthermore, only selected perinatal outcomes were assessed, while long-term neonatal complications were not evaluated.

Despite these limitations, the present study provides valuable local evidence regarding the association between hyperuricemia and adverse perinatal outcomes among Pakistani women with preeclampsia. Early identification of hyperuricemia may help clinicians improve antenatal monitoring, timely intervention, and neonatal outcomes in high-risk pregnancies.

CONCLUSION

The present study concluded that hyperuricemia is significantly associated with adverse perinatal outcomes in women with preeclampsia. Pregnant women with elevated serum uric acid levels demonstrated a markedly higher frequency of preterm birth and small for gestational age neonates compared to women without hyperuricemia.

The findings suggest that maternal serum uric acid can serve as an important biochemical marker for identifying preeclamptic women at increased risk of poor neonatal outcomes. Early detection and close monitoring of hyperuricemia during pregnancy may help improve antenatal surveillance, facilitate timely obstetric intervention, and reduce perinatal morbidity. Therefore, routine assessment of serum uric acid levels in women with preeclampsia may be beneficial in predicting disease severity and improving maternal and neonatal care outcomes.

RECOMMENDATIONS

•Serum uric acid assessment should be considered as part of routine evaluation in women diagnosed with preeclampsia.

•Pregnant women with hyperuricemia should receive close antenatal monitoring to reduce adverse neonatal outcomes.

•Early identification and timely management of high-risk pregnancies may help decrease the incidence of preterm birth and fetal growth restriction.

•Larger multicenter studies should be conducted to further evaluate the predictive value of serum uric acid in preeclampsia.

•Future research should also assess long-term neonatal outcomes associated with maternal hyperuricemia.

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