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Original Research Paper

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A COMPARATIVE STUDY OF SERUM URIC ACID, C-REACTIVE PROTEIN, AND SERUM CALCIUM IN PREECLAMPSIA AND NORMAL PREGNANCY AT SHADAN HOSPITAL

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ABSTRACT

Background: The lack of reliable biochemical markers for accurately diagnosing preeclampsia contributes significantly to adverse maternal and perinatal outcomes. This study aimed to investigate the relationship between serum uric acid, C-reactive protein (CRP), and serum calcium levels in patients with preeclampsia. **Methodology:** A prospective case-control study was conducted at Shadan Institute of Medical Sciences, Hyderabad, over a period of 12 months. A total of 84 antenatal women beyond 24 weeks of gestation were enrolled, including 42 with preeclampsia and 42 normotensive controls. Maternal levels of uric acid, calcium, and CRP were compared using independent sample t-tests, and ROC analysis was performed to assess the predictive value for preeclampsia. **Results:** The mean CRP value (7.22±1.09mg/L) and serum uric acid level (8.79±1.21mg/dL) were significantly elevated in the preeclamptic group, while serum calcium was notably lower (7.56±1.08mg/dL) compared to normotensive women ($p < 0.001$*). The area under the curve (AUC) for uric acid was 0.853 ($p < 0.001$*), demonstrating 73.3% sensitivity and 87.7% specificity. For serum calcium, the AUC was 0.809 ($p < 0.001$*), with 76.1% sensitivity and 93.1% specificity. When combined, the AUC for all three parameters was 0.919 ($p < 0.001$*), achieving 100% sensitivity and 86.4% specificity in predicting preeclampsia. **Conclusion:** Maternal hyperuricemia, elevated CRP, and decreased calcium levels are associated with preeclampsia. The combined assessment of these three biochemical markers provided the highest accuracy for predicting the condition.

KEYWORDS : Hyperuricemia, CRP, Hypocalcaemia, preeclampsia.

INTRODUCTION

Hypertension and proteinuria develop after 20 weeks of pregnancy in preeclampsia. This systemic condition can cause serious difficulties or death in both mother and fetus. Increasing uric acid levels in preeclampsia may indicate oxidative stress, tissue damage, and renal dysfunction, which may worsen the illness. Higher serum uric acid is an independent risk factor for cardiovascular disease and may affect vascular function and inflammation. Tissue ischemia and oxidative stress may limit renal excretion, causing hyperuricemia in pregnancy and endothelial damage, hypertension, and vascular problems.[1,2]

Serum calcium changes may also cause preeclampsia. Hypocalciuric and intracellular calcium increase vascular contractility and maternal blood pressure. Hypercalciuria in pregnancy-induced hypertension (PIH) may result from inadequate calcium absorption and reduced renal tubular function, which lowers serum calcium and raises intracellular calcium, worsening hypertension.[3]

A simple and inexpensive blood test can quantify C-reactive protein, another important biomarker. CRP levels are linked with endothelial cell damage, a significant preeclampsia risk factor. CRP's half-life is 19 hours, allowing quick elimination from the bloodstream as preeclampsia heals, making it a valuable disease severity predictor.[4]

Three biomarkers—serum uric acid, CRP, and serum calcium—are tested for their ability to predict eclampsia in pregnant women.[5] This study compares these indicators in preeclamptic and normotensive pregnant women to determine their relationship to eclampsia.

MATERIALS & METHODS

This prospective case-control study was conducted in the Department of Biochemistry, in collaboration with the Department of Obstetrics at the Shadan Institute of Medical Sciences. The study included singleton pregnant patients diagnosed with preeclampsia based on specific criteria: a blood pressure measurement exceeding 140/90 mmHg, assessed through medical history and clinical examination, alongside significant proteinuria (3+) after the 20th week of gestation. Control participants were healthy antenatal women exhibiting normal blood pressure and no proteinuria as determined by dipstick testing.

Exclusion Criteria: Patients with preeclampsia accompanied by other pregnancy complications or systemic diseases (such as liver or renal conditions), those with essential hypertension, individuals unwilling to provide informed consent, and cases with incomplete data were excluded from the study.

Procedure: Informed written consent was obtained from all participants, and demographic information—including age, gestational age, parity, and medical and family history—was recorded. A physical examination was conducted, and blood pressure measurements were taken twice for each participant using a manual mercury sphygmomanometer. Urinalysis was performed using a dipstick test to assess the degree of proteinuria. Participants with normal blood pressure and no proteinuria were classified as controls, while those presenting with elevated blood pressure and proteinuria were categorized as cases.

Sample Collection and Laboratory Analysis: After an overnight fast, blood samples were drawn from the antecubital vein using sterile techniques for the measurement of serum calcium and uric acid levels. For serum calcium, blood samples were allowed to clot, then centrifuged at 3000 revolutions per minute for 10 minutes. Serum calcium levels

were quantified using the O-Cresol Phthalein Complexone (OCPC) method on a biochemistry analyzer. Serum uric acid levels were measured via an enzymatic colorimetric assay using uricase and peroxidase enzymes. Serum C-reactive protein (CRP) was analyzed using a latex agglutination method on the biochemistry analyzer.

Sample Size Calculation: The sample size was estimated using the online calculator available at openpi.com, employing the Fleiss method with continuity correction. A two-sided confidence level of 95% and a power of 90% were considered. The ratio of controls to cases was assumed to be 1:1. The hypothetical exposure proportion among controls was set at 10%, while for cases, it was set at 50%. This estimation resulted in a calculated sample size of 38 for both cases and controls.

Statistical Analysis Method: Primary data were collected using paper-based Case Report Forms and subsequently entered into Microsoft Excel 2016. Statistical analysis was conducted using IBM SPSS Statistics Version 20. Categorical variables were summarized as frequencies and percentages, with cross-tabulations performed for selected parameters. Column proportions were compared using the Chi-square test, while average values were analyzed using the independent sample t-test. Receiver operating characteristic (ROC) curves were plotted to assess the diagnostic capability of the biochemical markers concerning preeclampsia, and the area under the curve (AUC) was calculated. Sensitivity and specificity were determined using contingency tables. A p-value of less than 0.05 was considered statistically significant, while a p-value of less than 0.01 was deemed highly significant.

RESULTS

A total of 84 women participated in the study, with 42 diagnosed with preeclampsia and 42 normotensive controls. The demographic characteristics and clinical parameters of both groups are summarized in Table 1.

The age distribution of participants revealed that 33.3% of the preeclamptic group were under 25 years of age compared to 21.4% in the normotensive group. However, the difference was not statistically significant (p = 0.1). The majority of participants in both groups were aged between 26 to 35 years, with a similar distribution across these age categories.

A significant difference was observed in BMI between the two groups (p = 0.01). In the preeclamptic group, 4.8% were classified as underweight, while none of the normotensive participants fell into this category. The prevalence of obesity (>30) was markedly higher in the preeclamptic group at 21.4% compared to 4.8% in the normotensive group. Additionally, 40.5% of preeclamptic women had a normal BMI, compared to 52.4% in the normotensive group.

Gestational age did not show a statistically significant difference between the groups (p = 0.1). Among preeclamptic women, 40.5% were in the 26-30 weeks gestational age category, while 33.3% of the normotensive group fell within this range. In the 31-35 weeks category, 59.5% of preeclamptic women were included, compared to 66.7% in the normotensive group.

Analysis of parity revealed no significant differences (p = 0.1) between the two groups. A higher percentage of nulliparous women (33.3%) were found in the preeclamptic group compared to 50% in the normotensive group.

In terms of gravidity, significant differences were noted (p = 0.01). The preeclamptic group had a higher proportion of women with gravidity of one (28.6%) compared to the normotensive group (50%). Conversely, a higher percentage of normotensive women had higher gravidity levels (3 or more pregnancies).

Table 1 Baseline Characteristics Among the Study Groups

Variables	Preeclamptic (n=42)		Normotensive (n=42)		p value
Age	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)	
< 25 years	14	33.3	9	21.4	0.1
26 to 30 years	9	21.4	11	26.2	
31 to 35 years	12	28.6	13	31.0	
>35 years	7	16.7	9	21.4	
BMI					
Underweight (≤18.5)	2	4.8	0	0	0.01
Normal (18.6 to 25)	17	40.5	22	52.4	
Overweight (25.1 to 30	14	33.3	18	42.9	
Obese (> 30)	9	21.4	2	4.8	
Gestational age					
26 - 30	17	40.5	14	33.3	0.1
31 - 35	25	59.5	28	66.7	
Parity					
0	14	33.3	21	50	0.1
1	13	31.0	14	33.3	
3	10	23.8	4	9.5	
3	3	7.1	3	7.1	
4	2	4.8	0	0	
Gravidity					
1	12	28.6	21	50	0.01
2	13	31.0	14	33.3	
3	10	23.8	4	9.5	
4	4	9.5	3	7.1	
5	3	7.1	0	0	

Table 2 Comparison of Biomarker levels Among the Study Groups

Variables	Preeclamptic (n=42)		Normotensive (n=42)		p value
Uric acid	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)	
Normal (3-7)	7	16.7%	27	64.3%	0.001
Increased (>7)	35	83.3%	15	35.7%	*
CRP					
Normal (6)	4	9.5%	31	73.8%	0.001
Increased (>6)	38	90.5%	11	26.6%	*
Calcium					
Normal (>9)	5	11.9%	29	69%	0.001
Decreased (≤9)	37	88.1%	13	31%	*

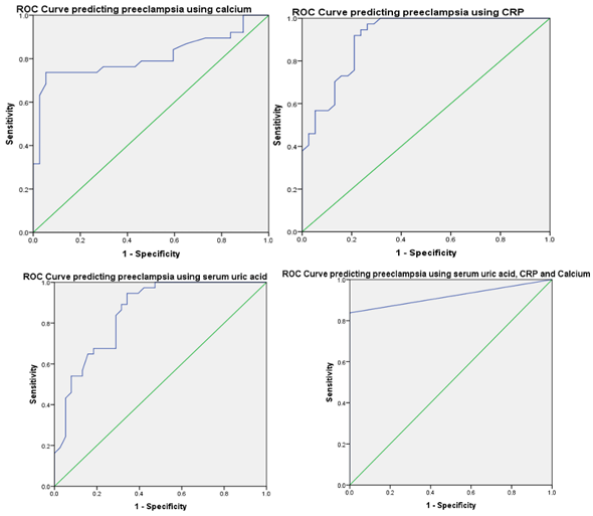
Table 3 Comparison of Average Biomarker levels Among the Study Groups

Study Groups	Uric acid	CRP	Calcium	p value
	Mean ± SD	Mean ± SD	Mean ± SD	
Normotensive (n=42)	6.08±1.90	3.40±2.61	9.89±1.23	0.001*
Preeclamptic (n=42)	8.79±1.21	7.22±1.09	7.56±1.08	0.001*
Total	7.43±2.10	5.31±3.76	8.22±1.03	0.001*

Uric acid levels showed a significant difference between the two groups (p = 0.001*). In the preeclamptic group, 83.3% of women had increased uric acid levels (>7 mg/dL), whereas only 35.7% of normotensive women were classified as such. Normal uric acid levels (3-7 mg/dL) were observed in 16.7% of preeclamptic women, compared to 64.3% in the normotensive group.

CRP levels were significantly elevated in the preeclamptic group (p = 0.001*). Specifically, 90.5% of women with

preeclampsia exhibited increased CRP levels (>6 mg/L), while only 26.6% of normotensive participants showed elevated levels. Normal CRP levels were found in 9.5% of the preeclamptic group compared to 73.8% in the normotensive group.



Calcium levels also demonstrated a significant difference ($p = 0.001^*$). In the preeclamptic group, 88.1% had decreased calcium levels (≤9 mg/dL), while only 31% of normotensive women exhibited low calcium levels. Conversely, only 11.9% of preeclamptic women had normal calcium levels (>9 mg/dL), compared to 69% in the normotensive group.

In the normotensive group (n=42), the mean uric acid level was 6.08 ± 1.90 mg/dL, while in the preeclamptic group (n=42), it was significantly higher at 8.79 ± 1.21 mg/dL ($p < 0.001^*$). This indicates a substantial elevation of uric acid levels associated with preeclampsia.

CRP levels also showed a marked difference between the two groups. The normotensive participants had a mean CRP level of 3.40 ± 2.61 mg/L, whereas the preeclamptic group exhibited a mean of 7.22 ± 1.09 mg/L ($p < 0.001^*$), suggesting increased inflammatory activity in preeclampsia.

Calcium levels were observed to be lower in the preeclamptic group, with a mean of 7.56 ± 1.08 mg/dL compared to 9.89 ± 1.23 mg/dL in the normotensive group ($p < 0.001^*$). This reduction further supports the biochemical disturbances often seen in preeclamptic patients.

Overall, the differences in biomarker levels between normotensive and preeclamptic groups were statistically significant across all measured parameters ($p < 0.001^*$), highlighting the biochemical changes associated with preeclampsia.

DISCUSSION

The study highlights significant differences in baseline characteristics and biomarker levels between preeclamptic and normotensive women. These findings offer valuable insights into the pathophysiology of preeclampsia, emphasizing the role of metabolic and inflammatory disruptions in its development.

While most baseline characteristics, such as age and parity, did not show statistically significant differences between the groups, BMI emerged as a notable factor. Preeclamptic women had significantly higher obesity rates, with 21.4% classified as obese compared to only 4.8% in the normotensive group ($p = 0.01$). This finding aligns with research suggesting that obesity is a significant risk factor for preeclampsia, likely due to its association with systemic inflammation and metabolic syndrome. Maternal obesity is consistently linked to higher rates of obstetric complications, including preeclampsia.[6]

The analysis of biomarkers further underscores the metabolic and inflammatory disturbances in preeclampsia. Uric acid levels were significantly elevated in the preeclamptic group, with 83.3% of women showing increased levels ($p = 0.001^*$). Elevated uric acid is a known marker of endothelial dysfunction and oxidative stress, which are critical factors in the pathogenesis of preeclampsia.[7] The strong association between high uric acid levels and adverse pregnancy outcomes, such as fetal growth restriction and emergency cesarean delivery, has been well documented.

CRP, a marker of inflammation, was also significantly higher in preeclamptic women (90.5% had elevated levels, $p = 0.001^*$). Chronic inflammation is believed to contribute to the vascular dysfunction seen in preeclampsia, supporting the hypothesis that preeclampsia is partly driven by an exaggerated maternal inflammatory response.[8]

Finally, calcium levels were significantly lower in preeclamptic women ($p = 0.001^*$), with 88.1% showing decreased levels. Calcium deficiency may exacerbate vascular contractility, leading to increased blood pressure and the development of preeclampsia. This finding is consistent with studies suggesting that calcium supplementation may reduce the risk of hypertensive disorders during pregnancy.[9]

The significant associations between elevated BMI, uric acid, CRP, and reduced calcium levels suggest that these biomarkers could serve as predictive tools for identifying women at risk of developing preeclampsia.[10] This highlights the potential for targeted interventions, such as weight management and anti-inflammatory therapies, to mitigate the risk and improve outcomes for both mother and fetus.

This study reinforces the importance of metabolic and inflammatory markers in the pathogenesis of preeclampsia. Future research should explore the utility of these biomarkers in early screening and prevention strategies.

CONCLUSION

This study underscores significant associations between preeclampsia and key metabolic and inflammatory markers, notably elevated BMI, uric acid, CRP, and reduced calcium levels. These findings support the role of systemic inflammation and endothelial dysfunction in preeclampsia pathogenesis. Obesity and elevated uric acid were prominent risk factors, aligning with previous research linking metabolic disturbances to adverse pregnancy outcomes. Early identification and management of these biomarkers could offer improved strategies for preventing and mitigating preeclampsia. Further research is needed to enhance biomarker-based screening and targeted interventions for high-risk pregnancies.

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