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# BIOCHEMICAL ASSESSMENT OF SERUM URIC ACID LEVEL IN RELATION TO SEVERITY OF PREECLAMPSIA IN A TERTIARY HEALTH CARE SETUP

Biochemistry

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## ABSTRACT

**Introduction:** Preeclampsia, a pregnancy-specific disorder of hypertension and proteinuria is known as "systemic syndrome of pregnancy". It is one of the major challenges for obstetrician, as it can set off grievous materno-fetal complications if left untreated. This has urged the need for prevention and earliest diagnosis of disorder so as to proceed with effective strategies for timely intervention. In this context, this study was sought to analyze serum uric acid, urea and creatinine in preeclampsia.

**Materials and Methods:** This study included 60 normotensive pregnant controls and 60 diagnosed preeclamptic cases after 20 weeks of gestation. The anthropometric characteristics and concentrations of serum uric acid, urea and creatinine were measured in both the study groups and statistically analyzed.

**Result** : Mean serum uric acid was significantly raised in preeclampsia as compared to normal pregnancy and it showed significant positive correlation with systolic/diastolic blood pressure. Other parameters like urea and creatinine were increased in preeclampsia indicating impaired renal function.

**Conclusion :** Serum uric acid may serve as a diagnostic marker and surrogate for clinical severity of preeclampsia. Screening for preeclamptic cases at an early stage allows for the vigilant antenatal surveillance and an appropriate timing of intervention to avert maternal and fetal morbidity and mortality. This will help to achieve the goal of safe motherhood and child survival.

## KEYWORDS

Preeclampsia, Serum Uric acid, Serum Urea and Creatinine

## INTRODUCTION

Preeclampsia (PE), the pregnancy-specific syndrome of hypertension and proteinuria that heralds the seizures of eclampsia, remains one of the pre-eminent enigmas in the domain of obstetrics. It has been elucidated being a "systemic syndrome of pregnancy", depicted by a de novo outset of high blood pressure (≥ 140/90 mmHg) and proteinuria (urinary protein > 300 mg in 24 hours urine) after 20 weeks of gestation in previously normotensive and non-proteinuric women.[1] Globally it strikes 7-10% of all the pregnancies and is distinguished by multi-organ cluster of alarming complications. In spite of advances in the discipline of medicine, it is even so accountable for high incidence of maternal and fetal morbidity and mortality.[2] It is accompanied with maternal complicacies like; Eclampsia, HELLP syndrome (Hemolysis, Elevated Liver Enzymes, and Low Platelet Count), pulmonary edema, abruptio placentae, Disseminated Intravascular Coagulation (DIC) and maternal death whilst in fetus, it may bring on intrauterine growth retardation, preterm birth and intrauterine death.[3]

One approach to curtail the untoward consequences of PE on maternal and fetal wellbeing is to recognize high risk women for developing the illness beforehand in pregnancy and to take measures with earlier interventions.[4] PE is well known to have a preclinical stage prior to signs and symptoms get to be clinically apparent in second half of pregnancy. In view of this "diagnostic delay", several tests have been sought to bring about the diagnosis of PE at the earliest.[5] Presently, no solitary biomarker is appropriate to foretell the occurrence of PE and a combination of indices would be most effectual.

Uric acid (UA) is a conventional marker of vascular damage, tissue injury and oxidative stress and also has been customarily ascribed to reflect impaired renal function.[6] Latterly, owing to such role, increased UA levels - hyperuricemia has been elicited as a contributor to the pathogenesis of PE. Hyperuricemia is one of the expeditiously detectable and usually the most consistent finding that oftentimes predates the beginning of hypertension and proteinuria in preeclamptic pregnancies.[7] Hence, Uric acid can be utilized for earlier diagnosis of PE and also it has been cited as a marker of disease severity.

Preeclampsia marked by extensive microangiopathic hemolysis due to endothelial dysfunction, inevitably jeopardizes glomerular dynamics and barrier function.[8] Consequently, renal perfusion and glomerular filtration are diminished which impedes the excretion of metabolic wastes products mainly urea and creatinine. These key renal function markers appear to be raised in PE.[3]

Even though the solitary curative treatment of preeclampsia is the termination of pregnancy, it could be managed expectantly with maternal blood pressure and fetal surveilling and seizure prophylaxis. Accordingly, timely prediction of PE and its intricacies is significant to circumvent maternal and perinatal complications.[10]

So, in the context of substantial attention being emplaced on maternal and child health in present era, this study was commenced to estimate the level of serum uric acid, urea and creatinine in preeclampsia and normal pregnancy. These non-protein nitrogenous metabolites are the markers of renal function as well. Over the years, a lot of focus has been aimed at research on the role of these biomarkers in preeclampsia with conflicting results. Such discordant reports have encouraged us to take on a comprehensive study on these facets to decipher the underlying intricacies.

## MATERIALS & METHODS

The Institutional Ethical Committee clearance was obtained. After written informed consent, 60 normal healthy pregnant controls and 60 diagnosed preeclampsia cases were enrolled in the study. The participants were 20 to 30 years age, primigravida with gestational age 20 weeks and above. Pregnant women with pre-existing hypertension, cardiac and renal disorders, liver disorders, multiple pregnancy and bad obstetric history were excluded from the study. The study and the control group were matched for maternal age, gestational age and body mass index. Anthropometric and demographic characteristics and biochemical data were obtained and recorded on structured data collection sheet designed for the study.

The diagnosis of PE was based on the definition of American College of Obstetricians and Gynecologists (ACOG, 2002) criteria as follows: systolic blood pressure > 140 mmHg (or rise of at least 30 mmHg) and/or diastolic blood pressure > 90 mmHg (or rise of at least 15 mmHg) manifested on two occasions 6 hours apart and proteinuria > 300 mg in a 24-hours urine collection or qualitative >1+ by dip stick test, after 20 weeks of gestation.[9] PE is of two degrees: Mild - BP ≥ 140/90 mmHg but < 160/110 mmHg and proteinuria (at least 1+). Severe - BP ≥ 160/110 mmHg and proteinuria (3+ or more) in the presence of warning signs of PE.[13]

We divided the subjects into 3 groups: Group I: 60 Normal pregnancy, Group II: 30 mild preeclampsia, Group III: 30 severe preeclampsia. Venous blood samples were obtained and analyzed for uric acid, urea and creatinine. Urine samples were collected for protein estimation by semi-quantitative dipstick method and graded as Trace to 4+.

**Statistical Analysis:** The Statistical Package for Social Sciences (SPSS) software was used for data analysis. The intergroup analysis of clinical characteristics was done by one-way analysis of variance (ANOVA) test. Pearson's correlation coefficient was used to evaluate the degree of association between various parameters in a group. The level of significance for all the inferential statistics was set at *p* value < 0.05.

## RESULT

A total of 120 subjects were enrolled in this study; 60 normotensive (group I), 30 with mild preeclampsia (group II) and 30 with severe preeclampsia (group III). The demographic data of the study participants is summarized in **Table 1**.

The comparative statistical analysis of biochemical parameters is illustrated in **Table 2**. Significant elevation in terms of serum uric acid, urea and creatinine was observed as compared to the control ones ($p < 0.05$).

We also found a significant positive correlation between serum uric acid levels and systolic/diastolic blood pressure among preeclamptic group (**Table 3**).

**Table 1. Comparison of Demographic Data in Normal Pregnancy, Mild Preeclampsia and Severe Preeclampsia Groups:-**

| Sr. No. | Demographic Characteristics | Controls | Mild Preeclampsia | Severe Preeclampsia | 'P' value |
|---|---|---|---|---|---|
| 1. | Age (years) | 26.50 ± 4.19 | 25.40 ± 5.68 | 26.91 ± 5.37 | - |
| 2. | BMI (Kg/m$^2$) | 25.35 ± 5.07 | 24.81 ± 4.19 | 26.09 ± 3.71 | - |
| 3. | Systolic BP (mmHg) | 114.82 ± 6.45 | 154.32 ± 9.21 | 176.29 ± 11.5 | **< 0.05*** |
| 4. | Diastolic BP (mmHg) | 76.8 ± 5.23 | 98.34 ± 5.82 | 118.53 ± 8.44 | **< 0.05*** |
| 5. | Gestational Age (Weeks) | 31.69 ± 6.17 | 32.51 ± 4.91 | 33.17 ± 5.74 | - |

**Table 2. Comparison of Biochemical Parameters in Normal Pregnancy, Mild Preeclampsia and Severe Preeclampsia Groups:-**

| Sr. No. | Biochemical Parameters | Controls | Mild Preeclampsia | Severe Preeclampsia | 'P' value |
|---|---|---|---|---|---|
| 1. | Uric Acid (mg %) | 4.91 ± 1.69 | 6.27 ± 2.35 | 7.86 ± 3.14 | **< 0.05*** |
| 2. | Urea (mg %) | 28.47 ± 8.54 | 41.35 ± 10.52 | 61.49 ± 13.76 | **< 0.05*** |
| 3. | Creatinine (mg %) | 0.73 ± 0.24 | 1.31 ± 0.62 | 2.17 ± 1.08 | **< 0.05*** |

**Table 3. Correlation of Serum Uric Acid with Systolic/Diastolic blood pressure among Mild Preeclampsia and Severe Preeclampsia Groups:-**

| Group | Biochemical Parameters ('r' Value) | | | 'P' Value |
|---|---|---|---|---|
| | | Systolic BP | Diastolic BP | |
| **Normal Pregnancy** | Uric Acid | 0.17 | 0.11 | - |
| **Mild Preeclampsia** | Uric Acid | 0.36 | 0.42 | **< 0.05*** |
| **Severe Preeclampsia** | Uric Acid | 0.49 | 0.53 | **< 0.05*** |

## DISCUSSION

Preeclampsia is a devastative pregnancy-related malady with little plausible pathophysiology revealed. It unfavorably influences maternal and fetal outcome because of all-embracing multi-organ involvement.[4] This has set forth anxiety in pregnant women and intrigued the concern of obstetricians all over.[1] Numerous tests have been endeavored to recognize pregnant women at substantial risk for PE at the earliest, beforehand the patient shows off progressive complications. Recently uric acid has gained so much interest and discourse as regards to its usefulness being a PE marker and a predictor of adverse materno-fetal outcome.[14] Furthermore, the obvious physiological alterations in renal function through normal pregnancy are magnified in PE because of placental ischemia and compromised placental function. Therefore, we analyzed and compared serum uric acid and renal parameters: urea and creatinine in preeclampsia and normal pregnancy.

In our study, we observed a significantly raised uric acid level in preeclampsia cases as compared to normotensive controls. This is in accordance with studies carried out by O Ekun et al[1], R Babu et al[15], R Ambad et al[16], B Ghazali et al.[13] Uric Acid showed significant positive correlation with systolic and diastolic blood pressure in PE women. This is in consonance with previous studies by R Babu et al[15], Nahar K et al[3], A Ryu et al[10], S Sogani et al.[12] Thus, the extent of rise in uric acid level was an indicator of degree of disease severity. In few studies uric acid did not show such association with blood pressure.[17,18]

Increase in serum urea and creatinine was noticed in preeclampsia. These variations were significant when compared with normotensive pregnancies. The study stands in line with O Ekun et al[1], R Babu et al[15], R Ambad et al[16], B Ghazali et al.[13] who also put out parallel findings. However, some researchers found no such conclusion denoting that aforesaid parameters are of slight use in prediction of PE.[2,9]

Raised uric acid level noted in preeclampsia is multifaceted. One of the most conventionally accepted justification is the altered renal handling subsequent to placental ischemia and reduced maternal glomerular filtration rate (GFR). This brings about increased reabsorption and decreased excretion of uric acid, analogous to the physiologic reaction to hypovolemia.[11] Hyperuricemia may be a vigilant response to combat the deleterious effects of intensified oxidative stress in PE.[8] Moreover, it may be owing to increased UA production caused by placental ischemia, trophoblast breakdown and cytokine release.[7]

In our study we noticed elevated urea and creatinine values in preeclampsia. PE is accompanied with a decrease in plasma rennin activity and rennin concentration than normal pregnancy.[4] Activity of mono amino oxidase is lower and serotonin is higher in placental tissue from preeclamptic women. These factors give rise to 20% reduction in renal perfusion and 32% reduction in GFR in PE. Ultimately, decreased urinary clearance, reduced GFR and increased reabsorption lead to the raised urea and creatinine in preeclampsia.[2]

Hyperuricemia antedates the signs and symptoms of preeclampsia and usually precedes any change in GFR.[19] It is not merely the most sensitive index of PE gravity but rather contributes directly to disease pathogenesis.[5] Accordingly, raised uric acid may be regarded as a risk factor for developing preeclampsia.[8] In our study, patients of PE displayed a notable impairment in renal function reflected by increased serum urea and creatinine.[15] Thus, it is also plausible that hyperuricemia might imply the presence of undiagnosed sub-clinical renal disease which may increase the menace of preeclampsia.[11]

Preeclampsia is one of the utmost concerns to obstetrician, as it can set off grievous - even fatal complications for both mother and fetus if left untreated. Effectual strategies should be formed and implemented towards the prevention and earliest diagnosis of the disorder.[19] Screening for high risk women and impeding the recurrence are also the fundamental aspects of disease management. Consequently, timely identification and meticulous supervision of preeclampsia cases are imperative.[8] This will allow for the vigilant antenatal surveillance and appropriate setting up of interventions in order to circumvent serious sequelae.

Small sample size and recruitment of study population from a single hospital are the limitations to this study. Further multicenter prospective studies with large samples are required to clinch the issue.

## SUMMARY & CONCLUSION

In the present study, raised serum uric acid level was observed in preeclamptic women, which displayed significant positive correlation with blood pressure with respect to normotensive pregnancies. Thus, serum uric acid may serve as a diagnostic marker and surrogate for clinical severity of the disorder. Moreover, preeclampsia has deleterious effects on renal function as indicated by deranged renal biomarkers. Maternal uric acid alongside urea and creatinine can be employed as predictor for the onset and severity of disease as well as a sensitive index of overall maternal and fetal outcome. This will allow for the well-timely implementation of preventive and management strategies to avert materno-fetal morbidity and mortality. Earlier diagnosis or recognition of preeclamptic manifestations can aid to curb and control the condition, limiting untoward sequelae and can assuredly reach the goal of safe motherhood and child survival.

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