Original Article

Biochemical Markers and Their Correlation with Fetal Outcomes in Preeclamptic Mothers

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Abstract

Objective: To assess the impact of serum uric acid, creatinine, and blood urea nitrogen (BUN) levels on fetal outcomes in preeclamptic mothers. It also examined correlations between uric acid and creatinine, and uric acid and BUN

Methodology: A cross-sectional comparative study was conducted at Liaquat University of Medical and Health Sciences (LUMHS) involving 86 pregnant women. Participants were divided into normotensive and preeclamptic groups. After obtaining verbal consent, blood samples were collected in a sitting position to measure serum uric acid, creatinine, BUN, and blood pressure.

Results: The mean age was 31.8±2.0 years in the normotensive group and 35.3±2.1 years in the preeclamptic group. Gestational age averaged 34.6 ± 2 weeks in normotensive women and 37.2 ± 1.3 weeks in preeclamptic women. Systolic and diastolic blood pressures were significantly higher in the hypertensive group. Serum levels of uric acid, creatinine, and BUN were also elevated in preeclamptic women, showing strong correlations with each other. These elevated markers were linked to poor fetal outcomes.

Conclusion: The study concluded that elevated serum uric acid, creatinine, and BUN levels, along with the uric acid-to-creatinine ratio, are significant predictors of hypertension and adverse fetal outcomes in pre-clamptic pregnancies.

Keywords: Preeclampsia, serum uric acid, serum creatinine, blood urea nitrogen (BUN).

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Introduction

Pre-eclampsia (PE) is a fatal pregnancy complication characterized by increased blood pressure and proteinuria in 24 24-hour urine sample after the 20th week of gestation.[1] Pre-eclampsia affects approximately 5 to 8% of pregnancies around the world and becomes a primary reason for morbidity and mortality.[2] Furthermore, the exact reason remains unknown; it is believed that it may occur due to a combination of endothelial dysfunction, abnormal placentation, and maladaptation of the immune system.

Pre-eclampsia is classified into two categories, mild and severe, with complications like abruptio placentae, organ failure, stroke, and restriction of intrauterine growth.[3] However, in extreme conditions, it may lead to eclampsia, a life-threatening condition with the development of seizures. Timely diagnosis and proper treatment of pre-eclampsia are vital to improve maternal and neonatal outcomes.[4]

Recent research suggests that disturbed metabolic processes and altered renal functions play a significant part in the pathophysiology of pre-eclampsia.[5] Metabolic abnormalities, including hyperuricemia, are potential markers for the disease. Uric acid is the metabolic product of purine excreted by the kidneys.[6]

Hence, in pre-eclampsia, renal dysfunction and higher production of uric acid may be the cause of increased levels of uric acid.[7] Studies also suggest that hyperuricemia is not only a common finding in pre-

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eclampsia but also contributes to the pathophysiology of the disease, causing endothelial dysfunction, decreased renal perfusion, and increased systemic vascular resistance.[8] Increased levels of uric acid are considered to cause oxidative stress, inflammation, and endothelial cell injury, which are the major contributors to the disease progression and management.[9]

Furthermore, the uric acid to creatinine ratio (UACR) has been suggested as an important diagnostic parameter for assessing renal function and predicting the severity of pre-eclampsia.[10] This ratio may reflect both the degree of renal impairment and the presence of oxidative stress, which had a significant part in the development of pre-eclampsia.[11] Studies suggest that UACR may relate to the severity of disease, maternal complications, and perinatal outcomes, making it a primary biomarker for pre-eclampsia.[12]

This study aims to correlate maternal uricemia with the uric acid-to-creatinine ratio in pre-eclamptic patients, to define its diagnostic and prognostic significance in predicting the onset and severity of pre-eclampsia. By assessing these biomarkers, we aim to understand their major role in the clinical treatment of pre-eclampsia, contributing to awareness that improves early detection and outcomes for mothers and babies.

Methodology

After the approval from the university research ethics committee of the Basic Medical Sciences, Liaquat University of Medical & Health Sciences, Jamshoro, letter no.: LUMHS/REC/-37, dated 28/03/23. This cross-sectional analytical study was conducted from April 23 to September 23 in the physiology department, in collaboration with the gynecology and obstetrical departments (both outdoor and indoor). Before the study, informed consent was obtained from all participants, and their confidentiality was ensured. It was designed to evaluate maternal uremia and the uric acid-to-creatinine ratio in preeclamptic mothers. This study involved collecting and analyzing blood samples to assess the link between biochemical markers and preeclampsia. The sample size was calculated using an Epi Info online calculator, based on the expected prevalence of pre-eclampsia and a 95% confidence level. A total of 86 participants were recruited (43 cases and 43 controls), selected using the purposive sampling method from antenatal patients in outdoor areas and wards.

Inclusion criteria were pregnant women aged between 18 and 40 years, who had gestational age ≥20 weeks with a singleton pregnancy. Exclusion Criteria were patients diagnosed with renal or hepatic diseases, patients with chronic hypertension or diabetes mellitus, and women with multiple pregnancies. Participants using medication affecting the metabolism of uric acid.

The maternal age, gestational age, and blood pressure readings were recorded. The detailed clinical history was taken to rule out exclusion criteria. In third trimester of pregnancy, A 5 mL venous blood sample was drawn in sterile conditions for the assessment of serum uric acid and creatinine levels, as well as blood urea nitrogen (BUN). Serum uric acid and creatinine levels were analyzed by an automated biochemical analyzer (BM-100C made in China).

Statistical Analysis was done by using SPSS version 23.0. Descriptive statistics were applied to summarize demographic and clinical characteristics. Independent t-tests were used to compare uric acid levels and uric acid-to-creatinine ratios between groups. A Pearson correlation was used to analyze the relationship between biochemical markers and blood pressure. A p-value < 0.05 was set to be considered statistically significant.

Results

Table I indicates the mean age (in years) of the Normotensive and hypertensive groups was 31.8 ± 2.049 and 35.3 ± 2.133, respectively. The gestational age (in weeks) of the normotensive and hypertensive groups was 34.6 ± 2 and 37.2 ± 1.3, respectively. The systolic and diastolic blood pressures were significantly elevated in the hypertensive group, at 151.9 ± 5 and 95± 4.5, respectively. The systolic and diastolic blood pressures in the normotensive group were 110.8 ± 4 mmHg and 75.4 ± 4.6 mmHg, respectively. The mean serum uric acid concentrations were significantly higher in the hypertensive group compared to the normotensive group, 6.9 ± 0.6 and 4.1 ± 0.4, respectively. The mean serum creatinine levels were significantly higher in the hypertensive group than in the normotensive group, at 0.57 ± 0.16 and 1.3 ± 0.23, respectively. The mean Blood Urea Nitrogen levels were significantly higher in the hypertensive group compared to the normotensive group: 5.3 ± 0.4 and 15.76 ± 2.8.

Table I: Basic Characteristics of the participants.

Variable	Normotensive (n=43)	Hypertensive (n=43)	P value
Age	31.8±2.049	35.3±2.133	<0.05
Gestational age	34.6 ± 2	37.2±1.3	<0.05
Systolic blood pressure (mmHg)	110.8 ± 4	151.9±5	<0.05
Diastolic blood pressure (mmHg)	75.4±4.6	95±4.5	<0.05
Serum uric acid (mg/dl)	4.1±0.4	6.9±0.6	<0.05
Serum creatinine (mg/dl)	0.57±0.16	1.3±0.23	<0.05
Blood urea nitrogen (BUN) MG/DL	5.3±0.4	15.76±2.8	<0.05

Pearson's Correlation Analysis of Serum Uric Acid with Serum Creatinine in the Normotensive and Hypertensive Groups.

Figure 1, The scatter plot illustrates the relationship between serum uric acid (x-axis) and serum creatinine (y-axis) in the normotensive group. The graph includes a fitted linear regression line with the equation y = 0.49 + 0.02 and an R-value of 0.004. The regression line has a very shallow positive slope of 0.02, indicating a minimal increase in serum creatinine levels with increasing serum uric acid levels.

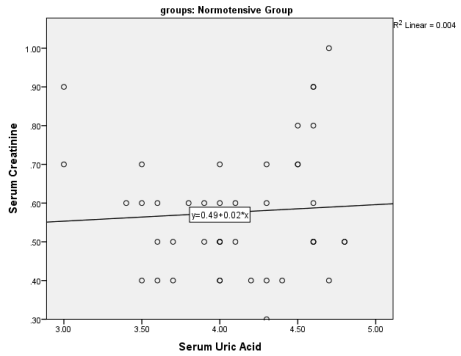

Figure 1. Pearson's correlation analysis of serum uric acid with serum creatinine in normotensive

Figure 2, The regression line has a moderately positive slope (0.180.18), indicating that as serum uric acid levels increase, serum creatinine levels also rise. The positive correlation suggests that elevated uric acid levels are associated with renal dysfunction in hypertensive pregnancies.

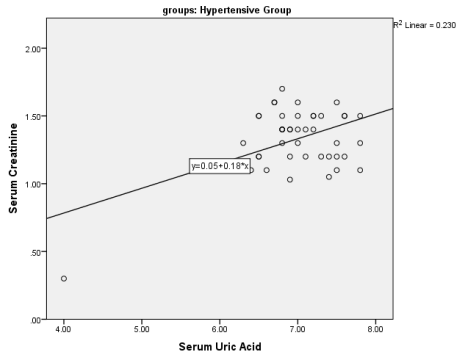

Figure 2. Pearson's correlation analysis of serum uric acid with serum creatinine in the hypertensive group.

Pearson's Correlation Analysis of Serum Blood Urea Nitrogen with Serum Uric Acid in Normotensive and Hypertensive Groups.

Figure 3. The regression line has a slight negative slope (-0.05 to 0.05), indicating a very weak inverse relationship between serum uric acid and blood urea nitrogen levels. As serum uric acid increases, BUN levels decrease slightly, but the change is minimal.

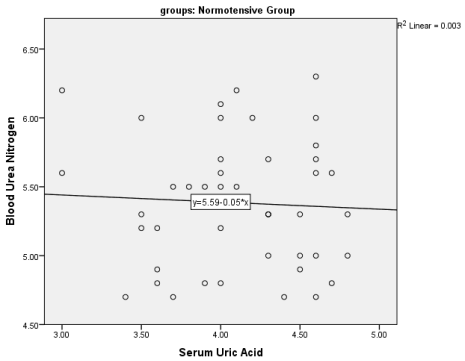

Figure 3, Pearson's Correlation Analysis of Serum Blood Urea Nitrogen with Serum Uric Acid in Normotensive.

Figure 4. The plot includes a linear regression line with the equation (y = -0.27 + 2.29). This indicates that Blood Urea Nitrogen increases with Serum Uric Acid, based on the slope (2.29). The R-value is 0.248, suggesting a weak positive correlation. Approximately 24.8% of the variation in Blood Urea Nitrogen can be explained by Serum Uric Acid**.**

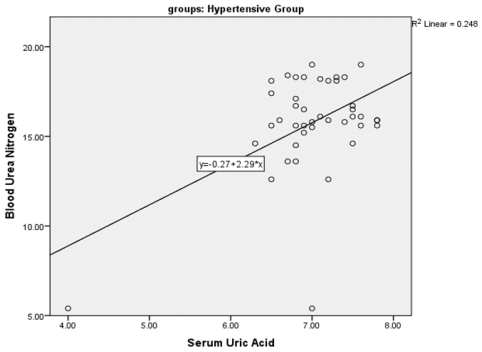

Figure 4. Pearson's Correlation Analysis of Serum Blood Urea Nitrogen with Serum Uric Acid in the Hypertensive Group.

The fetal outcome in both groups was analyzed. The fetal outcome in the normotensive group included full-term birth in 81.4%, pre-term birth in 9.3% and low birth weight was 9.3%. The fetal outcome in the hypertensive group showed full-term birth in 14%, pre-term birth 39.5%, stillbirth 4.7% low birth weight 37.2% and early neonatal death 4.7%. (Table II)

Table II: Fetal outcome in Normotensive and Hypertensive Group.

Groups	Full Term Birth	Preterm Birth	Still Birth	Low Birth Weight	Early Neonatal Death
Normotensive Group	81.4%	9.3%	--	9.3%	--
Hypertensive Group	14%	39.5%	4.7%	37.2%	4.7%

Discussion

Pre-eclampsia is a pregnancy-induced hypertensive disorder. The assessment of maternal serum uric acid and the uric acid-to-creatinine ratio has developed as a critical diagnostic and prognostic tool for the severity of pre-eclampsia.[13] In pre-eclampsia, hyperuricemia is frequently recognized to reduce renal clearance, raise oxidative stress, and placental ischemia, while increased serum creatinine concentrations indicate compromised glomerular filtration and renal damage. Our study provides an essential understanding of the differences in maternal and clinical parameters between normotensive and hypertensive groups, shedding light on the physiological disruptions associated with pre-eclampsia.

In this study, the mean age of hypertensive mothers (35.3 ± 2.133 years) was significantly higher compared to the normotensive mothers (31.8 ± 2.049 years). Progressive maternal age is considered a risk factor for pre-eclampsia, as it is related to reduced elasticity of vessels and increased susceptibility to endothelial dysfunction. [15] Hypertensive mothers had a longer gestational age (37.2 ± 1.3 weeks) than normotensive mothers (34.6 ± 2 weeks), which may reflect medical interventions to extend gestation while managing hypertensive complications. [16] The hypertensive group showed significantly elevated systolic (151.9 ± 5 mmHg) and diastolic (95 ± 4.5 mmHg) blood pressure compared to the normotensive group (110.8 ± 4 mmHg and 75.4 ± 4.6 mmHg). These findings support the diagnostic criteria for pre-eclampsia, which is characterized by constant hypertension due to systemic vasospasm and endothelial dysfunction. Uric acid levels were considerably higher in the hypertensive group (6.9 ± 0.6 mg/dL) than in the normotensive group (4.1 ± 0.4 mg/dL). Hyperuricemia, a prominent feature of pre-eclampsia, is known to reduce renal clearance and oxidative stress caused by placental ischemia. [17] Raised uric acid is increasingly predictive as a marker of disease severity and adverse perinatal outcomes. [10] Similar trends were found by Tan et al [18] who found that elevated serum uric acid concentrations are linked with preeclampsia and Moharan et al [19] agreed with our finding and stated that in pregnancy close monitoring of serum uric acid concentration may help for early diagnosis and proper management against gestational hypertension and pre-eclampsia. It helps to prevent the disease and its complications. Shakarami et al [20] stated that increased chances of developing pre-eclampsia even after adjusting for maternal age, gestational age, and BMI. According to Faraswati et al 21, serum uric acid can be a tool for diagnosing preeclampsia in pregnant women. This study is consistent with their research. Rayan A. M et al.[22] found inconsistent results with our finding, in which they found increased levels of serum uric acid, but the increase was not statistically significant.

The hypertensive group had considerably higher serum creatinine levels (1.3 ± 0.23 mg/dl vs. 0.57 ± 0.16 mg/dl in normotensive mothers), suggestive of reduced renal function. Pre-eclampsia-induced renal dysfunction is related to endothelial injury and glomerular endotheliosis. [23] Yadav BS et al [24] found that an imbalance of serum creatinine concentration in pregnant women was linked to increased chances of developing pre-eclampsia. Comprehensive history taking, thorough examination, and levels of uric acid may aid in the early diagnosis and proper management of pre-eclampsia, helping to prevent complications for both the mother and fetus. Vahdat M et al [25] creatinine level is lower in pre-eclamptic women. Our study shows increased levels of creatinine, which is inconsistent with the above research.

Hypertensive mothers had significantly higher BUN levels (15.76 ± 2.8 mg/dl vs. 5.3 ± 0.4 mg/dl in the normotensive group). Raised BUN imitates compromised renal filtration and increased protein catabolism, which are common in hypertensive disorders of pregnancy**.** [26] Increased uric acid, creatinine, and BUN concentrations in hypertensive mothers indicate systemic and renal involvement in pre-eclampsia. These markers can support early diagnosis and monitoring of disease progression. The significantly increased renal markers highlight the

importance of regular renal function tests in pre-eclamptic pregnancies to reduce complications.[27] Advanced maternal age is intensely linked with pre-eclampsia, underscoring the necessity for targeted antenatal care for high-risk women.[5] According to Khan JA et al, [28] the mean plasma blood urea nitrogen (BUN) concentrations were significantly raised in pre-eclamptic women compared to the normotensive pregnant women. This study is consonant with our research. Vazquez S et al [29] close observation of blood urea nitrogen BUN could be a good predictor of pre-eclampsia to detect fetal outcomes. This study is reconcilable with the above research. According to Ellery SJ et al, [30] Pre-Eclampsia has increased total creatinine content compared to normotensive controls. This study also detected the same findings as our study. Singh S et al [31]. Not only is hyperuricemia one of the most reliable indicators for the diagnosis of preeclampsia, but the ratio of serum uric acid and serum creatinine is a much more reliable indicator for the diagnosis of preeclampsia. Our study also concluded the same findings.

Elaine Luiza et al, [12] reported in their study that there is a correlation between serum uric acid and creatinine. Their findings are consistent with our study findings. Zia et al, [32] also stated that serum uric acid is significantly correlated with serum creatinine levels in preeclamptic mothers. Our study also gave the same results. Teka H et al, [33] reported full-term births were 10 to 13% Our study found full-term births were 14% so our study is consistent with their research.

Rahman F et al, [34] pre-term births were 36 to 40%, and our study shows pre-term birth 39.5%, so our study is consistent with their research. Das S et al [35] low birth weights were 35 to 39%, and our study shows low weight births, which were 37%, so our study is consistent with their research. Danko I et al, [36] early neonatal deaths were 5 to 6 %, and our study shows early neonatal death was 4.7%, so our study is consistent with their research.

Conclusion

Our study concluded that increased concentrations of serum uric acid, creatinine, and blood urea nitrogen (BUN) were associated with correlations between serum uric acid and serum creatinine, as well as between serum uric acid and BUN, and these correlations were linked to the outcomes of fetuses in preeclamptic pregnancies. Our results showed that pregnant women with hypertension, especially those with increased levels of these markers, have a higher risk of complications due to renal disease that may be present. These complications can be detrimental to both the mother and the baby. These complications can be harmful to both the mother and the baby.

The critical need for effective strategies to reduce complications associated with preeclampsia is evident. Our research supports the importance of early detection and intervention in managing elevated serum uric acid, creatinine, and BUN, as well as the correlation between serum uric acid and serum creatinine. By maintaining these markers within normal physiological limits, it may be possible to mitigate adverse outcomes and improve maternal and fetal health. This study provides valuable insights that can inform early detection and management practices, ultimately enhancing the care and outcomes for preeclamptic mothers and their babies.

List of Abbreviations: PE (Preeclampsia), BUN (Blood urea nitrogen), IUGR (Intrauterine Growth Restriction), GFR (Glomerular Filtration Rate), PIH (Pregnancy Induced Hypertension), UA/Cr ratio (Uric Acid to Creatinine Ratio), VEGF (Vascular Endothelial Growth Factor),

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