



**ORIGINAL RESEARCH PAPER**

**Gynaecology**

**ESTIMATION OF FIRST TRIMESTER SERUM URIC ACID LEVELS AS A PREDICTOR OF PREECLAMPSIA AMONG SINGLETON PREGNANT PATIENTS ATTENDED AT A TERTIARY CARE INSTITUTION.**

**KEY WORDS:** gestational hypertension, hyperuricemia, preeclampsia, uric acid

**Dr.P.S.Jikki Kalaiselvi**

Professor of Obstetrics & Gynaecology, A.C.S.Medical College, Chennai.

**Dr.B.Gayathri**

Assistant Professor ,Department of Obstetrics & Gynaecology, Karpaga Vinayaga Institute of Medical Sciences, Palayanoor post, Maduranthagam.

**S.Padmanaban**

Research Scientist B(Non Medical), NIRRH Field unit, KMC Hospital

**ABSTRACT**

**BACKGROUND**

The association of elevated serum uric acid with the development of hypertension is established outside of pregnancy. We investigated whether first trimester uric acid was associated with the development of the following: gestational hypertension or preeclampsia, these outcomes stratified by presence of hyperuricemia at delivery since this denotes more severe disease, preterm birth or small for gestational age (SGA).

**METHODS**

Uric acid was measured in 191 maternal plasma samples from a prior prospective cohort study that were collected at a Tertiary care Hospital, Chennai.

**RESULTS**

Among total number of 191 maternal subjects, 16 were Pre eclampsia patients. The biomarker level of serum uric acid among cohort study(pre eclampsia) subjects were in the mean of 5.51 and No pre eclampsia patients were 3.570 and by the two independent t test, both are statistically significant. Receiving Operating Curve denotes optimal cut off criterion is >4.6 for pre eclampsia patients. The Area Under curve is 0.922825, which is atmost perfect prediction with a youden Index value = 0.7994.

**CONCLUSIONS**

First trimester elevated uric acid was associated with later preeclampsia and more strongly with preeclampsia and gestational hypertension with hyperuricemia.

**Introduction**

5 to 10% of all pregnancies are complicated by hypertensive disorders. Preeclampsia is a multisystem disorder associated with significant fetal and maternal morbidity and mortality. Incidence of preeclampsia ranges from 5-15% and in India incidence is 8-10%. Preeclampsia associated with hypertension, proteinuria and edema which is evident after 20 weeks gestation and resolves after delivery. So understanding of pathophysiology is very important to search for the marker that predicts the occurrence of preeclampsia. According to many studies preeclampsia is associated with abnormal placentation and endothelial dysfunction.

Predictive tests will enable to discriminate high risk and low risk patients to develop preeclampsia. It will also identify the patients who may develop clinically significant diseases so it may help to identify those patients for targeted prophylaxis once a therapy is identified.

Serum uric acid in first trimester can be a good predictor of development of preeclampsia and its estimation is a simple biochemical screening test to predict the development of preeclampsia.

Hyperuricemia is associated with many complications such as hypertension, metabolic syndrome, chronic kidney disease and diabetes in non-pregnant adults. They are high risk factors for the development of Preeclampsia. Hyperuricemia frequently occurs before the development of hypertension and proteinuria in pregnancy.

Serum uric acid is not only a biomarker for the preeclampsia, it can also play an important role in the pathogenesis of preeclampsia. So it was found to have a pathogenic role in the development of preeclampsia. Serum uric acid is a simple screening test in the first trimester to predict high risk patients who are prone to develop preeclampsia.

Preeclampsia is responsible for 16% of maternal mortality even in developed countries according to World Health Organization (WHO). We can prevent 50% of these preeclampsia related deaths. Thus early identification of high risk pregnancies may enhance development of new strategies for antenatal monitoring to detect the disease at earliest. So we can intervene appropriately to improve maternal and perinatal outcome.

**Role of Uric Acid in the Pathogenesis of Preeclampsia**

Uric acid is an end product of metabolism of purine compounds and its daily synthesis is about 400mg and from dietary sources about 300mg. Normal uric acid pool in males is about 1200 mg and in females is about 600 mg.

75% of serum uric acid is excreted in urine and its remainder is degraded to allantoin in the gastrointestinal tract by the bacterial enzymes. 98-100% of uric acid is reabsorbed in proximal convoluted tubule and it is secreted into the distal proximal convoluted tubule and further it is absorbed in to the distal convoluted tubule.

Net excretion of uric acid is 6-12% and normal serum urate level in males ranges from 2.5-8mg/d and in females ranges from 1.9-7.5mg/dl.

**Aim of the Study**

- To estimate whether an elevated uric acid level in the first trimester is associated with an increase in occurrence of preeclampsia.
- To predict the cut off value of uric acid for the outcome preeclampsia.

**Methodology**

A total of 197 antenatal patients who attended the antenatal clinic of the department of obstetrics and gynaecology, Government Kilpauk Medical College, were selected based on inclusion and exclusion criteria after obtaining their consent. All selected women were subjected to a detailed history

comprising of age,parity,body weight and height,LMP, medical history,drug history,previous obstetric history,previous H/o preeclampsia.

They were subjected to clinical examination and BP was recorded. Routine laboratory investigations were done.

On the next day fasting sample was taken from these patients for measuring serum uric acid level.Serum uric acid was measured by autoanalyzer.

- These patients were regularly followed up in the antenatal OP once in 4 weeks till 28 weeks then once in two weeks till their delivery and thorough clinical examination were done focusing their blood pressure and urine albumin.All details were entered.The patients who developed preeclampsia were grouped as preeclampsia cohort.
- The patients who were normotensive till delivery were grouped as normal cohort.
- The factors taken for analysis were age distribution, obstetric score, body mass index, history of preeclampsia in previous pregnancies and the serum uric acid.
- The predictive value of serum uric acid is determined by the ROC Curve.

Definitions used for the diagnosis of preeclampsia was according to International Society for the Study of Hypertension in Pregnancy [ISSHP],hypertension is defined as systolic blood pressure of >140 mmHg or diastolic blood pressure of >90mmHg.

A rise in the systolic blood pressure of 30mmHg or rise in the diastolic blood pressure of 15mmHg, atleast 4 hours apart associated with proteinuria of at least1+ or 1g/L on dipstick.

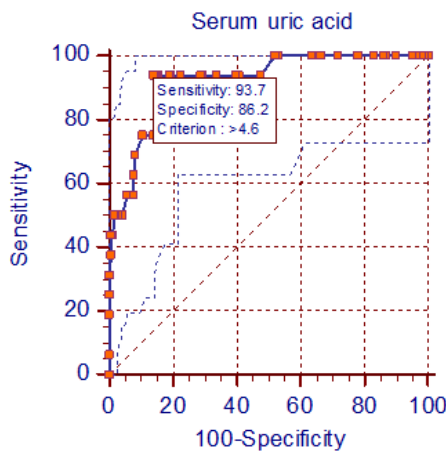
**Results and Analysis:**

**Table:1**

Group Statistics					
Pre eclampsia(yes-1/No-0)	N	Mean	Std. Deviation	Std. Error Mean	P
Serum uric acid YES	14	5.571	1.7920	.4789	<0.00001 SIGNIFICANT
NO	183	3.570	.9511	.0703	

From the above,we infer that all pre eclampsia patients were in the mean level 5.571 and control patients were in the mean level of 3.570 and statistically significant. This clearly indicates that uric acid levels were elevated for pre eclampsia patients.

**Diagram:1**



**ROC curve**

Variable	Serum_uric_acid
Classification variable	Pre_eclampsia_yes_1_No_0_
Sample size	197
Positive group :	Pre eclampsia(yes-1/No-0) = 1
Negative group :	Pre eclampsia(yes-1/No-0) = 0

Disease prevalence (%) unknown

**Area under the ROC curve (AUC)**

Area under the ROC curve (AUC)	0.922825
Standard Errora	0.0321
95% Confidence intervalb	0.876286 to 0.955970
z statistic	13.173
Significance level P (Area=0.5)	<0.0001

**Youden index**

Youden index J	0.7994
Associated criterion	>4.6

This ROC curve clearly tells at the optimum cutoff criterion for uric acid is >4.6 for likely to go Pre eclampsia.

**Conclusion**

After analysing and comparing the results between preeclampsia cohort and normal cohort it was concluded that:

- The serum uric acid level was high among preeclampsia patients in the first trimester.
- Thus there exists a positive correlation between elevated serum uric acid level in the first trimester and occurrence of preeclampsia.
- The mean cut off value of serum uric acid level for the prediction of preeclampsia in my study is 5.571

Therefore serum uric acid level in the first trimester can be a good predictor for preeclampsia if we combine with other clinical and biochemical parameters to improve the prediction. This ROC curve clearly tells at the optimum cutoff criterion for uric acid is >4.6 for likely to go Pre eclampsia.

- Long term cohort studies are needed to investigate whether patients with hyperuricemia early in pregnancy are at risk for developing hypertensive diseases with more adverse outcomes during pregnancy and future risk of metabolic syndrome, cardiovascular disease,diabetes and hypertension.

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