



## ASSESSMENT OF SERUM URIC ACID LEVELS IN PRE-ECLAMPSIA PATIENTS OF SUB-HIMALAYAN REGION.

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### ABSTRACT

**Background:** Pre-eclampsia is one of the most common but least understood complication of pregnancy that causes maternal as well as fetal mortality and morbidity. The present study was designed to estimate serum uric acid levels in pre-eclampsia patients of Sub-Himalayan region.

**Methods:** The study design consisted of two groups viz. control group (N=60) and pre-eclampsia group (N=60). Blood pressure of the subjects was measured. Urine samples were collected for urinary micro proteins (MPR) and blood samples were analyzed for serum uric acid levels.

**Results:** Increased blood pressure and urinary MPR were used to establish pre-eclampsia. A significant increase was observed in uric acid levels in pre-eclampsia group as compared to the control group ( $p < 0.001$ ).

**Conclusion:** The present study exhibited hyperuricemia as one of the changes in pre-eclamptic women in Sub-Himalayan region and suggests for early screening and management of uric acid levels in pregnant females.

**KEYWORDS :** Hyperuricemia, Micro proteins, Normal pregnancy, Pre-eclampsia, Sub-Himalayan.

### INTRODUCTION

Pre-eclampsia is one of the most common complication of pregnancy that causes maternal as well as fetal mortality and morbidity.<sup>1</sup> As per the American College of Obstetrics and Gynaecology (ACOG), pre-eclampsia is defined as a pregnancy disorder related to new onset hypertension occurring after 20 weeks of gestation and commonly near term.<sup>2</sup> Pre-eclampsia is the most common but least understood disorder of pregnancy that affects about 5-7 % of all the pregnancies.<sup>1</sup> Worldwide, 500,000 babies and 76,000 women die every year of this disorder with high prevalence in low socioeconomic countries as compared to those in developed countries.<sup>3</sup> Various risk factors related to pre-eclampsia include diabetes (pregestational and gestational), chronic hypertension, renal disease, nulliparity, multifetal gestation, pre-eclampsia in previous pregnancy, maternal age of more than 35 years, systemic lupus erythematosus, thrombophilia, assisted reproductive technology and obstructive sleep apnea.<sup>4</sup> Research advances have been made in understanding the pathophysiology of pre-eclampsia but obstetricians are faced with challenge to efficiently predict pre-eclampsia in first trimester of pregnancy and to ascertain high risk group females, so that preventive measures can be initiated in the early stages to improve placenta and management of pre-eclampsia.<sup>3</sup>

In the recent years, uric acid has received much focus in relation to its utility as a marker for pre-eclampsia and an indicator of adverse maternal-fetal outcome however, the clinical correlation of this association is still not clear.<sup>5</sup> In normal pregnancies, a decrease in serum uric acid levels can be attributed to an increase in the renal blood flow, glomerular filtration rate, expansion of blood volume due to pregnancy and uricosuric action of estrogen.<sup>6</sup> But in the later stages of pregnancy, serum uric acid levels tend to rise until the end of pregnancy, as a result of increased fetal production, reduced binding to albumin and decreased renal clearance.<sup>7,8</sup> However, in pre-eclamptic pregnancies the augmentation in serum uric acid levels may be associated with decreased uric acid excretion but uricemia precedes proteinuria.<sup>9,10</sup>

Additionally, increased oxidative stress and pro-inflammatory factors may also contribute to hyperuricemia in turn leading to the progression of disease.<sup>5</sup> Therefore, the role of maternal uric acid in pre-eclampsia and in subsequent adverse maternal or fetal outcome is unclear. Moreover, as per literature no known study has addressed the role of serum uric acid in pre-eclamptic patients of Sub-Himalayan region. So, keeping in mind the above-mentioned facts present study was designed to carry out a comparative assessment of serum levels of uric acid in pre-eclampsia and normal pregnant females of Sub-Himalayan region.

### MATERIALS AND METHODS

A comprehensive study was carried out in Department of Biochemistry in collaboration with Department of Obstetrics and Gynaecology, Dr. Rajendra Prasad Government Medical College, Kangra at Tanda, District Kangra, Himachal Pradesh, India after obtaining approval from the Institutional Ethics Committee vide letter number HFW-H-DRPGMC/Ethics/2019/217 Dated: 21-12-2019,

#### Patients

Sampling population comprised of adult pregnant females coming to the Centralized Collection Centre of Hospital and Out-patient Clinic of Department of Obstetrics and Gynaecology of Hospital diagnosed with pre-eclampsia. Volunteer pregnant females willing to serve as control group were also recruited for the study.

After obtaining written consent from subjects, present history, past history, menstrual history, obstetrical history and general physical examination was documented on a predesigned proforma. The subjects were divided into two groups viz. 60 healthy pregnant controls and 60 pregnant patients with pre-eclampsia. Subjects with chronic hypertension, medical, surgical and gynaecological disorders, seizures in pregnancy, eclampsia, immunocompromised state, malignancy, history of alcohol consumption, smoking and hydatidiform mole were excluded from the study.

## Methods

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) was measured by mercury sphygmomanometer (Pagoda, Chennai, India) in subjects after 20 weeks of period of gestation from the left arm in sitting position with a resting phase of 10 minutes. Thereafter, blood pressure was measured again after an interval of four hours.

Whole blood sample of approximately 3 ml was collected from median cubital vein after venipuncture; and serum samples were analyzed for uric acid concentration. Additionally, 3 ml of urine sample was collected in sterile urine container for estimation of 24 hours urinary micro proteins (MPR). The quantitative analysis of serum uric acid (uricase-peroxidase method)<sup>11</sup> and 24 hours urinary MPR (pyrogallol red method)<sup>12</sup> was carried out on XL-300 autoanalyzer (Erba, Mannheim, Germany) using commercially available kits (Transasia Bio-Medicals Ltd., Baddi, India).

## Statistical Analysis

Data was analyzed using independent samples t-test between the groups by Statistical Package for Social Sciences (SPSS) software version 20. Data was expressed as mean  $\pm$  standard deviation (SD) for continuous variables. Values with  $p < 0.005$  calculated at 95 % confidence limit, were considered statistically significant.

## RESULTS

A significant increase was observed in the SBP value in pre-eclampsia group ( $159.33 \pm 11.84$  mm Hg) as compared to the control group ( $115 \pm 8.03$  mm Hg) ( $p < 0.001$ ) (Table 1). Similarly, a significant augmentation was also seen in the mean DBP value in pre-eclamptic group ( $100.43 \pm 7.82$  mm Hg) as compared to the control group ( $79.06 \pm 5.04$  mm Hg) ( $p < 0.001$ ) (Table 1).

**Table 1: Mean Values Of Systolic Blood Pressure And Diastolic Blood Pressure In Control Group And Pre-eclampsia Group.**

Parameters	Controls (N=60)	Pre-eclampsia (N=60)
SBP (mm Hg)	$115 \pm 8.03$	$159.33 \pm 11.84^*$
DBP (mm Hg)	$79.06 \pm 5.04$	$100.43 \pm 7.82^*$

\*Significantly different from Control group. \* ( $p < 0.001$ )

**Table 2: Mean Values Of 24 Hours Urinary Micro Proteins And Serum Uric Acid In Control Group And Pre-eclampsia Group.**

Test Parameter	Controls (N=60)	Pre-eclampsia (N=60)
24 hours urinary MPR (mg/day)	$17.46 \pm 3.85$	$814.51 \pm 185.73^*$
Uric Acid (mg/dl)	$4.53 \pm 0.58$	$7.88 \pm 0.76^*$

\*Significantly different from Control group. \* ( $p < 0.001$ )

A substantial rise was noted in the urinary MPR values in pre-eclampsia group ( $814.51 \pm 185.73$  mg/day) as compared to the control group ( $17.46 \pm 3.85$  mg/day) ( $p < 0.001$ ) (Table 2). The mean uric acid value for control group was  $4.53 \pm 0.58$  mg/dl whereas, for the pre-eclampsia group was  $7.88 \pm 0.76$  mg/dl. A considerable increase was observed in uric acid levels in pre-eclampsia group as compared to the control group and the results were statistically significant ( $p < 0.001$ ) (Table 2).

## DISCUSSION

Blood pressure as one of the diagnostic components is defined to be a new onset gestational hypertension at or after 20 weeks of gestation and SBP  $\geq 140$  mm Hg and DBP  $\geq 90$  mm Hg measured at two occasions 4-6 hours apart along with other factors such as micro proteinuria contribute to the diagnosis of pre-eclampsia.<sup>3</sup> The present study exhibited a significant increase in blood pressure in pre-eclampsia group (SBP  $\geq 140$  mm Hg and DBP  $\geq 90$  mm Hg) as compared to the

control group. Brown et al., (2018) have shown that chronic hypertensive pregnant women are at greater risk of developing pre-eclampsia.<sup>13</sup> Moreover frequent monitoring and management of blood pressure in females is required so that gestational hypertension may not proceed to pre-eclampsia otherwise leading to the risk of maternal stroke, low birth weight and prolonged neonatal intensive care.<sup>14</sup>

A significant augmentation in the urinary MPR levels was observed in pre-eclampsia group as compared to control group in the present study. A similar increase in the urinary MPR levels has been reported by Kumar and Singh (2019) in a prospective cohort study carried out in a rural tertiary care centre in Northern India.<sup>15</sup> The presence of micro proteinuria ( $\geq 300$  mg/day) is known to be as one of the diagnostic criteria in patients of pre-eclampsia.<sup>3</sup> The collection of 24-hours urine sample for MPR estimation is one of the recommended methods as it is accurate and not affected by dehydration in mother, bacterial infection in urine and variation in excretion.<sup>16</sup> The present study exhibited a significant increase in serum uric acid levels in pre-eclampsia group as compared to control group. In a recent study, elevated maternal serum uric acid values were related to increased severity of disease and poor maternal and fetal outcome. In females with severe pre-eclampsia and eclampsia, the mean serum uric acid levels were  $7.88 \pm 3.11$  and  $8.79 \pm 3$  respectively and were highly significant.<sup>15</sup> Similar results have been reported in a study conducted by Thangaratinam et al., (2006) and another study by Kumar et al., (2017) stating that increased uric acid concentration in blood of pre-eclamptic mothers was eventually associated with the poor fetal outcomes that mainly involved low birth weight and hyperuricemia was also associated with the progression of pre-eclampsia.<sup>17,18</sup> In an observational study conducted by Ryu et al., (2019) in a tertiary care center in South Korea, hyperuricemia in pregnant females was attributed to oxidative stress along with the renal function impairment, a consequence of reduction in glomerular filtration rate and placental ischemia.<sup>19</sup>

Hyperuricemia is known to severely effect placental and maternal vasculature as increased uric acid is known to impair endothelial function by inhibiting vascular endothelial growth factors and reduce nitric oxide levels. It can also enters fetal circulation freely thereby, blocking fetal angiogenesis and contribute to fetal complications. Moreover, hyperuricemia also contributes to the etiology of pre-eclampsia, by diminution of normal trophoblast invasion and vascular remodeling of spiral artery.<sup>20</sup> Additionally, uric acid can also lead to the activation of pro-inflammatory cytokines by acting as a mediator of inflammation.<sup>5</sup> Other factors affecting uric acid levels may include enzymatic defect in purine metabolism, increased cell turn over or altered kidney function.<sup>21</sup> Therefore several factors may be responsible for increased uric acid levels in pre-eclampsia patients. Since, the findings of present study are only suggestive. A longitudinal study with larger patient group can be done to arrive at definite conclusions.

## CONCLUSION

The present study exhibited hyperuricemia in pre-eclamptic women of Sub-Himalayan region suggesting for an important role of uric acid in the pathogenesis of pre-eclampsia. Additionally, the present study suggests for early screening and management of uric acid levels in pregnant females so as to prevent occurrence of pre-eclampsia and identify greater risk for fetal and maternal morbidities.

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