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Original Research Article

## Level of serum uric acid in patients with preeclampsia compared to controls and its relation to feto-maternal outcome

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### ABSTRACT

**Background:** Uric acid is the final product of the purine metabolism in humans. The two final reactions in its production which catalyze the conversion of hypoxanthine to xanthine and the latter to uric acid are catalyzed by the enzyme xanthine oxidoreductase. The role of uric acid in the progression of prediabetes to diabetes has been known. Serum uric acid has been shown to be associated with cardiovascular disease, hypertension, and chronic kidney disease. The present study was done to see the level of uric acid in preeclampsia and healthy pregnant controls, to relate serum uric acid results to the severity of hypertension and its relation to fetomaternal outcome in patients attending OPD at RMC Ajmer.

**Methods:** 100 cases of preeclampsia of age group between 20-40 year and gestational age  $\geq 28$  weeks and 100 normal healthy women with similar gestational age and age group were included in the study and maternal serum uric acid was estimated in both groups.

**Results:** Mean serum uric acid levels in preeclampsia was  $7.65 \pm 0.81$  mg/dl and  $3.21 \pm 0.72$  mg/dl in control group. Perinatal complication was more in case group, 74 % were preterm compared to 11% in control group. Mean birth weight in study group was 2.07 kg, of which 24% babies were VLBW 52% were LBW, and 24% babies had normal birth weight, in control group mean birth weight was 2.82 kg. The difference was found to be statistically significant (p value 0.001). In the study group, the MSUA concentration is found higher in LBW and VLBW babies compared to normal birth weight babies.

**Conclusions:** There is a positive correlation between SUA & severity of preeclampsia, and a significant adverse fetal outcome is observed with raised MSUA in preeclamptic patients.

**Keywords:** Birth Weight, Gestational Age, Preeclampsia, Pregnancy, Uric acid

### INTRODUCTION

Preeclampsia is a serious pregnancy complication. It is a multi-system disorder characterized by hypertension (blood pressure  $\geq 140/90$  mmHg), proteinuria (24-hr urinary protein  $\geq 0.3$  g) with or without pathological edema, beyond 20th week of gestation in previously normotensive and nonproteinuric woman. This pregnancy specific syndrome can affect virtually every organ

system.<sup>1</sup> Gestational hypertension is a common first clinical presentation of preeclampsia. Pre-eclampsia is still one of the most important causes of maternal and foetal mortality.<sup>2</sup> The aetiology of preeclampsia still remains unexplained. Though endothelial dysfunction is considered to play a central role in pathophysiology of it.<sup>3</sup> There was no screening test reliable enough to diagnose pre-eclampsia. Uric acid is one of the most sensitive indicators of disease severity in pregnancy induced

hypertensive disorders and can be of great help in monitoring the cause of disease process.<sup>4</sup> Several studies have demonstrated a correlation between elevated maternal serum uric acid and adverse maternal and foetal outcome.<sup>5</sup> Uric acid is a product of purine degradation catalysed by the enzyme xanthine oxidase. In normal pregnant women serum uric acid concentration initially falls 25-30% due to elevation in renal clearance secondary to increased GFR or reduced proximal tubular reabsorption due to changes in its production rate. Later in pregnancy the serum uric acid levels increase due to foetal production, decreased uric acid clearance and decreased binding to albumin.<sup>6</sup> Uric acid is filtered, reabsorbed and secreted by the kidney. The most commonly accepted explanation for hyperuricemia is increased reabsorption and decreased excretion of uric acid.<sup>7</sup>

Uric acid is a potent mediator of inflammation. Uric acid stimulates monocytes to produce pro-inflammatory cytokines IL-1 $\beta$ , IL-6, TNF- $\alpha$ . Uric acid promotes endothelial dysfunction per se which could promote hypertension, vascular disease and renal disease.<sup>8</sup> Therefore, the present study was designed to assess the association of uric acid levels with severity of preeclampsia and its relation to fetomaternal outcome.

## METHODS

Present cross-sectional comparative study was conducted among 200 antenatal women visited at OPD of department of Obstetrics and Gynaecology at RMC, Ajmer during December 2019 to November 2018 after ethical permission of institutional ethical committee. Inclusion Criteria of participants were pregnant women, Gestational age  $\geq 28$  weeks, Patient diagnosed as preeclampsia based on BP  $\geq 140/90$  urine protein  $\geq 1+$  dipstick and exclusion criteria were known hypertensive before, known diabetic, known renal disease patients, known gout patients, those who received chemotherapy within 4 weeks, those on thiazide diuretics.

100 Patients diagnosed as having Preeclampsia with gestational age  $\geq 28$  weeks and age between 20-40 years and 100 controls with similar gestational age and age group. Blood samples were collected under aseptic precautions in plain vial for serum uric acid estimation. Serum samples were analyzed by semi-automated biochemistry analyzer. Uric acid estimation was done by uricase peroxidase method, serum urea and creatinine, serum ALT, and AST to rule out renal and liver disease.

The data was collected from the patients using a semi structured questionnaire. 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, demographic region etc. They were subjected to clinical examination and BP was recorded.

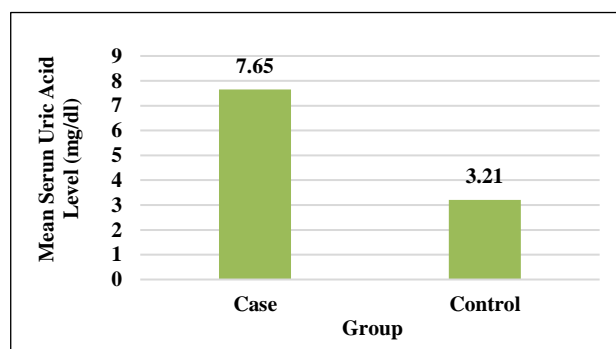
Routine laboratory investigations were done. On the next day fasting sample was taken from these patients for measuring serum uric acid level. Serum uric acid was measured by modified trinder peroxidase method using TBHB. Normal value in female: 2.6-6.0 mg/dl and in male 3.5-7.2 mg/dl. Explanation of procedure to all women participating in study was done. Participants were divided in two groups: cases were women with preeclampsia and controls were women without preeclampsia.

Descriptive statistics included computation of percentages, means and standard deviations. The independent t test (for quantitative data within two groups) was used for quantitative data comparison of all clinical indicators. Chi-square test used for qualitative data whenever two or more than two groups were used to compare. Level of significance was set at  $P \leq 0.05$ .

## RESULTS

Table 1 shows that almost 58% and 74% participants were belonged to  $< 24$  years age group in case and control group respectively. Mean age of participants were 23.9 years with 3.4 SD and 25.4 years with 4.8 SD in case and control group respectively. Around 57.0% and 58.0% participants were residing in rural area in case and control group respectively. Almost 74.0% and 50.0% cases were un-booked in case and control group respectively. Almost 58.0% and 16.0% participants were belonged to lower socio-economic group in case and control group respectively. Regarding gravidity, 54.0% and 40.0% participants were primigravida in case and control group respectively. Around 90.0 and 100.0% participants have no history of preeclampsia in case and control group respectively. Mean gestation age was 35.8 weeks with 2.42 SD and 38.1 weeks with 1.63 SD and mean birth weight was 2.1 kg with 0.6 SD and 2.8 kg with 0.4 SD in case and control group respectively. Almost 76.0% and 89.0% babies were delivered by LSCS in case and control group respectively.

Figure 1 shows that mean value of serum uric acid level was 7.65 mg/dl and 3.21 mg/dl in case and control group respectively and difference was statistically significant ( $p < 0.05$ ).



**Figure 1: Mean serum uric acid level.**

Table 2 shows fetal outcome in both groups, in study group perinatal morbidity was very high as compare to control, 58% babies were normal, 34% babies were admitted in NICU and 08% were IUFD ,while in control group 92% babies were normal and only 08% babies were admitted in NICU. The neonatal mortality in NICU babies of study group was very high, out of 34 admitted babies 14 were expired ( $p < 0.001$ ).

Table 3 compares maternal outcome in both groups, 18% patient had good outcome and discharged on time, 58% had average outcome with different minor ante, intra and postpartum complications, 6% had abruptio placentae, 12% APE, 02% ARF and 04% had PPH in study group as compare to control group all had good outcome which was statistically significant ( $p < 0.001$ ).

**Table 1: Clinico-demographic characteristics of study participants (N=200).**

Variables	Case (n=100)	Control (n=100)
<b>Age (in years)</b>		
<24	58	74
25-29	40	26
>29	2	00
Mean age $\pm$ SD	23.9 $\pm$ 3.4	25.4 $\pm$ 4.8
<b>Residence</b>		
Rural	57	58
Urban	43	42
<b>Booking Status of case</b>		
Booked	26	50
Un-booked	74	50
<b>Socio-economic Class</b>		
Upper Middle	26	40
Upper Lower	16	44
Lower	58	16
<b>Gravidity</b>		
Primigravida	54	40
Multigravida	46	60
<b>History of Preeclampsia</b>		
Present	10	0
Absent	90	100
<b>Gestational Age (in week)</b>		
Mean $\pm$ SD	35.8 $\pm$ 2.42	38.1 $\pm$ 1.63
<b>Birth Weight</b>		
<1.5	24	0
1.5-2.5	52	30
>2.5	24	70
Mean $\pm$ SD	2.1 $\pm$ 0.6	2.8 $\pm$ 0.4
<b>Mode of Delivery</b>		
LSCS	76	89
Vaginal	24	11

**Table 2: Fetal outcome among study participants (N=200).**

Outcome	Case (n=100)	Control (n=100)
IUFD	8	00
NICU Admission	34	08
Low Birth Weight	76	30
Fetal Growth Restriction	38	10
Death	14	00

**Table 3: Maternal outcome among study participants (N=200).**

Outcome	Case (n=100)	Control (n=100)
Abruptio Placenta	6	0
APE	12	0
ARF	2	0
PPH	4	0

## DISCUSSION

The ultimate goal of any protocol for management of preeclampsia must be maternal safety, delivery of a healthy live mature newborn. As some amount of expectant management exists in all treatment protocols it would be advantageous to predict development of severe PIH. The principle findings have been evolved from this study were as there is a positive correlation between SUA and both SBP and DBP, hence as the SUA concentration increased both systolic and diastolic blood pressure increased.<sup>9</sup> The observed mean serum uric acid level in all preeclampsia cases was 7.65 $\pm$ 0.081mg/dl compared to 3.21 $\pm$ 0.072 mg/dl in control, which was compatible with Ahmed A et al, found in preeclampsia 7.35 mg/dl as compare to 4.47 mg/dl in control group, Pramanik T et al, in Nepal (2012-2013) [6.27 $\pm$ 1.37 vs 4.27 $\pm$ 0.61 mg/dl] in pre-eclamptic patients compared to their healthy counterparts and ALZuabidi ZFM et al, in Iraq in preeclampsia was 7.68 $\pm$ 0.79 mg/dl as compare to 4.18 $\pm$ 1.17 mg/dl in control group.<sup>10-12</sup> The mean serum uric acid level in mild and severe preeclampsia cases in this study was 7.13 mg/dl and 8.45 mg/dl respectively which was close to the study of Thanna RC et al, found in mild preeclampsia, and severe preeclampsia patients were 7.23 $\pm$ 0.83 mg/dl, 8.59 $\pm$ 0.58 mg/dl respectively as compared to controls which was 4.12 $\pm$ 0.65 mg/dl.<sup>13</sup> There is a significant increase in perinatal mortality in severe preeclamptic patients with hyperuricemia, more so in preterm group, compared to control When it is compared with MSUA concentration, highest MSUA concentration was in study preterm group and as the MSUA concentration increased the mean gestational age decreased.<sup>14</sup> The study done by Magnann et al, found a positive correlation between increasing/raised SUA and IUGR and preterm birth.<sup>15</sup> The perinatal mortality in present study was 22% in study group and 0% in control group, and the difference was found statistically

significant ( $p < 0.05$ ). Study done by Magann et al, found that there is a positive correlation between increasing/raised SUA level and increased incidence of perinatal mortality, stillborn.<sup>15</sup> In our study we observed that maternal outcome was significantly affected adversely in preeclampsia cases compared to normotensive patients which was supported by study done by Patel T et al, was reported a comparison between the two groups revealed that hyperuricemia in patients with hypertensive disorders of pregnancy was a strong risk factor for several maternal complications with an increased risk of eclampsia by 4.2 fold and cesarean section by 3.4 fold in patients with a uric acid level 6 mg/dl as compared to those with a level of  $< 6$  mg/dl.<sup>16</sup>

## CONCLUSION

Present study found that preeclampsia is associated with rise in serum uric acid level, the higher the blood pressure in preeclampsia the higher the rise in serum uric acid level, increased gravidity is not associated with hyperuricemia, fetal outcome is worsen with rise in serum uric acid level, maternal outcome also worsen with rise in serum uric acid level. In spite of the many hidden facts about this disease improved perinatal outcome, maternal wellbeing can be achieved to a satisfactory level by establishing specialized referral centers fully equipped with facilities for proper neonatal and maternal handling, antenatally, during labour and further follow up afterwards.

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