

**Research Article**

## **Serum Uric acid level in preeclampsia and its correlation to maternal and fetal outcome**

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### **Abstract**

**Introduction:** Preeclampsia and Eclampsia are serious complications of pregnancy. They are the leading causes of morbidity and mortality in the world and one of the leading causes for perinatal mortality also. Biochemical parameters like serum levels of Urea, Uric Acid, Creatinine, LDH, Transaminases increase significantly in Preeclampsia/eclampsia.

**Aim of the study:** Aim of the study was to Estimate the level of serum uric acid in preeclampsia/eclampsia, Correlate Hyperuricemia with the severity of Preeclampsia and Study its effect on maternal and fetal outcome.

**Study design:** Prospective study, conducted at the Government Lady Goschen Hospital, Mangalore, Karnataka India, during the years from June 1997 to June 1999, with recent updates.

**Method:** 100 consecutive patients with preeclampsia/Eclampsia all having singleton pregnancy were included in the study. Necessary laboratory investigations from samples of blood and urine were performed. Special investigations like Ultrasonography and funduscopy were conducted. Maternal and perinatal complications were studied in patients with preeclampsia with elevated uric acid levels.

**Results:** In patients with serum uric acid level of >5.5mg/dl, 86.4% had perinatal deaths and 60 % of patients with uric acid levels > 5.5 mg/dl had preterm delivery. All the babies born to mothers who had this value had birth weight < 2.5 kgs, 68% of them being Small for Gestational Age.

**Conclusions:** Hence by serial monitoring of serum Uric acid level we would be able to ascertain the severity and progression of the disease process and prompt termination of pregnancy would prevent maternal complications, improve fetal outcome and reduce perinatal mortality.

**Keywords:** Preeclampsia, Hyperuricemia, Perinatal mortality

## **1. Introduction**

Preeclampsia diagnosed by the gestational onset of hypertension and proteinuria, increases perinatal mortality by five fold<sup>1</sup> and kills 50,000 women yearly worldwide.<sup>2</sup> Its management, delivery to halt the progression of the pathophysiology, is responsible for 15% of preterm births in developed countries.<sup>3</sup> In preeclampsia, vasospasm and glomerular endotheliosis lead to reduction in renal perfusion and glomerular filtration. Renal function deteriorates in 2 stages: the first involves the impairment of tubular function and reduction in uric acid clearance and development of hyperuricemia. Later glomerular filtration becomes impaired and proteinuria develops. An increase in plasma urate is therefore an early sign in the evolution of preeclampsia. (1976)<sup>4</sup>. It has been cited as a better predictor of fetal risk than blood pressure.<sup>5</sup> It identifies women in increased risk of adverse maternal and particularly fetal outcome<sup>6</sup>. A recent publication stated 'The utility of measuring serum uric acid level in hypertensive disorders of pregnancy is limited'<sup>7</sup>. In our study, we had focused on whether inclusion of uric acid would be an indicator of adverse maternal and fetal outcomes like eclampsia, abruptio placentae, preterm delivery, low birth weight and perinatal mortality.

## **2. Materials and Methods**

### **2.1 Study Population**

This observational study was conducted over a period of twenty four months (June 1997-June 1999). All the patients who fulfilled the diagnostic criteria of Preeclampsia (>20 weeks of pregnancy with high arterial blood pressure, proteinuria and edema) admitted in the Obstetric ward, at the Government Lady Goschen Hospital, Mangalore, Karnataka State in South India, intending to eventually deliver in the above named hospital were included in this study. Patients who had preexisting diabetes or hypertension or renal disease were excluded from the study.

100 consecutive patients with preeclampsia were included in this study, detailed history, clinical evaluation, blood and urine investigations, Ultrasonography were performed. A normotensive group of 100 normotensive pregnant women were also recruited in this study. All were singleton pregnancy and were comparable with the study group in age, parity, period of gestation.

## 2.2 Blood Pressure Measurements

Upper arm blood pressure was measured using the Mercury Sphygmomanometer (ELKO B.P APPARATUS) after 5 minutes of rest, according to standard protocols. All of the participants were seated in an upright position with back support. A cuff was placed around the non-dominant upper arm, which was supported at the level of the heart; with the bladder midline over the brachial artery pulsation, the average of 3 separate measurements was taken.

Preeclampsia was classified into mild and moderate-severe based on the blood pressure recordings. Blood Pressure of 140/ 90 mm of Hg. was taken as the cut-off point for mild preeclampsia, while a B.P of 160/100 mm of Hg. was the starting point for moderate to severe preeclampsia. Eclampsia group was based on the occurrence of convulsions in a patient with pre-eclampsia.

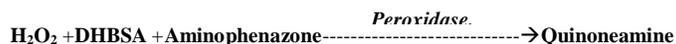
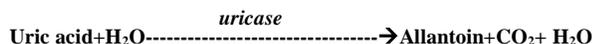
Renal function tests: 5 ml of blood was taken in a bottle without any anticoagulant to determine serum levels of uric acid, creatinine, and urea by using an auto analyzer.

## 2.3 Method of determination of urea<sup>4</sup>:

**2.3.1 Enzymatic assay:** Preliminary hydrolysis of urea with urease followed by quantitation of ammonium ion with *glutamate dehydrogenase*

**2.3.2 Determination of creatinine:** using Jaffe reaction creatinine in a protein free supernatant of plasma or serum is reacted with alkaline picrate to form a color complex whose intensity is measured at 5-10nm.

*Determination of uric acid: The estimation of uric acid involves the following reactions*



(DHBSA –DiHydroxy Benzene Sulphonic Acid)

**2.4 Statistical analysis:** Results were tabulated as Mean and Standard Deviations.

## 3. Results

A total of 200 patients were examined; 100 were patients with preeclampsia/ Eclampsia and 100 were normotensive pregnant mothers. In our study majority were primigravidae, 65% of cases of preeclampsia/Eclampsia were unbooked, the patients age was in the range of 18—38 yrs, peak incidence of preeclampsia was seen in 26—30 yrs of age group. Gestational age ranged from 24—40 weeks. The mean value of blood urea level was 15.34 mg/dl, in normotensive pregnant patients, 20.84mg/dl in mild preeclampsia, 31.10mg/dl in moderate-severe preeclampsia and 48 mg/dl in Eclampsia. The mean value of serum uric acid level was 3.07mg/dl in normotensive gravidas, 4.03 mg/dl in mild preeclampsia, 5.57 mg/dl in moderate-severe preeclampsia and 6.47 mg/dl in Eclampsia. The mean serum uric acid levels increased proportionately with the severity of the disease.

All patients who had abruption were in moderate –severe preeclampsia group with uric acid levels > 5.5 mg/dl. In patients with serum uric acid level level of >5.5mg/dl, 86.4% had perinatal deaths and 60 % of patients with uric acid levels > 5.5 mg/dl had preterm delivery. All the babies born to mothers who had this value had birth weight < 2.5 kgs, 68% of them being Small for Gestational Age.

**Table 1. Study of range and mean levels of serum uric acid in control and preeclampsia groups**

Group	Range (mg/dl)	Mean (mg/dl)
Control	2.3—4	3.07
Mild preeclampsia	3.2—5.7	4.03
Moderate to severe preeclampsia	4.1—8.9	5.57
Eclampsia.	4.8—9.3	6.47

**Table II. Correlation of Serum uric acid with Abruptio placentae**

Serum Uric Acid (mg/dl)	Abruptio placentae	
	(n=)	Percentage
Normal (<5.5 )	Nil	Nil
Abnormal (>5.5)	8	100%

All cases (100%) of abruptio placentae were seen in moderate –severe preeclampsia group with serum uric acid level > 5.5 mg/dl.

**Table III. Correlation of serum uric acid level with preterm delivery**

Serum uric acid( mg/dl)	Preterm (<37 weeks)	Term (>37 weeks)
	n	n
3—3.9 (n=7)	2	5
4—4.9 (n=44)	14	30
5—5.9(n=22)	18	4
6—6.9 (n=6)	5	1
>7 (n=1)	1	NIL.

60% of patients who had preterm delivery had serum uric acid level > 5.5 mg/dl.

**Table IV. Correlation of serum uric acid level with perinatal mortality**

Serum uric acid( mg/dl)	Perinatal deaths	
	N	(%)
3—3.9 (n=7)	Nil	Nil
4—4.9 (n=44)	Nil	Nil
5—5.9 (n=28)	7	22.6
6—6.9 (n=15)	10	66.67
>7 (n=6)	5	83.33

86.4 % of perinatal deaths were seen in patients with serum uric acid >5.5 mg/dl.

Table V. Correlation of Serum Uric acid with Birth weight

Serum uric acid( mg/dl)	Birth weight			
	<2.5kgs		>2.5kgs	
	SGA	AGA	SGA	AGA
3—3.9 (n=7)	Nil	Nil	Nil	7
4—4.9 (n=44)	16	20	nil	8
5—5.9 (n=22)	11	9	Nil	2
6—6.9 (n=6)	5	1	Nil	Nil
>7 (n=1)	1	Nil	Nil	Nil

SGA-small for gestational age; AGA-appropriate for gestational age

Birth weight of all the babies born to patients with serum uric acid >5.5 mg/dl was <2.5 kg, 68% of them being small for gestational age.

#### 4. Discussion

The data analyzed by us indicate that women with preeclampsia, elevated uric acid concentration indicate pregnancies at increased risk for SGA and preterm delivery compared with women with preeclampsia in the absence of hyperuricemia. In this study the increased incidence of preterm delivery reflects the severity of disease rather than natural history. Most early deliveries with hypertension and proteinuria were medically indicated preterm inductions and births<sup>13</sup>.

Among blood urea, serum creatinine and serum uric acid only latter was analyzed because hyperuricemia is a characteristic biochemical feature of preeclampsia known to be caused by an early tubular retention of urate which occurs before any measurable decrease in the GFR<sup>9,14</sup>. In the present study, the mean uric acid levels in the control group was found to be 3.07mg/dl., in the mild preeclampsia 4.03mg/dl, moderate-severe preeclampsia 5.57mg/dl and eclampsia 6.47mg/dl. The mean serum uric acid levels increased proportionately with the severity of disease. Nawal Kishore and S.Tandon made similar observations. In their study mean serum uric acid level was 3.8mg/dl in normotensive gravidas and 5.2 mg/dl in mild preeclampsia, 5.63mg/dl in moderate to severe preeclampsia, and 7.2mg/dl in eclampsia group<sup>8</sup>. All the patients who had abruption were in moderate to severe preeclampsia group with serum uric acid 5.5mg/dl. Elevated uric acid has been related to eclamptic seizures<sup>9</sup>. In patients with serum uric level >5.5mg/dl, 86.4% had perinatal deaths. All the mothers with serum uric acid levels above 5.5mg/dl delivered babies with birth weight less than 2.5 kg., 68% among them were small for gestational age. Mustaphi et.al<sup>10</sup> made similar observations. In their series a rise in serum uric acid level above 5.5mg/dl was associated with increased perinatal morbidity and mortality. Kang DH et al<sup>11</sup> found an increased risk of early delivery and SGA. The possibility has been suggested; recently that uric acid might itself be causally related to hypertension.<sup>11,12</sup>

#### 5. Conclusions

The pregnant women with preeclampsia associated with elevated serum uric acid levels were at a greater risk for ante partum complications and adverse pregnancy outcome. Hence by serial monitoring of serum uric acid level which is inexpensive we would be able to know the severity and progression of the disease process. Prompt termination of pregnancy in such cases would prevent maternal complications; improve fetal outcome thereby reducing perinatal mortality.

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