

## Correlation Between Salivary and Serum Uric Acid Levels In Preeclampsia.

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### Abstract:

**Background:** Among hypertensive disorders of pregnancy, preeclampsia contributes to about 7- 10% of all pregnancies. Hyperuricemia is a common finding and often precedes clinical manifestations of preeclampsia. There are several studies to suggest positive correlation between serum uric acid levels and adverse maternal and fetal outcomes. This study is to determine the correlation between salivary and serum uric acid levels in preeclampsia.

**Materials and Methods:** The Study was performed among 50 preeclamptic subjects in the Department of Obstetrics and Gynecology at SRIHER over a period of 6 months. In this study, Group 1 was Non severe Preeclampsia (n = 20) and Group 2 was Severe Preeclampsia (n = 30). In both the groups, salivary and serum uric acid levels were monitored. Uric acid was determined by Uricase method.

**Results:** There was a statistically significant correlation between salivary uric acid levels of group 1(3.31mg/dl) and group 2 (4.87mg/dl) with p value < 0.001 and serum uric acid levels of group 1 (4.99mg/dl) and 2 (6.26mg/dl) with p value < 0.001.

**Conclusion:** Salivary uric acid level in pre-eclamptic patients has a linear correlation with serum uric acid. Increase in salivary and serum uric acid levels has an adverse effects on maternal and fetal outcomes. Hence salivary uric acid can be used to prognosticate patients with preeclampsia. As salivary sample collection is noninvasive and easy compared to serum sample, salivary uric acid can be approached to monitor patients with preeclampsia. Salivary uric acid test kits can be employed for home monitoring and follow up of patients with mild preeclampsia.

**Keywords:** Salivary uric acid, Serum uric acid, cohort study, Preeclampsia.

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### I. INTRODUCTION

Hypertensive disorders in pregnancy forms a part of 'Deadly Triad' with high maternal and perinatal morbidity and mortality<sup>1</sup>. Preeclampsia contributes to about 7-10% of all pregnancies<sup>4</sup>.

Oxidative stress is the major underlying factor in all pathological consequences occurring in preeclampsia which ultimately lead to poor placental perfusion. Uric acid is generated during purine degradation. Purine metabolism by xanthine oxidase or xanthine dehydrogenase ( XO or XDH) leads to the production of uric acid along with the free radical superoxide (O<sub>2</sub>), which contributes to oxidative stress<sup>3</sup>. Therefore uric acid acts both as pro-inflammatory and pro-oxidant agent.

Hyperuricemia is almost present in all cases of pregnancies with pre-eclampsia<sup>8</sup>. The hypothesized reasons for higher levels of uric acid in preeclampsia include abnormal renal function, increased tissue lysis, metabolic acidosis, and increased activity of xanthine dehydrogenase<sup>1</sup>.

In pregnant who continue to develop preeclampsia, serum uric acid is elevated as early as 10 weeks of gestation. This elevation of serum uric acid levels occurs much before the clinical manifestation of the disorder including reduced glomerular filtration<sup>5</sup>. But higher serum uric acid level has historically been attributed to reduced renal clearance. Hypovolemia, seen very early during preeclampsia can in turn cause hyperuricemia by increased uric acid reabsorption<sup>6</sup>. Higher incidence of preterm labor and intra uterine growth retardation has been noted in pregnant with hyperuricemia.

Estrogen is uricosuric. In men and post-menopausal women, uric acid concentrations are higher due to lower blood estrogen levels. In pregnancy, due to the combined effects of increased blood volume, higher

estrogen levels and increased glomerular filtration rate, uric acid concentration initially falls by 25 to 35%. However, concentration slowly rises to that observed in non-pregnant women by term gestation (4-6 mg/dL).<sup>3</sup>

High serum uric acid levels are associated with other conditions including chronic hypertension, obesity, cardiovascular disorders, gout, renal or liver diseases. Salivary uric acid can be used as a non-invasive biomarker for prognostication of preeclampsia<sup>2</sup>. Salivary uric acid levels may be raised in few conditions like dental caries and oral cavity infections.

Positive correlation between high serum uric acid concentrations and adverse maternal and perinatal outcomes has been proved by several studies done earlier<sup>3,4</sup>. This present study aims to determine the correlation between salivary uric acid and serum uric acid levels in patients with preeclampsia.

## II. MATERIALS AND METHODS

**Study Design:** Prospective observational study

**Study Period:** September 2019 to September 2020

**Place Of Study:** Department of Obstetrics and Gynecology, SRIHER

**Study Case Selection:** Antenatal women with preeclampsia attending OPD in the Department of Obstetrics and Gynecology and those admitted in antenatal ward after 20weeks of gestation till delivery at SRIHER.

**Sample Size:** 50

Study Group 1 – Non severe Preeclampsia

Study Group 2 – Severe Preeclampsia

**Inclusion Criteria:**

Antenatal women with preeclampsia after 20weeks of gestation till delivery.

**Exclusion Criteria:**

Diabetes Mellitus, Chronic Hypertension, Cardiovascular disorders, Gout, Renal/Liver disorders, Connective tissue disorders, Oral cavity infections and Dental caries.

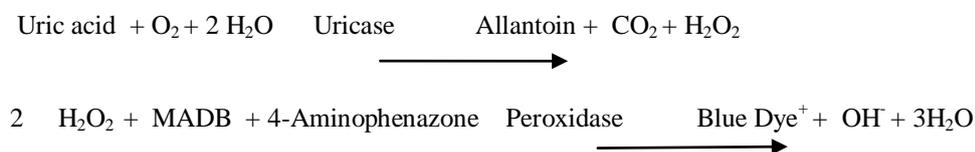
**Methodology:**

After obtaining informed consent, the study subjects are advised to rinse the mouth with water. 10 minutes later, 2ml of saliva is collected in a wide bore vial and 2ml of blood from antecubital vein is collected at the same time. Follow up levels were not measured. The samples collected before delivery were used for the analysis.

Both Salivary and Serum Uric acid levels are estimated by Uricase method

Uric acid is converted to allantoin and hydrogen peroxide by the enzyme uricase. The Trinder reaction is utilized to measure H<sub>2</sub>O<sub>2</sub>. The formed hydrogen peroxide reacts with N,N-bis(4-sulfobutyl)-3,5-dimethylaniline, disodium salt (MADB) and 4-aminophenazone produces a chromophore by peroxidase enzyme, which is read biochromatically at 660/800nm. The amount of dye formed will be proportional to the uric acid concentration in the sample.

### CHEMICAL REACTION SCHEME



## III. OBSERVATION AND RESULTS

In this study, 50% of subjects delivered vaginally and 50% of subjects delivered by cesarean section in study group 1 (Non severe Preeclampsia) and 10% of subjects delivered vaginally and 90% of subjects underwent cesarean section in study group 2 (Severe Preeclampsia).

The maternal mean age in study group 1 (Non severe Preeclampsia) was 27.70 years and in study group 2 (Severe Preeclampsia) was 29.43 years.

Totally 31 Primigravidae were included in this study of which 9 in study group 1 and 22 in study group 2 and totally 19 multigravidae were included of which 11 in study group 1 and 8 in study group 2. In this study, no statistically significant difference was noted in the age and parity of the subjects in both the study groups.

**Table 1:** Correlation of Salivary Uric Acid and Serum Uric Acid in Study Group 1 (Non-Severe Preeclampsia)

	No. of Subjects	Min	Max	Mean	SD
Salivary Uric Acid (mg/dl)	20	0.2	7.9	3.31	2.44
Serum Uric Acid (mg/dl)	20	2.2	7.1	4.99	1.47

In Study group 1, salivary uric acid ranged from 0.2 to 7.9mg/dl and mean salivary uric acid was 3.31mg/dl. Serum uric acid in group 1 ranged from 2.2 to 7.1mg/dl and mean serum uric acid was 4.99mg/dl (Table 1). There is statistically significant linear correlation between salivary uric acid and serum uric acid levels in study group 1(Non severe preeclampsia).

**Table 2:** Correlation of Salivary Uric Acid and Serum Uric Acid in Study Group 2 (Severe Preeclampsia)

	No. Of Subjects	Min	Max	Mean	SD
Salivary Uric Acid (mg/dl)	30	2	9.3	4.87	1.79
Serum Uric Acid (mg/dl)	30	3.3	10.5	6.26	1.71

In Study group 2, salivary uric acid ranged from 2 to 9.3mg/dl and mean salivary uric acid was 4.87mg/dl. Serum uric acid in group 2 ranged from 3.3 to 10.5mg/dl and mean serum uric acid was 6.26mg/dl (Table 2). There is statistically significant linear correlation between salivary uric acid and serum uric acid in group 2 (Severe Preeclampsia). The rise in salivary and serum uric acid levels were associated with the severity of preeclampsia.

**Table 3:** Intergroup Comparison of Salivary Uric Acid and Serum Uric Acid

	Salivary Uric acid (mg/dl)				Serum Uric acid (mg/dl)			
	Min	Max	Mean	SD	Min	Max	Mean	SD
Study Group 1	0.2	7.9	3.31	2.44	2.2	7.1	4.99	1.47
Study Group 2	2	9.3	4.87	1.79	3.3	10.5	6.26	1.71
	p< 0.001				p< 0.001			

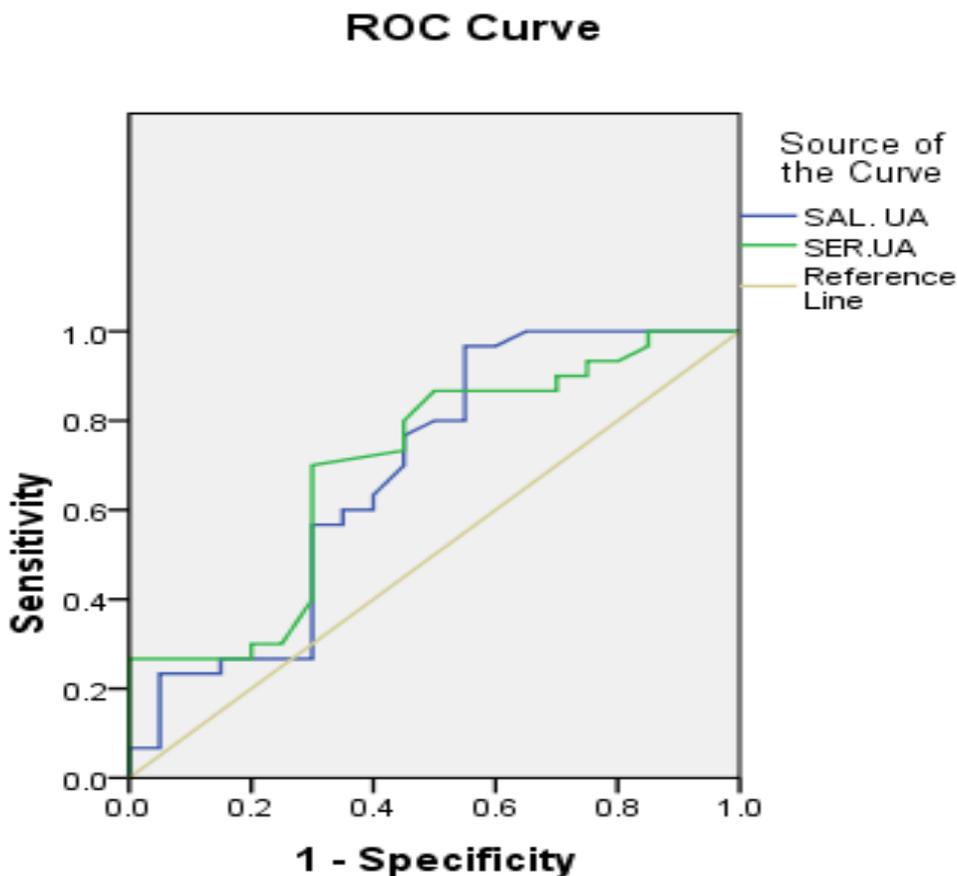
There was a statistically significant correlation between salivary uric acid levels in group 1(3.31mg/dl) and 2 (4.87mg/dl) with p value< 0.001 and between serum uric acid in group 1 (4.99mg/dl) and 2 (6.26mg/dl) with p value< 0.001(Table 3)

**Table 4:** Correlation of Maternal Outcome with Salivary Uric Acid and Serum Uric Acid In Both The Study Groups

Parameters	No. Of Subjects	Mean Salivary Uric acid (mg/dl)	Mean Serum Uric acid (mg/dl)
Eclampsia	2	4.8	4.7
HELLP Syndrome	3	4.37	6.1
Abruption	1	4.8	5.5
PRES (Posterior Reversible Encephalopathy Syndrome)	1	7	8.3
Hypertensive Retinopathy	2	7.6	7.6

The incidence of complications of preeclampsia like Eclampsia, HELLP syndrome, Abruptio placenta, PRES and Hypertensive retinopathy was higher in group 2 (Severe Preeclampsia). Mean salivary and serum uric acid levels in patients with complications ranged from 4mg/dl to 8.3 mg/dl (Table 4).

The incidence of prematurity, Intra Uterine Growth Restriction, Doppler changes, Low Birth Weight and NICU admissions were higher with elevated mean salivary uric acid and serum uric acid levels.



Diagonal segments are produced by ties.

The test result variable(s): SAL. UA, SER.UA has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Area under the curve findings were 0.685 for salivary uric acid and 0.697 for serum uric acid. ROC curve analysis also showed that there is no much variation between the areas covered by salivary uric acid and serum uric acid. (Figure 1).

#### IV. DISCUSSION

In our study, mean salivary uric acid in study group 1 was 3.31mg/dl and that in study group 2 was 4.87mg/dl. Mean serum uric acid in study group 1 was 4.99mg/dl while that in study group 2 was 6.26mg/dl.

A study by Urmila Singh<sup>1</sup>, reported that uric acid is found in the saliva of patients with preeclampsia and has linear correlation with serum uric acid which is similar to this study. Studies by Soukup et al.<sup>2</sup>, Bahaa et al<sup>7</sup> also support this.

The rate of maternal complications like cesarean section, eclampsia and abruptio placenta and fetal complications like prematurity, Intra Uterine Growth Restriction, low Apgar were higher in study group 2 which were similar to the findings in the study done by Patel tejal et al<sup>4</sup>.

Study by Soukup et al.<sup>2</sup> also found that salivary uric acid levels were significantly higher in patients with metabolic syndrome.

Studies by Shannon A. Bainbridge<sup>3</sup> and Patel Teja<sup>4</sup> concluded that serum uric acid can be used as a sensitive index of severity of preeclampsia and it plays direct role in the pathological processes of preeclampsia.

In this study, we observed that there exists a linear correlation between salivary uric acid and serum uric acid. We also found that there is association between adverse maternal and fetal outcomes and increase in salivary uric acid values. Hence Salivary Uric acid can be approached to monitor patients with preeclampsia. Smaller sample size and lack of a specific cutoff value for salivary uric acid above which it causes adverse outcomes were the limitations of the study. Wider studies with larger population should be done to derive the cutoff value for salivary uric acid.

## V. CONCLUSION

Salivary uric acid level in pre-eclamptic patients has a linear correlation with serum uric acid. Increase in salivary uric acid level has an adverse effect on maternal and fetal outcome. Hence, salivary uric acid can be used to prognosticate patients with preeclampsia. As salivary sample collection is noninvasive and easier compared to serum sample, salivary uric acid can be employed to monitor patients with preeclampsia. Salivary uric acid test kits can be used for home monitoring and follow up of patients with mild preeclampsia.

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