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## Estimation of Serum Uric Acid Levels in First Trimester as a Predictor of Pre-Eclampsia

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### Abstract

**Background:** Pre-eclampsia is a life-threatening multisystem disorder, unique to pregnancy, complicating approximately 5-8% in developing countries. It is the 2nd most important cause of maternal mortality in the world. The search for an ideal predictive test for pre-eclampsia remains a major challenge for obstetricians. We in the current study tried to evaluate the serum uric acid levels with maternal and fetal outcomes. **Methods:** N=100 cases attending ANC at Prathima Institute of Medical Sciences, Naganoor, Karimnagar were included in the study. selected patients are subjected to detailed history comprising of age, parity, body weight and height, LMP, medical history, drug history, previous obstetric history, previous history of preeclampsia. They were subjected to clinical examination and BP will be recorded. Routine laboratory investigations are done, along with the serum uric acid (1<sup>st</sup> trimester) serum uric acid level was measured by the autoanalyzer. **Results:** The normal maximum serum uric acid concentration in the first trimester is 4.2 mg/dl the values below this were taken as negative for high serum uric acid levels. Those above the value of 4.2 mg/dl were taken as positive for a high level of serum uric acid levels. Pre-eclampsia was absent at the mean serum uric acid levels of less than 3.60 mg/dl and mild pre-eclampsia was noted in cases with serum uric acid range of 4.3 to 4.5 mg/dl and severe eclampsia was noted with serum uric acid levels > 4.6 mg/dl the correlation value 'r' was +0.57 and the p-value was <0.001 was significant. **Conclusion:** positive correlation between serum uric acid levels and development of pre-eclampsia in later weeks of pregnancy. There is a study on was a positive correlation between serum uric acid levels and SBP and DBP and gestational hypertension. Increased serum uric acid levels in the first-trimester help to determine fetal and maternal outcomes. Increased levels are associated with a high risk of HELLP syndrome, Low APGAR scores, and increased NICU Admissions.

**Keywords:** Pregnancy, High risk, pre-eclampsia, Uric acid, pregnancy complication

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### Introduction

Hypertensive disorders i.e., Pre-eclampsia (PET) complicate about 5-10% of all pregnancies, it is one of the members of the deadly triad along with hemorrhage and infection that contributes to maternal mortality and morbidity. Pre-eclampsia (PET) predominantly affects women in their first pregnancy (2-8% of first pregnancies).<sup>[1]</sup> Its incidence varies across the world depending on

the population under study. It is most common in Latin America and the Caribbean, and often reported as more severe in women of black ethnicity.<sup>[2, 3]</sup> It forms a part of the 'triad' responsible for the majority of maternal deaths across the world – the other two being hemorrhage and sepsis. pre-eclamptic toxemia occurs after 20 weeks of gestation in a singleton pregnancy and resolves after delivery.<sup>[4]</sup> Etiology and understanding of pathophysiology are very important to search for the marker that

predicts the occurrence of pre-eclampsia. according to many studies, preeclampsia is associated with abnormal trophoblastic invasion of uterine vessels, abnormal immunological tolerance between maternal, placental (paternal), and fetal tissues, and maladaptation to cardiovascular inflammatory changes of normal pregnancy. [5-7] Genetic factors like inheriting predisposing genes also play a role in the etiology of PET. pathophysiological changes which include abnormal trophoblastic invasion, spiral artery narrowing, atherosclerosis, infarcts, endothelial cell injury seen in the placenta, are seen in preeclamptic women. Vasospasm, endothelial cell injury, increased pressor response, prostaglandins involvement, and derangement. [8-11] Nitric oxide production and endothelial production are involved in all organs of the body. [12] All the pathophysiological changes begin with early pregnancy i.e., in the 1st trimester of gestation that is when an early invasion of trophoblastic changes takes place. During early pregnancy measurements of various biological, biochemical markers implicated in the pathophysiology of PET have been proposed to predict its development. The biochemical marker which are been proposed which are suggested of renal dysfunction are seen. Uric acid, microalbuminuria, urinary calcium, microtransferrin urea, cystatin C, etc. 10. Predictive tests will enable to discriminate high and low-risk patients to develop preeclampsia. It will also identify who may develop the clinically significant disease during pregnancy. Hence it may help to identify the patients for targeted prophylaxis once the high risk is identified. Serum uric acid in the 1st trimester can be a good predictor of preeclampsia and its estimation is a simple, biochemical screening test to predict the development of preeclampsia.

## Materials and Methods

The present study was conducted in the Department of Obstetrics and Gynecology, Prathima Institute of Medical Sciences, Naganoor, Karimnagar, Telangana State. Institutional Ethical committee Permission was obtained for the study. Written consent was obtained from all the participants of the study.

### **Inclusive Criteria**

1. Primi/ multigravida with a singleton pregnancy with a gestational age up to 12 weeks.
2. All selected patients between the age group of 18-35 will be screened for serum uric acid in the early first trimester and will be followed up till delivery.

### **Exclusion Criteria**

1. Multiple pregnancies
2. Women with a history of renal disease hypertension, diabetes mellitus, hypothyroidism, or hyperthyroidism.
3. Hydatidiform Mole, Malignancy, Hematological Disorders, etc.

Pre-eclampsia was diagnosed in women who had a blood pressure of 140/90 mm Hg or more on two occasions each 6 hours apart associated with proteinuria of at least 300 mg per 24 hours or at least 1+ on dipstick testing. Severe preeclampsia was defined as a blood pressure of 160/110 mm Hg or above measured on two occasions each 6 hours apart [18, 20 CHR]. Eclampsia is a convulsive condition associated with pre-eclampsia [18 CHR]. Successive pregnant females based on the inclusion and exclusion criteria were selected and included in the study. During the study period, a total of n=100 cases were studied. All selected women are subjected to detailed history comprising of age, parity, body weight and height, LMP, Medical History, Drug History, previous obstetric history, previous history of pre-eclampsia. They are subjected to clinical examination and BP will be recorded. Routine laboratory investigations are done. On the next day, a fasting sample was taken from these patients for measuring serum uric acid levels. Serum uric acid level will be measured by the auto analyzer "SIEMENS Dimension clinical chemistry system" and the reagent used was Uricase- Bacterial (8 IU/mL) for detection of serum uric acid. These patients are regularly followed up in the antenatal OPD once in the 4 weeks till 28 weeks then once in two weeks till there is delivery and thorough clinical examination done focusing their blood pressure and urine albumin. All the details are noted. The patients who developed preeclampsia are grouped as pre-eclampsia Cohort. The patients who are normotensive till delivery are grouped as a normal cohort. The factors taken for

analysis are age, distribution, obstetric score, body mass index, history of preeclampsia in previous pregnancies, serum uric acid, outcome-mode of delivery, APGAR score, birth weight, NICU admission.

**Statistical analysis**

The data were validated and analyzed with the help of statistical software SPSS version 20. The unpaired t-test/Mann-Whitney Test was applied for comparing the mean uric acid levels with the maternal outcomes. Qualitative variables were correlated using the Chi-Square test /Fisher's exact test and p-value < 0.05 was considered statistically significant.

**Results**

In the current study out of n=100 cases based on the age group < 20 years were 5% between 21 – 25 years were 33% and between 26 – 30 years were 40% and > 30 years were 22%. Cases diagnosed with preeclampsia were 9%. The distribution of cases based on pre-eclampsia is given in table 1.

**Table 1:** Distribution of study subjects based on age group in both the groups

|                    |         | Group (N=100) |                   |
|--------------------|---------|---------------|-------------------|
|                    |         | Normal (%)    | Pre-eclampsia (%) |
| Age group in years | <20     | 05            | 0                 |
|                    | 21 – 25 | 31            | 2                 |
|                    | 26 – 30 | 35            | 5                 |
|                    | > 30    | 19            | 3                 |
| Total              |         | 91            | 9                 |

In most of the cases, 76% were belonging to gravida 1 and 2 and the frequency of pre-eclampsia was also greater in this group with n=6 out of n=9 total cases of pre-eclampsia found in this study the distribution of cases has been depicted in table 2. Based on the gestational age 8 weeks cases were 3% followed by 9 weeks 5%, 10 weeks where 23% 11 weeks cases were 36%- and 12-weeks cases were 33%. Out of the n=9 cases of pre-eclampsia n=6 cases were in 12 weeks 3 cases in 11 weeks and n=1 cases in 10 weeks.

The normal maximum serum uric acid concentration in the first trimester is 4.2 mg/dl the values below this were taken as negative for high serum uric acid levels. Those above the value of 4.2 mg/dl were taken as positive for a high level of serum uric acid levels. Table 3 depicts the results obtained of serum uric acid

levels. The chi-square test p values were 0.00154 is significant.

**Table 2:** Distribution of Obstetric index among study subjects in both the groups

|                 |           | Group (N=100)    |                         |
|-----------------|-----------|------------------|-------------------------|
|                 |           | Normal Frequency | Pre-eclampsia Frequency |
| Obstetric Index | Gravida 1 | 51               | 4                       |
|                 | Gravida 2 | 25               | 2                       |
|                 | Gravida 3 | 06               | 3                       |
|                 | Gravida 4 | 05               | 1                       |
|                 | Gravida 5 | 04               | 0                       |
| Total           |           | 91               | 9                       |

**Table 3:** Distribution of Serum Uric Acid analysis among both the groups

|                        |                        | Group (N=100)    |                         |
|------------------------|------------------------|------------------|-------------------------|
|                        |                        | Normal Frequency | Pre-eclampsia Frequency |
| Serum Uric Acid levels | < 4.2 mg/dl (Negative) | 68               | 1                       |
|                        | > 4.2 mg/dl (Positive) | 23               | 8                       |
| P value                |                        | 0.00154*         |                         |

\* Significant

Out of the n=69 cases of serum uric acid levels < 4.2 mg/dl gestational hypertension were found in n=22(31.88%) cases and in cases of serum uric acid positive gestational hypertension was found in n=25(80.65%) out of n=31 cases given in table 4. HELLP syndrome was found in n=2 cases and both the cases were positive for serum uric. NICU admissions were required in n=08 (25.80%) of the serum uric acid positive cases and n=13 (18.84%) of serum uric acid negative cases.

**Table 4:** Distribution of frequency of gestational hypertension and NICU Admissions

|                          |         | Group (N=100)                          |  |
|--------------------------|---------|--|--|
|                          |         | Serum uric acid > 4.2 mg/dl (Positive) | Serum uric acid < 4.2 mg/dl (Negative) |
| Gestational Hypertension | Absent  | 06 (19.35%)                            | 47 (68.11%)                            |
|                          | Present | 25 (80.65%)                            | 22 (31.88%)                            |
| NICU Care                | Absent  | 23 (74.19%)                            | 56 (81.16%)                            |
|                          | Present | 08 (25.80%)                            | 13 (18.84%)                            |

Pre-eclampsia was absent at the mean serum uric acid levels of less than 3.60 mg/dl and mild pre-eclampsia was noted in cases with serum uric acid range of 4.3 to 4.5 mg/dl and server eclampsia was noted with serum uric acid levels

> 4.6 mg/dl the correlation value 'r' was +0.57 and the p-value was <0.001 was significant.

## Discussion

The present study is concerned with the association of elevated serum uric acid levels in the prediction of preeclampsia and the study of maternal and perinatal outcomes in elevated serum uric acid levels. In non-pregnant women, serum uric acid level is 2.5-5.6 mg/dl is the reference range for females. During pregnancy serum uric acid for the first trimester is 2.0-4.2 mg/dl, second trimester 2.4-4.9 mg/dl, and the third trimester is 3.1-6.3 mg/dl. There is a decreased trend of serum uric acid level in the first trimester and second trimester and third trimester of pregnancy. The cited reasons for this change of decreasing trend of uric acid level is (i) due to haemodilution and increase renal plasma flow. (ii) decreasing oncotic pressure in the blood. (iii) increase in glomerular filtration rate. There is a pathological change in trophoblastic invasion is a known factor as a cause of preeclamptic toxemia (PET). This pathological change takes place well before the clinical manifestation. Hence assessment of uric acid in the first trimester is necessary as a predictor of pre-eclamptic toxemia. In the present study 100 pregnant women who are included in the study are subjected to serum uric acid estimation in the first trimester and its association with the development of preeclampsia with the maternal and fetal outcomes are studied. out of n=100 patients, n=31 was uric acid positive (>4.2 mg/dl) and n=69 was uric acid negative (<4.2 mg/dl) and out of n=9 cases of mild preeclampsia was seen in n=3 cases, moderate in n=2 cases, and severe in n=4 cases. Ellora Devi et al., studying PIH in relation to platelet count and serum uric acid levels found out of total n=76 cases including n=60 cases of PIH of varying severity, the result was the mean uric acid level(mg/dl)  $3.88 \pm 0.51$  in control group  $5.32 \pm 0.70$  in mild PIH,  $6.8 \pm 0.97$ -moderate to severe PIH. They concluded that uric acid estimation can be used as a good indicator of the severity of PIH. Habibunnisha et al.,<sup>[14]</sup> in their study on n=80 cases diagnosed with pre-eclampsia with age-matched controls found the mean serum uric acid levels in pre-eclampsia was  $7.52 \pm 0.77$  mg/dl as compared to  $3.70 \pm 0.74$  mg/dl in controls. These

observations are in accordance with the results observed in this study. In this study, we found 2% of cases with HELLP syndrome, and both the cases were positive for high serum uric acid levels the mean serum uric acid levels in these cases were  $7.15 \pm 2.25$  mg/dl. Robert et al.,<sup>[15]</sup> have shown that 2.8% of patients with increased serum uric acid concentrations had HELLP syndrome. In the current study NICU admissions were required in n=08 (25.80%) of the serum uric acid positive cases and n=13 (18.84%) of serum uric acid negative cases. OM Ayankunle et al.,<sup>[16]</sup> in their study found Babies with low birth weight, poor Apgar scores (at 1st and 5th minute of life), and those who required neonatal unit admission occurred more significantly among the pre-eclamptic women when compared with the controls.

## Conclusion

The present study found a positive correlation between serum uric acid levels and the development of pre-eclampsia in later weeks of pregnancy. There is a study on was a positive correlation between serum uric acid levels and SBP and DBP and gestational hypertension. Increased serum uric acid levels in the first-trimester help to determine fetal and maternal outcomes. Increased levels are associated with a high risk of HELLP syndrome, Low APGAR scores, and increased NICU Admissions. Therefore, routine estimation of serum uric acid in the first trimester must be done for the determination of pre-eclampsia.

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**Source of support: Nil**

**Ethical Permission: Obtained**

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