



# Study of Correlation between Hyperuricemia and Hypertension

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## ABSTRACT

**Background:** Hypertension is one of the current emerging community health problems, which is very common affecting one in four individuals. Hyperuricemia is predictive for the development of both hypertension and coronary artery disease. Since there are various etiological factors associated with hypertension so it is very difficult to predict which one is the most common cause of hypertension. In this study is carried out to investigate the existence of an association between serum uric acid and essential hypertension.

**Methods:** In this hospital based case control study, a total of 75 newly diagnosed essential hypertensive cases, 75 prehypertensive cases and 50 normotensive healthy controls, aged 20-50 years of both sexes were enrolled after excluding gout, diabetes mellitus, cardiovascular diseases, renal diseases, metabolic syndrome, secondary hypertension or history of having relevant drugs by taking detailed history and physical examination. Serum uric acid was measured in all study cases as well as control subjects.

**Results:** The results of our study revealed that the mean serum uric acid level and the frequency of subjects with increased serum uric acid level were significantly higher in newly diagnosed cases of essential hypertension as compared to prehypertensive and normotensive controls ( $p < 0.001$ ). Serum uric acid correlated positively with systolic blood pressure (SBP) ( $r = + 0.23$ ,  $p < 0.05$ ) and diastolic blood pressure (DBP) ( $r = + 0.09$ ,  $p > 0.05$ ). These results indicate a definite association between hyperuricemia and essential hypertension.

**Conclusions:** In the present study, Elevated level of SUA is significantly linked with PreHT and EHT after controlling various confounding factors. The present study showed that the number of hyperuricemic individuals and mean SUA level were significantly higher in newly diagnosed cases of hypertension as compared to prehypertensive and normotensive control.

**Keywords:** Serum uric acid, Borderline hypertension/Prehypertension, Essential hypertension

## I. INTRODUCTION

Life is not merely to be alive, but to be healthy and wealthy. Despite incredible improvement in health since 1950, cardiovascular disease remains among the leading causes of death worldwide. Hypertension (HT) is the most common risk factor for cardiovascular morbidity and mortality. This positive relationship between blood pressure (BP) and cardiovascular risk has been shown to exist not only in those with higher BP but also in individuals with high-normal BP/prehypertension.<sup>1</sup> Prehypertension as the name suggests that it precedes the hypertension. Trends in hypertension prevalence in India have shown a high prevalence of hypertension in both urban and rural areas. The prevalence rates of hypertension among urban population are 36.4% and rural people are 21.2%.<sup>2</sup> Hyperuricemia (HU) is frequently associated with life style related diseases.<sup>3,4</sup> As regards BP, elevated level of serum uric acid has been identified as an independent predictor of hypertension incidence and progression.<sup>5</sup>

Hyperuricemia is present in 25 -60% of individuals with untreated primary hypertension and nearly 90% in adolescent with essential hypertension of recent onset.<sup>6</sup> Experimental models have demonstrated that an elevated concentration of serum uric acid (SUA) increases blood pressure without affecting the morphology of the kidney, and that lowering uric acid can normalize blood pressure.<sup>7,8</sup> Hyperuricemia is also more common in primary hypertension than in secondary hypertension, at least in adolescents.<sup>6</sup> Consequently, if HU contributes to hypertension, it should also contribute to prehypertension (PreHT). Since PreHT is the pre-stage of hypertension respectively, it can be expected that HU will be more often present in persons suffering from prehypertension. A report shows that borderline hypertension (systolic BP 130-139 and/or diastolic BP 85-89 mmHg) carry a significant cardiovascular risk and there is a need to reduce this blood pressure.<sup>9</sup> This study was done to study the



relationship between SUA and EHT as well as to find out the correlation coefficient between SUA levels and BP in individual with EHT.

## METHODS

### Inclusion criteria

A total of 200 subjects of age group between 20-50 years, irrespective of sex were included in this study. All the subjects were divided into three groups:

□ □ Control group: 50 subjects with normal blood pressure (SBP= 90-119 mmHg, DBP= 60-79 mmHg) or any other condition known to cause hyperuricemia.

□ □ PreHT group: 75 cases of prehypertension (SBP= 120-139 mmHg, DBP= 80-89 mmHg).

□ □ HT group: 75 cases of newly diagnosed essential hypertension (SBP= 140-159 mmHg, DBP= 90-99 mmHg). The diagnosis of PreHT and EHT is established according to JNC7 criteria.<sup>10</sup>

### Exclusion criteria

□ □ Pregnant hypertensive patients (Gestational hypertension)

□ □ Patients with Secondary hypertension due to any cause

□ □ Patients with gout

□ □ Patients with diabetes mellitus

□ □ Smokers

□ □ Alcohol consumers

□ □ Patient taking antihypertensive, lipid lowering agents and hypouricemic agents.

After obtaining a written voluntary informed consent from all the subjects, data was

collected in the detailed proforma along with requisite physical examination.

Then blood sample (3 ml) was drawn after an overnight fast (12 h) by venous puncture and serum was separated by a centrifugation at 3000rpm for 10 minutes. Serum was used to determine participant's S. uric acid, S.creatinine and fasting blood glucose level by Modified Trinder method, Jaffe's method and enzymatic method

respectively.<sup>11-13</sup> Serum creatinine and fasting blood glucose was estimated to exclude renal disorder and diabetes mellitus respectively.

The data was analysed by using standard statistical software. Significance testing of difference for mean  $\pm$  SD of three groups was done by analysis of variance test

(ANOVA). The correlation between SUA and BP was assessed by Pearson coefficient of correlation. Association between hypertension and hyperuricemia was tested by Chi-square test and Odds ratio. A p-value of  $<0.05$  was used to establish statistical significance.

## II. RESULTS

In the present study the difference in the mean age, mean BMI, mean systolic and diastolic BP of control, preHT and HT group were highly significant ( $p < 0.0001$ ). The mean & std. deviation of serum uric acid level were  $4.91 \pm 0.88$  mg/dl,  $5.89 \pm 0.97$  and  $6.56 \pm 0.64$  mg/dl in control, preHT and HT group respectively ( $p < 0.001$ ).

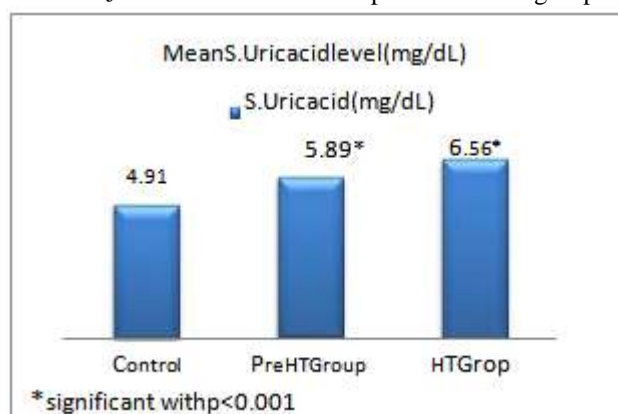


Figure 1: Comparison of mean of serum uric acid level among different groups.



**Table 1: Characteristics of study population among different groups.**

Variables	Control	PreHTgroup	HTGroup	Pvalue
	Mean± SD	Mean± SD	Mean± SD	
Gender(F/M)	26/24	35/40	28/47	
Diet(Nonveg/Veg.)	16/34	37/38	45/30	
Age(Yrs.)	37.46±8.09	35.84± 6.5	40.25±7.71	0.0014
BMI(Kg/m <sup>2</sup> )	21.89±1.47	24.27± 2.6	27.34±2.77	<0.0001
SBP(mmHg)	114.06±16.77	134.00±5.1	160.04±11.49	<0.0001
DBP(mmHg)	74.66±6.22	86.45±2.93	92.00± 10.15	<0.0001
S.Uricacid(mg/dL)	4.91±0.97	5.89±0.97	6.56±0.76	<0.001

Serum uric acid was found to be positively and significantly correlated with systolic blood pressure (SBP) ( $r= +0.23$ ,  $p<0.05$ ), whereas no significant

correlation was found between serum uric acid and diastolic blood pressure (DBP) ( $r= +0.09$ ,  $p>0.05$ ).

**Table 2: Distribution of the study subjects with hyperuricemia in HT, PreHT group and control group (P value reached from chi square test).**

Particulars	PreHTv/s	Control	HTv/sPreHTGroup		HTGroup	v/sControl
	PreHT	Control	HTGroup	PreHT	HTGroup	Control
Totalno.ofsubject	75	50	75	75	75	50
SubjectwithHyperuricemia	15	7	28	15	28	7
Percentage	25%	14%	37.33%	25%	37.33%	14%
OddsRatio	1.53		2.38		3.66	
pvalue	>0.05		<0.01		<0.01	

This study showed that 25% of prehypertensive cases had hyperuricemia as compared to 14% in control (OR=1.53,  $p>0.05$ ) indicating that hyperuricemic individual have 1.53 times more risk of developing prehypertension as compared to the one with lower value of serum uric acid whereas among HT group, 37.33% of cases had hyperuricemia as compared to 14% in control (OR=3.66,  $p<0.01$ ), indicating that hyperuricemic individual have 3.66 times more risk of developing essential hypertension as compared to those with lower serum uric acid level. These results indicate a definite association between hyperuricemia and essential hypertension. Hyperuricemia is defined as SUA level  $\geq 7$  mg/dl (in men) or  $\geq 6.0$  mg/dl (in women).<sup>14</sup>

### III. DISCUSSION

An elevation in serum uric acid (SUA) has been associated with an increased risk for the development of hypertension.<sup>15,16</sup> Serum uric acid levels have been associated cross-sectionally with BP and longitudinally with hypertension incidence and future increase in BP.<sup>6,17,18</sup> The hyperuricemia observed in untreated hypertension may reflect the decrease in renal blood flow and early hypertensive nephrosclerosis. This can lead to local tissue

ischemia.<sup>19</sup> In addition to the release of lactate that blocks urate secretion in the proximal tubule; ischemia also results in increased uric acid synthesis. With ischemia, ATP is degraded to adenine and xanthine, and there is also increased generation of xanthine oxidase. The increased availability of substrate (xanthine) and enzyme (xanthine oxidase) results in increased uric acid generation. Others factors like alcohol abuse, obesity, insulin resistance and diuretic use may also contribute to the fact that serum uric acid is associated with hypertension.

Nevertheless, some studies find uric acid predictive for the development of cardiovascular disease, hypertension and renal disease despite controlling for associated risk factors. This raises the possibility that uric acid may have a role in the pathogenesis of in hypertension and cardiovascular disease.

The present study showed an increased trend in mean serum uric acid level and number of hyperuricemic individuals from control to prehypertensive cases and prehypertensive to hypertensive cases ( $p<0.001$ ) and serum uric acid was found to be positively and significantly correlated with systolic blood pressure (SBP) ( $r= +0.23$ ,  $p<0.05$ ) whereas no significant correlation was found between serum uric acid and diastolic blood pressure (DBP) ( $r= +0.09$ ,  $p>0.05$ ).

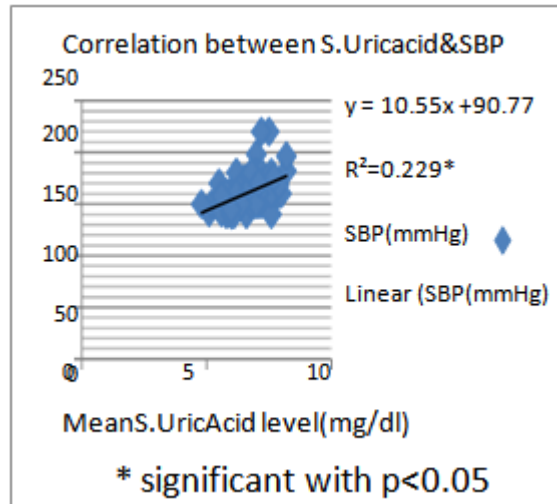


Figure 2: Correlation between serum uric acid level &SBP.

Our results were similar to the several other studies.<sup>20-25</sup> In favour of our study Assob JCN et al observed that the serum uric acid level in prehypertensive group was significantly higher

than control group ( $p < 0.0001$ ) and SUA was found to be positively correlated with SBP and DBP ( $p < 0.0001$ ).<sup>26</sup>

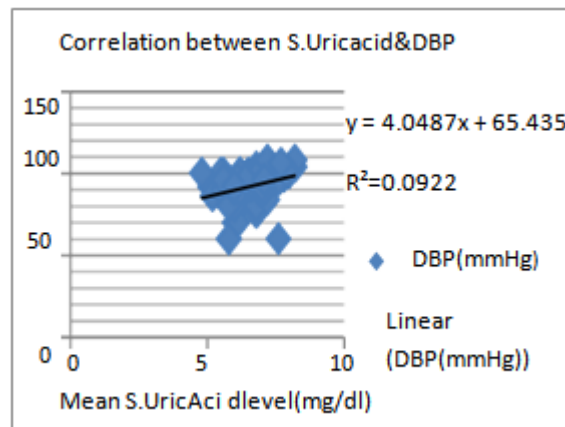


Figure 3: Correlation between serum uric acid level &DBP.

In contrast to our study, Hamdani IHAL observed no significant difference in serum uric acid level between hypertensive patients and control group.<sup>27</sup> Another study carried out by Vucak J et al did not find an association between hyperuricemia and hypertension (OR 1.68).<sup>28</sup>

The possible mechanisms for the occurrence of high blood pressure in high serum uric acid includes: (a) uric acid induced activation of rennin angiotensin system and action on glomerular apparatus (b) increased insulin resistance and increased insulin level, causing decreased

excretion of uric acid, sodium, potassium from kidney tubules and (c) uric acid action in proliferation of vascular smooth muscles, endothelial dysfunction with decrease nitric acid production.<sup>29-35</sup> Initially uric acid causes constriction of vessels by activation of the renninangiotensin system and decreased circulating nitric oxide by endothelial dysfunction which results in hypertension.

This hypertension type is salt resistant and this can be reversed by decreasing uric acid. As time passes, uric acid uptake into vascular smooth muscle cells causes cellular proliferation and secondary arteriosclerosis that impairs pressure



natriuresis, causing hypertension this type of hypertension is salt driven/salt sensitive, renal independent and independent of SUA level.<sup>36</sup> It is therefore hypothesized that if SUA were important in the genesis of primary hypertension, then the relation would be greatest in the new and recent onset hypertensive subjects. Taken together, these data suggest that SUA could be an independent association factor for the development of HT in the healthy general and prehypertensive population.

#### IV. CONCLUSION

In the present study, Elevated level of SUA is significantly linked with PreHT and EHT after controlling various confounding factors. The present study showed that the number of hyperuricemic individuals and mean SUA level were significantly higher in newly diagnosed cases of hypertension as compared to prehypertensive and normotensive control. SUA was found to be positively and significantly associated with SBP in newly diagnosed cases of hypertension. In the present study, we found patient with PreHT and EHT often exhibited hyperuricemia as comorbidity even if they were not taking medication. There is a future perspective that hypertension can be treated by lowering SUA levels particularly in new and recent onset primary hypertension.<sup>37</sup> Thus it is important to monitor SUA level among prehypertensive and newly diagnosed essential hypertensive patients.

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