

Association of High Serum Uric Acid Levels and Poor Perinatal Outcome

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ABSTRACT

Background and objectives: Pre-eclampsia (PE) is one of the medical complications of pregnancy and contributes significantly to maternal and perinatal morbidity and mortality. Hyperuricemia is often associated with preeclampsia.

The objective of this study was to assess serum uric acid in group of women with pre-eclampsia and to evaluate its effect on perinatal outcome.

Materials and methods: This is a hospital-based cross-sectional study conducted at Smt. N.H.L. Municipal Medical college, Ahmedabad. 70 patients were included between 1st January 2019 to 15th September 2019 and all sociodemographic data was collected. Blood samples were obtained to assess serum uric acid besides other investigation and fetal outcome (in terms of gestational age at birth, birth weight, fetal growth restriction, admission to neonatal care unit (nicu) and intrauterine death) was evaluated.

Results & conclusion: Serum uric acid was ≥ 6 mg/dL in 43(61.4%) pre-eclamptic women. This study revealed significant association between increased level of serum uric acid and bad fetal outcome (in terms of gestational age at birth, birth weight, fetal growth restriction, admission to neonatal care unit and intrauterine death)

This study revealed significant association between high levels of serum uric acid among pre-eclamptic women and significant poor fetal and perinatal outcome.

I. INTRODUCTION

Uric acid is end product of purine metabolism. Hyperuricemia is considered a risk factor for hypertension, cardiovascular and renal disease [1]. Its normal range in nonpregnant adult is 2.5 to 5.6 mg/dl, while during pregnancy, its normal range in 1st trimester is 2.0 to 4.2 mg/dl, in 2nd trimester is 2.4 to 4.9 and in 3rd trimester is 3.1 to 6.3 [2]. Hyperuricemia is a common finding in pre-eclamptic pregnancies. The elevation of uric acid in pre-eclamptic women often precedes hypertension, proteinuria and the clinical manifestations used to diagnose the disorder [3]. There are several potential origins for uric acid in pre-eclampsia; abnormal renal function, increased tissue breakdown, metabolic acidosis, and increased activity of the enzyme xanthine oxidase (XO) [1]. The association of hyperuricemia with pre-eclampsia has been known since 1971 [1]. The severity of pre-eclampsia increases with increasing uric acid, questions whether uric acid may play a role in the pathophysiology of pre-eclampsia or is it a marker of disease [4,5,6].

Uric acid is filtered, reabsorbed, and secreted by the kidney. Hypovolemia, an early change in pre-eclampsia, increases uric acid reabsorption which could increase serum uric acid concentrations. However, increased uric acid precedes the reduction in plasma volume. Increased uric acid production from maternal, fetal, or placental tissues through heightened tissues breakdown (i.e. Increased substrate availability) and/or increased XO activity could also explain the increased concentration. The specific stimuli responsible for increased XO activity in pre-eclamptic women are unclear. The possible causes can be placental ischemia-reperfusion injury, reduced antioxidant capacity and oxidative stress. [7]

In women with preeclampsia there is impaired trophoblastic invasion of the placenta and ischemic metabolite formation [8]. These ischemic metabolites are responsible for peripheral vasoconstriction in glomeruli and glomerular endotheliosis results in decreased GFR and increased uric acid net reabsorption from proximal convoluted tubule leading to increased level of serum uric acid [9].

Numerous reports have demonstrated a relationship between uric acid concentrations and severity of disease [10,11-13]. It is one of the most consistent and earliest detectable changes in pre-eclampsia and has been cited as a better predictor of fetal risk than blood pressure. According to Roberts, James M., et al 2005 hyperuricemia was evident in 16% of women with gestational hypertension without proteinuria and 75% of women with clinically diagnosed preeclampsia (PE). Hyperuricemia among pregnant hypertensive women was associated with an excess of adverse fetal outcomes. The rate of fetal growth restriction and preterm birth was prevalent among hypertensive women with elevated concentration of uric acid even in the absence of proteinuria disorder. Uric acid elevation often precedes clinical manifestations of the disease including reduced glomerular filtration rate [14].

However, several other studies showed that serum uric acid is a poor predictor of PE [15-17].

However, we have observed in our institute that hyperuricemia in women with preeclampsia causes significant perinatal outcome, so our hypothesis is that increased uric acid in preeclampsia is responsible for poor perinatal outcome. To prove our hypothesis, we have undertaken this study.

Aim and Objectives

1. To estimate the serum uric acid levels in pregnant women with pre-eclampsia.
2. To evaluate the perinatal outcome in relation to the serum uric acid level in women presented with pre-eclampsia.

II. MATERIALS AND METHODS

This study was carried out at Smt. N.H.L. Municipal Medical College, Ahmedabad from 1st January 2019 to 15th September 2019. To achieve the aim of the study, cross-sectional design was adopted. Approval from ethical committee of college was obtained. The sample size was 70 pregnant women with ≥ 30 weeks of gestation with different severity of gestational hypertension. A consent form was signed from patients. After diagnosing pre-eclampsia, blood samples were sent for measuring serum uric acid besides other routine investigations when they were admitted in ward. The serum uric acid concentration is maintained relatively low in healthy pregnant women. The cut off value for serum uric acid was taken as 6.0 mg/dl.[2]

The study sample was divided into two groups, the first group with serum uric acid level <6 mg/dL, the second group with serum uric acid level ≥ 6 mg/dL. Perinatal outcome including gestational age at birth, induction of labour, mode of delivery, birth weight, fetal growth restriction, admission to neonatal care unit, intrauterine death measured in both groups. Other socio-demographic parameter like age, educational status, occupation and parity was also recorded.

The inclusion criteria for all women were enrolled in current study were pregnant women with gestational age ≥ 30 weeks presented with hypertension $\geq 140/90$ mm hg, proteinuria [18]. Patients with history of gout, renal disease, cardiovascular disease, diabetes, liver disease, bleeding disorders and congenital anomaly of fetus were excluded.

* *In both groups there are three twin pregnancies, so there are 30 neonates in group of patients with uric acid level less than 6 mg/dl and there are 46 neonates in group of patients with uric acid level more than or equal to 6 mg/dl.*

Statistical analysis was done by using the statistical **chi square test.**

The results were analysed by Chi square, and **$p \leq .05$ was considered as statistically significant [8].** Appropriate tables have been used for data representation.

III. RESULTS

Out of 70 pre-eclamptic pregnant women with a different degree of hypertension (mild, severe) there were 43(61.4%) with serum uric acid equal or more than 6 mg/dL(High serum uric acid group) and 27(38.5%) with serum uric acid less than 6 mg/dL(Normal serum uric acid group) as shown in table 1.

Table 1:

Total patients	High serum uric acid (≥ 6 mg/dl)	Low serum uric acid (<6 mg/dl)
70	43(61.4%)	27 (38.6%)

Table 2: Distribution of sample according to sociodemographic criteria

Socio demographic data		Number	Percentage (%)
Age in years	18 to 35	65	93
	>35	5	7
Educational status	Illiterate	1	1.42
	Primary	29	41.42
	Secondary	40	57.16
Occupation	Housewife	67	96
	Other	3	4
Parity	0	20	29
	1	22	31
	2 to 4	26	37
	>4	2	3

Tables for Distribution of sample according to fetal outcome at different levels of serum uric acid:

3. Weeks of gestation at termination:

Weeks	<34 weeks	34 to 36 weeks	≥37 Weeks
Uric acid			
Normal	0	2	25
High	2	17	24

Chi square test value is 10.767, which is statistically significant at $p < .05$.

4. Mode of delivery:

Mode of delivery	Cesarean section	Vaginal birth
Uric acid		
Normal	9	18
High	34	9

p Value is .00013, The result is significant at $p < .05$.

5. vaginal delivery: spontaneous v/s induction of labour.

Induction of labour	Present	Absent
Uric acid		
Normal	2	16
High	8	1

p Value is .000602, The result is significant at $p < .05$.

* In both groups there are three twin pregnancies, so there are 30 neonates in group of patients with uric acid level less than 6 mg/dl and there are 46 neonates in group of patients with uric acid level more than or equal to 6 mg/dl.

6. Birth weight:

Birth weight	Normal (≥2.5 kg)	Low (<2.5 kg)
Uric acid		
Normal	23	7
High	25	21

p Value is .048656, The result is significant at $p < .05$

7. Fetal growth restriction (FGR):

FGR Uric acid	Absent	Present
	Normal	26
High	37	6

p Value is .164096, The result is not significant at $p < .05$.

8. Admission to NICU (Neonatal intensive care unit)

Admission to NICU Uric acid	Admitted	Not admitted
	Normal	3
High	22	24

p Value is .000602, The result is significant at $p < .05$.

9. Intra uterine fetal death (IUFD):

IUFD Uric acid	Absent	Present
	Normal	26
High	42	1

p Value is .736203, The result is not significant at $p < .05$.

IV. DISCUSSION

In our study 61.4% (43) of preeclamptic pregnant women had serum uric level equal or more than 6 mg/dl. Majority of females (93%) were from age group of 18 to 35 years, none of them had education level more than secondary high school.

Among the group of normal serum uric acid levels only 7.4% (2) patients delivered at less than 37 weeks, while in the group of high serum uric acid levels 44% (17) pregnancies were terminated between 34 to 36 weeks, 5% (2) pregnancies were terminated below 34 weeks, which is statistically significant. This suggests that high incidence of prematurity in hyperuricemic women.

Among the group of normal serum uric acid levels 33% (9) patients were delivered by caesarean section, while in the group of high serum uric acid levels 79% (34) of them delivered by caesarean section and this result is almost equal to Sultana, Razia, et al. [19]. This suggests that high incidence of caesarean section in hyperuricemic women.

Among the group of normal serum uric acid levels only 11% (2) vaginal deliveries were induced, while in the group of high serum uric acid levels 89% (8) deliveries were induced. This suggests that high incidence of induction of labour in hyperuricemic women.

Among the group of normal serum uric acid levels, 23% (7) babies were born with low birth weight less than <2.5 kg, while in the group of high serum uric acid levels 49% (21) babies were born with birth weight less than 2.5 kg which is comparable to Yassae, F. [20]. This suggests that high incidence of low birth weight in neonates born to hyperuricemic women.

14% (6) babies had fetal growth restriction (FGR) who were born mothers with high serum uric acid levels, 4% (1) baby had fetal growth restriction (FGR) who were born mothers with normal serum uric acid levels.

Out of 30 neonates born to pre-eclamptic women with normal serum uric acid levels only 10% (3) were admitted to NICU. Out of 46 neonates born to pre-eclamptic women with hyperuricemia, 47% (22) neonates were admitted to NICU. This data suggests significant association between serum uric acid and admission to NICU. This suggests that high incidence of NICU admission in neonates born to hyperuricemic women.

V. CONCLUSION

The measurement of serum uric acid is thus of great prognostic value for fetus. Estimation of serum uric acid level in pregnancies complicated by pre-eclampsia helps to assess the severity of illness, and to identify fetuses those are likely to have perinatal morbidity in terms of prematurity, low birth weight, NICU admission. Our study shows strong association between high serum uric acid levels and high rates of prematurity, caesarean section, induction of labour, low birth weight, NICU admission. We can improve outcome of such pregnancies by timely intervention.

LIMITATIONS

- Small sample size
- Such study can be carried out at wider level involving different classes of patients.
- This is cross sectional study. Prospective COHORT study will give large picture of motor and sensory development of baby.

ACKNOWLEDGMENT

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