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Original Research

To evaluate the serum uric acid in hypertensive patients with reference to age and BMI

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ABSTRACT:
Aim: To evaluate the serum uric acid in hypertensive patients with reference to age and BMI. **Methods:** This cross-sectional study was conducted in the Department of medicine, Government District Hospital , Sri ganganagar, Rajasthan. 50 patients with hypertension and 50 normotensive age and sex-matched otherwise healthy subjects were included in this study. 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. 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 Cockroft-Gault formula. Hyperuricemia was defined if SUA levels above 7.0 mg/dL in males and above 6.0 mg/dL in females. **Results:** The frequency of hyperuricemia was higher in the hypertensive group in comparison to the normotensive control group (28% vs. 6%, $p<0.001$). Serum uric acid level was higher in the hypertensive subjects than the controls (6.30±0.88 vs. 5.58±0.54 mg/dL, mean±SD, $p<0.001$). In the hypertensive group, subjects with stage II HTN had higher serum uric acid than those with stage I HTN (6.66±0.83 vs. 5.92±0.78 mg/dL, mean±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. **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.
Keywords: hyperuricemia, serum uric, normotensive, hypertensive

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INTRODUCTION

Essential hypertension is a rise in blood pressure with overall prevalence of 26.4% with undetermined cause that includes 90% of all hypertensive cases and is a highly important public health challenge in its burden of morbidity and mortality because of its complications, including cardiovascular, cerebrovascular, and renal diseases. In (90%) of individuals, its etiology cannot be determined; therefore, the essential hypertension term is employed.[1] It is (80– 95%) more common than secondary hypertension (5–20%) which is due to other aetiologies that raises blood pressure.[2] Uric acid (UA) is the end product of purine metabolism in humans, and nearly 70% of UA are eliminated by the renal system, while the rest is eliminated by the intestines.[3] Uric acid acts as an antioxidant (> 50% of the antioxidant capacity of the blood) by exerting a strong reducing effect together with bilirubin and ascorbic acid vitamin C) during the early stage.[4] When uric acid levels are too low and in its latter stage, the reducing effect also decreases. As a result, reactive oxygen products cannot be scavenged and neutralized which finally leads to the development of oxidative stress.[5-8] There is convincing evidence from animal studies that elevated uric acid has a detrimental effect on blood pressure (BP) and renal function. Administration of uric acid causes a rise in arterial BP in rat models[9] and sustained elevation of uric acid results in salt-sensitive hypertension and irreversible

renal damage characterized by both arteriolar and glomerular damage.[10] Furthermore, the xanthine oxidase inhibitor allopurinol lowers BP in adolescents with hypertension and hyperuricemia[11] and both allopurinol and the uricosuric drug probenecid lower BP in obese adolescents with prehypertension.[12] A recent meta-analysis found that allopurinol lowers BP by 3/2 mm Hg in adults,[13] although this has never been tested in a specifically designed prospective study. Despite these results, there is still debate about a causal role for uric acid and the potential cardiovascular benefits of allopurinol may reflect either uric acid reduction or other mechanisms, such as superoxide anion reduction.[14]

MATERIAL AND METHODS

This cross-sectional study was conducted in the Department of medicine, Government District Hospital, Sri ganganagar, Rajasthan. 50 patients with hypertension and 50 normotensive age and sex-matched otherwise healthy subjects were included in this study.

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.[15] Patients with diabetes, ischemic heart disease, congestive cardiac failure, gout, overweight/obesity (BMI >25 kg/m2), 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.

METHODOLOGY

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.[15]

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. 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.[16] 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 Cockroft-Gault formula.[17] Hyperuricemia was defined if SUA levels above 7.0 mg/dL in males and above 6.0 mg/dL in females.[18]

STATISTICAL ANALYSIS

Data were processed and analyzed using SPSS (Statistical Package for Social Sciences) Version 23.0. 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). The frequency of hyperuricemia was higher in the hypertensive group in comparison to the normotensive control group (28% vs. 6%, p<0.001). Serum uric acid level was higher in the hypertensive subjects than the controls (6.30±0.88 vs. 5.58±0.54 mg/dL, mean±SD, p<0.001). In the hypertensive group, subjects with stage II HTN had higher serum uric acid than those with stage I HTN (6.66±0.83 vs. 5.92±0.78 mg/dL, mean±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.

Table 1: Characteristics of the study participants

Variables	Subgroups	HTN group (n=50) mean±SD or n (%)	Control group (n=50) mean±SD or n (%)	p
Age (years)		51.73±5.72	49.86±5.92	0.14
	Male	30 (60%)	28(56%)	
Gender	Female	20 (40%)	22 (44%)	0.77
	Smoker	10 (20%)	8 (16%)	
Smoking status	Non-smoker	40 (80%)	42 (84%)	0.42
BMI (kg/m2)		24.59±1.24	24.44±1.14	0.23
SBP (mmHg)		156.68±7.43	121.30±5.80	<0.001
DBP (mmHg)		95.23±4.36	78.50±4.65	<0.001
S. creatinine (mg/dL)		0.97±0.22	0.95±0.19	0.19
eGFR (mL/min/1.73m2)		88.89±7.2	96.88±8.6	<0.001
FPG (mmol/L)		97.55±11.29	93.22±11.48	0.04
Total Cholesterol (mg/dL)		176.55±21.58	178.98±13.98	0.42
LDL-Cholesterol (mg/dL)		103.60±11.09	102.51±6.97	0.57
HDL-Cholesterol (mg/dL)		42.48±6.97	44.87±3.18	0.03
Triglyceride (mg/dL)		151.47±35.30	171.43±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=50) mean±SD or n (%)	Control group (n=50) mean±SD or n (%)	p
S. uric acid (mg/dL)	6.30±0.88	5.58±0.54	<0.001
Hyperuricemia	14 (28%)	3 (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=50)		Normotensive subjects (n=50)	
	r	p	r	p
Age (year)	0.03	0.74	0.28	0.04
SBP (mmHg)	0.50	<0.001	0.42	0.003
DBP (mmHg)	0.19	0.03	0.24	0.07
BMI (kg/m2)	0.13	0.13	-0.54	<0.001
eGFR (mL/min/1.73m2)	0.04	0.66	0.21	0.11

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

Hypertension and other cardiovascular complications have played great attention as a potential clinical condition predicting the development of hyperuricemia in metabolic syndrome patients and in turn compromising the management of the disease itself and its progression. 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.[19] 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.[20] 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.[21-27] 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.[28]

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.[29-31] In Bangladesh study, the observed prevalence of hyperuricemia in hypertensive and normotensive subjects were 25.4% and 9.8%, respectively.[32] In the present study, hyperuricemia was observed in 28% of hypertensive patients and 6% of normotensive controls, which was similar to most of the studies dine 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.[32]

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.[33,18] 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.[28] In contrast to the findings of Poudel et al, authors observed no significant correlation between serum uric acid level and age in hypertensive subjects.[28]

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.

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