



ELEVATED LEVELS OF SERUM URIC ACID IN PRE-ECLAMPTIC WOMEN

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ABSTRACT

The purpose of the present study is to estimate serum uric acid levels in preeclamptic, eclamptic and normotensive groups to identify women who are at high risk of developing the disease early in pregnancy. The study may provide possible biochemical parameter in toxemias of pregnancy. This is because early identification of biochemical markers of the disease would not only facilitate to identify those at increased risk for pre-eclampsia but also help in determining those patients likely to benefit from interventional measures. This study was conducted in the Department of Biochemistry, Gandhi Medical College, Secunderabad, Telangana, State, India. The cases for the study were selected from the antenatal outpatient, Gandhi Hospital, Secunderabad. A total of 34 subjects were selected and categorized into three groups. 22 among 34 women, were Pregnancy Induced Hypertensive (B.P. >140/90 mmHg), who were considered as the experimental group and remaining 12 were normotensive (B.P. <140/90 mmHg) taken as controls (n =12). The experimental group was further categorized into two groups, having 16 women in preeclampsia (n = 16), and six in eclampsia (n = 6). The data obtained was subjected to statistical tests of mean and standard deviation utilizing the SPSS-7.5 version. One-way analysis of variance (ANOVA) was utilized to compare the mean serum uric acid levels among pregnant women. The serum uric acid levels studied in various study groups showed a significant increase in pre-eclamptic (n = 16) and eclamptic (n = 6) the difference being statistically significant at $p \leq 0.001$. The mean serum uric acid level values for women with pre-eclampsia (5.80 ± 0.59 mg/dl, n = 16) and eclampsia (6.37 ± 0.25 mg/dl, n = 6) were significantly higher than those of controls (4.56 ± 0.36 mg/dl, n = 12) which is statistically significant at $p < 0.001$. Moreover, it was also experimentally found that the individual values of observed SUA in preeclamptics and eclamptics were relatively higher than those of the average values of normotensives. Although mean serum uric acid values are elevated in women with preeclampsia, the clinical utility of serum uric acid values in differentiating various hypertensive diseases of pregnancy appears to be limited. In the setting of chronic hypertension, however, a serum uric acid level of $> \text{ or } = 5.5$ mg/dl could identify women with an increased likelihood of having superimposed preeclampsia.

KEY WORDS: Eclampsia, pre-eclampsia, pregnancy induced hypertension, serum uric acid.



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INTRODUCTION

Pre-eclampsia or Preeclampsia (PE) is a hypertensive, multi-system disorder of pregnancy characterized by high blood pressure and a large amount of protein in the urine¹. It contributes to both maternal and perinatal morbidity and mortality in both developed and developing countries². It is well known that pre-eclampsia is one of the most potential complications contributing to preterm labour, perinatal mortality, maternal mortality, intra-uterine growth retardation, low birth weight infants and many such related complications. Raised serum uric acid (SUA) is one of the characteristic findings in preeclampsia. The association between raised serum UA and pre-eclamptic pregnancies was first reported almost a century ago³. Several studies have reported a positive correlation between elevated maternal serum UA and adverse maternal and fetal outcomes⁴⁻⁹. Over the years, a lot of interest has been directed at the studies on the role of serum uric acid (SUA) in the pathogenesis of pregnancy induced hypertension, preeclampsia. A number of important studies are available which confusingly and often conflictingly describe the dependence of this parameter levels in pre-eclamptic and normotensive groups. The SUA levels were found to be significantly elevated in the pre-eclamptics (with reference to the normotensives) in a number of studies^{9, 10-16}. Many biochemical markers of pre-eclampsia have been recognised in maternal serum and serum uric acid is one among the others. The results of some studies in normotensive pregnant women suggest that SUA levels begin to rise before the appearance of hypertension and proteinuria¹⁷. It is important therefore, to identify women who are at high risk of developing the disease early in pregnancy. This is because early identification of biochemical markers of the disease would not only facilitate to identify those at increased risk for pre-eclampsia but also help in determining those patients likely to benefit from interventional measures. This study, therefore involves estimations of serum uric acid levels in pre-eclamptic, eclamptic and normotensive groups.

Clinical prediction of preeclampsia may facilitate initiation of timely management to avert mortality and morbidity in the mother and as well as infant.

MATERIALS AND METHODS

This study was conducted in the Department of Biochemistry, Gandhi Medical College, Secunderabad, Telangana, State, India. The cases for the present study were selected from the antenatal outpatient, Gandhi Hospital, Secunderabad according to specific criteria like women with age group between 18-28 years, primigravide with known last menstrual period and gestational age between 20-30 weeks. If menstrual history and examination findings were not correlating, ultrasonography was done to find out the exact period of gestation. Those with known hypertension, diabetes mellitus, multiple pregnancy and ultrasound proven congenital malformation in the fetus were excluded. Consent from the pregnant women was taken to participate after explaining the objective of the study. A total of 34 subjects were selected in this study. All the 34 patients included in the present study were subjected to a detailed history taking, systematic examination, obstetric examination and routine antenatal investigations. 22 among 34 women, were Pregnancy Induced Hypertensive (B.P. >140/90 mmHg), who were considered as experimental group and remaining 12 were normotensive (B.P. <140/90 mmHg) taken as controls (n =12). The experimental group was further categorized into two groups, having 16 women in Pre-eclampsia (Group II, n = 16), and six in eclampsia (Group III, n = 6).

Collection of samples

3 ml of venous whole blood sample was collected from each subject in a plain, dry and properly labelled bottle under strict aseptic conditions. Precautions were taken to prevent haemolysis. Samples were brought to Clinical Biochemistry Laboratory, Gandhi Hospital and were centrifuged after clotting at 3500 rpm at 4°C for 30 min for separating the serum and

retraction at room temperature. Clear serum was collected and subsequently analysed for serum uric acid level measured in triplicates by colorimetric assay¹⁸. The mean of the three values was considered as the serum uric acid concentration of the study subject.

STATISTICAL ANALYSIS

The data obtained was subjected to statistical tests of mean and standard deviation utilizing the SPSS-7.5 version. To compare the mean

serum uric acid levels among pregnant women, one-way analysis of variance (ANOVA) was utilized. The results were considered significant at $p \leq 0.001$ level of significance.

RESULTS

The mean serum uric acid levels in various study groups are presented in Table 1.

Table 1
The mean serum uric acid levels in various study groups selected for the present study

Subjects	Mean \pm SD
Control group (I)	4.56 \pm 0.36
Pre-eclampsia (Group II)	5.80 \pm 0.59
Eclampsia (Group III)	6.37 \pm 0.25
p	0.000

p at 0.001% level of significance

Table 2
Serum uric acid levels in various study groups

S. No.	Control (Group I) mg/dl	Pre-eclampsia (Group II) mg/dl	Eclampsia (Group III) mg/dl
1	4.2	5.0	6.3
2	4.6	5.0	6.6
3	5.0	5.3	6.7
4	4.6	6.8	6.3
5	4.7	6.3	6.7
6	4.3	5.6	6.0
7	4.0	6.3	
8	4.3	5.6	
9	4.7	5.3	
10	5.3	5.7	
11	4.7	6.7	
12	4.3	6.0	
13		5.6	
14		5.3	
15		5.3	
16		5.0	
Mean	4.56	5.80	6.37
SD	\pm 0.36	\pm 0.59	\pm 0.25
SE	0.10	0.15	0.10

This study was carried out with the view to establish the correlation between severity of toxemias of pregnancy and serum uric acid level. The study may provide possible biochemical parameter in toxemias of pregnancy. The serum uric acid levels studied in various study groups showed a significant increase in group II (pre-eclamptic, n = 16) and

groups III (eclamptic, n = 6) the difference being statistically significant at $p \leq 0.001$. The mean serum uric acid level values for women with pre-eclampsia (5.80 \pm 0.59 mg/dl, n = 16) and eclampsia (6.37 \pm 0.25 mg/dl, n = 6) were significantly higher than those of controls (4.56 \pm 0.36 mg/dl, n = 12) which is statistically significant at $p < 0.001$. Moreover, it was also

experimentally found that the individual values of observed SUA in pre-eclampsics and eclampsics were relatively higher than those of the average values of normotensives (Fig 1). The difference in the mean serum uric acid

concentration in the two groups was however statistically significant ($p < 0.001$) with higher values in the pre-eclampsia and eclampsia groups.

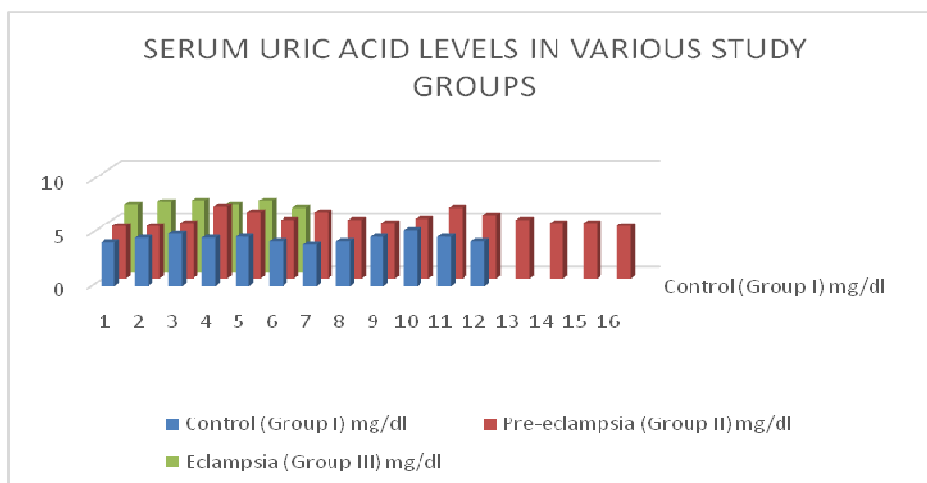


Figure 1
Serum uric acid levels in variuos study groups

DISCUSSION

Toxemia of pregnancy is a common complication of pregnancy, particularly in our country. Pre-eclampsia and eclampsia are the two major categories of toxemias of pregnancy. Various factors are involved in the development of toxemias of pregnancy. The study may provide possible biochemical parameters in toxemias of pregnancy. Toxemia of pregnancy is characterized by the appearance, during gestation or within 7 days of delivery, of a constellation of abnormalities which include hypertension, edema and proteinuria when hypertension is more severe, convulsions and coma may occur (eclampsia). Preeclampsia is responsible for approximately 70% of hypertension cases seen during gestation. Etiology of preeclampsia and eclampsia includes abnormal trophoblast invasion, coagulation abnormalities, vascular endothelial damage, cardiovascular maladaptation, immunological phenomena, genetic predisposition and dietary deficiencies or excesses. Increased uric acid levels in pre-eclamptic and eclampsia are also due to increased purine catabolism. Serum uric acid

levels were seen to be increased significantly in both preeclampsia and eclampsia. Hyperuricemia is associated with the severity of the preeclampsia and foetal outcome. Traditionally the high uric acid concentration in preeclampsia has been attributed to renal dysfunction. Preeclampsia is characterized by hyperurecemia and signs of increased formation of reactive oxygen species and decreased levels of antioxidants. Preeclampsia is also characterized by increased turnover of trophoblast tissue, which can result in higher xanthine and hypoxanthine concentrations and higher levels of circulating cytokinins. Increased uric acid concentration precedes the signs and symptom of the disease and frequently antedates any change in glomerular filtration rate. A correlation between high serum uric acid and severity of disease and perinatal mortality has been suggested earlier.¹⁹proposed that increased production of uric acid occurs in addition to altered renal handling. Uric acid is an antioxidant and has been proposed as potentially important in pregnancy. Therefore, high serum uric acid levels act as

both marker of preeclampsia and also a protective agent against free radicals. Preeclampsia leads to altered renal excretion of uric acid leading to increased levels of serum uric acid²⁰. Increasing levels of uric acid are observed to be associated with increasing number of maternal complications in various studies. Severe pre-eclampsia leads to maternal complications, such as abruption, eclampsia, renal failure and fetal complications, such as low birth weight including preterm and small gestational age and increased perinatal mortality. According to ²¹, in women with preeclampsia who developed convulsions, there invariably was a further rise in the plasma uric acid levels. Monitoring the serum uric acid levels, we were able to identify a serum uric acid value that could be used to differentiate hypertensive disease. Hence, monitoring of plasma uric acid level in those with pre-eclampsia will help to predict those women that will develop eclampsia. In several study reports it was found that the extent of the elevation in SUA level in pre-eclamptics was an indicator for the degree of severity of this disorder^{9-11, 22, 13, 14}. Elevated SUA levels have also been interpreted to act as an important cofactor involved in the pathogenesis and manifestation of pre-eclamptic disorder¹². It has been proposed recently that increased oxidative

stress and formation of reactive oxygen species (ROS), as another contributing source of hyperuricemia noted in pre-eclampsia apart from renal dysfunction²². Uric acid (as also creatinine and to some extent urea), possessing water soluble or hydrophilic antioxidant characteristics, may delay or inhibit cellular damage mainly through the free radical scavenging property; it also presents strong antioxidant activity towards ROS in aqueous phase²³. Uric Acid contributes to about 60% of free radical scavenging activity in human serum²⁴. The observed uric acid elevation may be a protective response, capable of opposing harmful effects of free radical activity and oxidative stress. Elevated serum uric acid concentrations predict the development of hypertension²⁵. Uric acid thus may function as a marker of oxidative stress tissue injury dysfunction. However, in several studies it was concluded that the measured elevated SUA level can be taken as an unreliable indicator for development of hypertension^{26, 27}. Another review inferred that uric acid (SUA) is not a consistent predictive factor for the development of preeclampsia, but its level generally increases once the disease manifests and plasma levels of uric acid may often correlate with disease severity²⁸.

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