

## Original Research Article

# Serum uric acid level in Bangladeshi adults with essential hypertension

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## ABSTRACT

**Background:** The association of hyperuricemia with various cardiovascular risk factors has often led to the debate of whether hyperuricemia is an independent risk factor for essential hypertension (HTN). The current study was conducted to see the relationship between serum uric acid and essential HTN in Bangladeshi adults.

**Methods:** In this cross-sectional study, conducted in a tertiary hospital of Bangladesh, 155 patients with essential hypertension (newly detected or on treatment) aged  $\geq 18$  years and 100 age-sex matched normotensive subjects were investigated. Serum uric acid, plasma glucose, serum creatinine, and lipid profile were measured in all in fasting samples.

**Results:** The frequency of hyperuricemia was higher in the hypertensive group in comparison to the normotensive control group (29.7% vs. 6.0%,  $p < 0.001$ ). Serum uric acid level was higher in the hypertensive subjects than the controls ( $6.10 \pm 0.88$  vs.  $5.38 \pm 0.54$  mg/dL, mean  $\pm$  SD,  $p < 0.001$ ). In the hypertensive group, subjects with stage II HTN had higher serum uric acid than those with stage I HTN ( $6.46 \pm 0.83$  vs.  $5.72 \pm 0.78$  mg/dL, mean  $\pm$  SD,  $p < 0.001$ ). In the hypertensive group, uric acid level showed significant positive correlations with both systolic and diastolic blood pressure though in the control group, uric acid showed such correlation with systolic BP only.

**Conclusions:** Patients with essential hypertension had higher serum uric acid compared to normotensive controls; uric acid level showed positive correlations with systolic and diastolic BP in the hypertensive subjects.

**Keywords:** Essential hypertension, Hypertension, Hyperuricemia, Uric acid

## INTRODUCTION

Hypertension (HTN) is a significant public health problem due to its high prevalence all around the globe. Around 7.5 million deaths or 12.8% of the total of all annual deaths worldwide occur due to high blood pressure.<sup>1</sup>

The prevalence of HTN is high in Bangladesh; like other parts of the world, HTN and its complications are one of

the leading causes of death and disability in here.<sup>2</sup> The pathogenesis of essential HTN, which constitutes around 95% of all causes of HTN, is not clearly understood. Many factors may contribute to its development, including peripheral resistance vessel tone, endothelial dysfunction, autonomic tone, insulin resistance, and neurohumoral factors.<sup>3</sup> Some studies have found higher frequencies of hyperuricemia in hypertensive patients in comparison to healthy subjects.<sup>4-9</sup> Elevated serum uric acid has been identified as a potential independent risk factor for the development of essential HTN in the

general population.<sup>10-14</sup> Few studies have evaluated the association between high uric acid and essential HTN in Bangladesh; we conducted this study to fill this lacuna.

## METHODS

This cross-sectional study was conducted during the period from July 2016 to June 2018 in the Department of Medicine of a tertiary hospital of Bangladesh. Patients with essential hypertension attending the Medicine Outpatient Department (OPD) of the hospital during the study period were the study population. Considering the prevalence of hypertension of 11.3% with 5% significance level and 5% margin of error, the estimated sample size was 154; for this study, 155 subjects with hypertension were enrolled; 100 normotensive age and sex-matched otherwise healthy subjects from the accompanying persons of the patients, and hospital staffs (doctors, nurse, and others) were enrolled in the comparison group.<sup>15</sup>

Patients of both genders aging >18 years with essential hypertension (newly detected or on treatment) according to the seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7) criteria were selected in the hypertensive group.<sup>16</sup> Patients with diabetes, ischemic heart disease, congestive cardiac failure, gout, overweight/obesity (BMI >25 kg/m<sup>2</sup>), alcohol abuse, renal insufficiency, secondary hypertension, lymphoproliferative or myeloproliferative disorders, any acute illness and subjects on levodopa, ethambutol, pyrazinamide, nicotinic acid, cytotoxic drugs, aspirin, thiazide diuretics, and ACE inhibitors were excluded. Consecutive convenient sampling was applied to select samples.

### Measurement of blood pressure

Blood pressure (BP) was measured in the right arm placed at the heart level using aneroid sphygmomanometer with an adequate cuff size with the subjects were rested quietly for at least 5 minutes in a sitting position with the feet on ground and back supported after removing tight clothing from the arm. Systolic blood pressure (BP) and diastolic blood pressure (DBP) were measured twice at an interval of 5 minutes. The averages of SBP and DBP were recorded in the data collection sheet, and this average of two readings was used for classification of BP according to the JNC-7 criteria:

- Normal: SBP <120 and DBP <80 mmHg
- Pre-hypertensive: SBP 120-139 or DBP 80-89 mmHg
- Stage I HTN: SBP 140-59 or DBP 90-99 mmHg
- Stage II HTN: SBP ≥160 or DBP ≥100 mmHg.<sup>16</sup>

Anthropometric measurements: Anthropometric measurements included height and body weight, which

were measured by standard instruments following the recommended procedures while the subject was wearing light clothing without shoes.

### Biochemical assessments

Fasting venous blood was collected from all of the study subjects after 8-12 hours of overnight fasting for measurement of plasma glucose, serum creatinine, serum uric acid, lipid profile. All biochemical assays were analyzed on a semi-automated analyzer. The serum uric acid level was measured by the uricase method, serum creatinine by Jaffe method, triglyceride, total cholesterol, and HDL cholesterol by enzymatic method. LDL-cholesterol was calculated using the Friedewald equation.<sup>17</sup> Glucose was measured by the glucose oxidase method in the venous blood samples collected in EDTA tubes. The estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft-Gault formula.<sup>18</sup> Hyperuricemia was defined if SUA levels above 7.0 mg/dL in males and above 6.0 mg/dL in females.<sup>19</sup>

### Ethical consideration

The study protocol was approved by the Institutional Ethics Committee of the hospital. Informed written consent was taken from each of the patients before taking any interviews after describing the purpose and methods of the study, confidentiality of the interviews, risks, and benefits of participating in the study. All information was collected confidentially with complete respect to the patient with and without any force or pressure.

### Statistical analysis

Data were processed and analyzed using SPSS (Statistical Package for Social Sciences) Version 22.0. Quantitative data were expressed as mean and standard deviation (SD), and comparison was made by the Student's t-test. Qualitative data were expressed as frequency and percentage, and comparison was carried by the Chi-square test. p-value ≤0.05 was considered as statistically significant.

## RESULTS

The hypertensive and the control groups were indifferent to age, gender, smoking status, BMI, serum creatinine, total cholesterol, and LDL-Cholesterol levels. Systolic BP, diastolic BP, and FPG were higher in the hypertensive group. Estimated GFR, HDL-Cholesterol, and TG levels were higher in the healthy control group (Table 1). The mean uric acid level of the hypertensive patients was found significantly higher compared to normotensive subjects; the frequency of hyperuricemia was also higher in the hypertensive group (Table 2). Again, serum uric acid level was significantly higher those with stage II HTN compared to those with stage I HTN (6.46±0.83 vs. 5.72±0.78 mg/dL, p<0.001) (not shown in Table).

**Table 1: Characteristics of the study participants.**

Variables	Subgroups	HTN group (n=155) mean±SD or n (%)	Control group (n=100) mean±SD or n (%)	P
Age (years)		50.63±6.62	48.96±6.82	0.126
Gender	Male	91 (58.7%)	56 (56%)	0.736
	Female	64 (41.3%)	44 (44%)	
Smoking status	Smoker	33 (21.3%)	16 (16%)	0.416
	Non-smoker	122 (78.7%)	84 (84%)	
BMI (kg/m <sup>2</sup> )		23.49±1.14	23.34±1.04	0.203
SBP (mmHg)		155.58±8.33	120.20±6.70	<0.001
DBP (mmHg)		94.13±5.26	77.40±5.55	<0.001
S. creatinine (mg/dL)		0.86±0.12	0.84±0.09	0.175
eGFR (mL/min/1.73m <sup>2</sup> )		87.79±8.1	95.98±9.5	<0.001
FPG (mmol/L)		96.45±12.19	92.12±12.38	0.031
Total Cholesterol (mg/dL)		174.55±21.58	176.98±13.98	0.456
LDL-Cholesterol (mg/dL)		101.60±11.09	100.51±6.97	0.514
HDL-Cholesterol (mg/dL)		41.38±7.87	43.97±4.08	0.027
Triglyceride (mg/dL)		149.47±35.30	169.43±32.59	<0.001

BMI= Body mass index; SBP= Systolic blood pressure; DBP= Diastolic blood pressure; eGFR= Estimated glomerular filtration rate; FPG= Fasting plasma glucose, p-value by Student's t-test or Chi-square test as applicable

**Table 2: Serum uric acid in the study participants.**

Variables	HTN group (n=155) mean±SD or n (%)	Control group (n=100) mean±SD or n (%)	P
S. uric acid (mg/dL)	6.10±0.88	5.38±0.54	<0.001
Hyperuricemia	46 (29.7%)	6 (6%)	<0.001

p-value by Student's t-test or Chi-square test as applicable

**Table 3: Correlation of serum uric acid level with other variables.**

Parameters	Hypertensive subjects (n=155)		Normotensive subjects (n=100)	
	r	p	r	p
Age (year)	0.027	0.738	0.271	0.057
SBP (mmHg)	0.493	<0.001	0.414	0.003
DBP (mmHg)	0.186	0.021	0.238	0.096
BMI (kg/m <sup>2</sup> )	0.123	0.126	-0.532	<0.001
eGFR (mL/min/1.73m <sup>2</sup> )	0.036	0.655	0.200	0.163

by Pearson's correlation test

The correlations of serum uric acid level with other variables are shown in Table 3. In hypertensive patients, serum uric acid level showed significant positive correlations with systolic and diastolic blood pressure. In the control group, a significant positive correlation of serum uric acid level with systolic blood pressure was observed though uric acid and diastolic blood pressure did not show significant correlations; uric acid showed a significant negative correlation with BMI.

**DISCUSSION**

The current study conducted in the medicine OPD of a tertiary hospital of Bangladesh demonstrated a higher frequency of hyperuricemia among patients with essential

hypertension in comparison to the normotensive controls; the hypertensive subjects also had higher serum uric acid than the controls. Also, the patients with stage II HTN had higher serum uric acid than those with stage I HTN. The uric acid level was found to have significant positive correlations with both systolic and diastolic BP in the hypertensive patients.

The involvement of serum uric acid as an independent risk factor for cardiovascular disease is already known.<sup>20</sup> In recent years, uric acid levels have become a novel topic of research due to the increase in the prevalence of hyperuricemia cases and the accumulated evidence that hyperuricemia increases the risk for hypertension onset and lack of optimal blood pressure control.<sup>10-14,21</sup> The

plausible mechanism for the development of hypertension in hyperuricemia includes: (a) uric acid-induced activation of the renin-angiotensin system and action on glomerular apparatus; (b) increased insulin resistance and hyperinsulinemia, causing decreased excretion of uric acid, sodium, potassium from renal tubules; and (c) uric acid action in the proliferation of vascular smooth muscle; endothelial dysfunction with decrease nitric acid production.<sup>22-28</sup> However, there are numerous confounding factors including metabolic syndrome, diabetes mellitus, chronic kidney disease, obesity, alcohol consumption, salt intake, fluid volume status, etc. in the association of hyperuricemia and hypertension.<sup>7</sup>

Worldwide, many researchers have found a higher frequency of hyperuricemia in subjects with essential HTN than the normotensive subjects though a wide variation in the reported frequencies observed. In Australia, Bauer et al. reported 31% of subjects with essential HTN to have hyperuricemia; the frequency was 55.4% in Egypt, 37.4% in Pakistan, 28.8% in Nepal, and two studies from India reported 37% and 46% hypertensive subjects to have hyperuricemia.<sup>4-9</sup> In a previous study in Bangladesh, the observed prevalence of hyperuricemia in hypertensive and normotensive subjects were 25.4% and 9.8%, respectively.<sup>29</sup> In the present study, hyperuricemia was observed in 29.7% of hypertensive patients and 6.0% of normotensive controls, which was similar to most of the studies done in this part of the world. The mean serum uric acid level was higher in the hypertensive patients than the normotensive controls in the present study. Previous researchers had similar observations.<sup>4-9,29</sup>

Among the hypertensive subjects of the current study, those with stage II HTN had significantly higher uric acid than those with stage I HTN. The higher uric acid levels with higher stages of HTN were also described by Neki et al, and Meti et al.<sup>8,19</sup> Moreover, both the systolic and diastolic BP had significant positive correlations with serum uric acid levels in the hypertensive subjects of this study. Poudel et al, and Shah et al, had similar observations.<sup>7,9</sup> In contrast to the findings of Poudel et al, authors observed no significant correlation between serum uric acid level and age in hypertensive subjects.<sup>7</sup>

Limitations of the study this was a cross-sectional study, so any inference on the causal relationship between uric acid and hypertension was beyond the limit of the study. Blood pressure was only measured during one visit, so some might be misclassified owing to the white coat effect. The study population was drawn from outpatients of a hospital that may not form a representative sample of the general population. A small sample size also limits the power of analysis.

## CONCLUSION

Patients with essential hypertension had higher serum uric acid compared to normotensive controls; patients

with stage II HTN had higher uric acid than those with stage I HTN in this study. Serum uric acid level showed positive correlations with systolic and diastolic BP in the hypertensive subjects. Large scale longitudinal studies are needed to establish the role of hyperuricemia in the pathogenesis of essential hypertension.

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