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ORIGINAL ARTICLE

To investigate the levels of serum uric acid in individuals with essential hypertension, with a particular focus on the impact of age and body mass index

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ABSTRACT:

Aim: This study aims to investigate the levels of serum uric acid in individuals with essential hypertension, with a particular focus on the impact of age and body mass index. **Methods:** This study comprised a sample of 100 individuals diagnosed with hypertension and 100 age and sex-matched healthy participants with normal blood pressure. The uricase method was employed to measure the serum uric acid level, while the Jaffe method was utilized to measure the serum creatinine. Additionally, the enzymatic method was employed to measure the triglyceride, total cholesterol, and HDL cholesterol. The Friedewald equation was utilized to compute the LDL-cholesterol. The glucose oxidase method was employed to measure glucose levels in venous blood samples that were collected in EDTA tubes. The Cockroft-Gault formula was utilized to compute the estimated glomerular filtration rate (eGFR). The condition of hyperuricemia is characterized by serum uric acid (SUA) levels that exceed 7.0 mg/dL in males and 6.0 mg/dL in females. **Results:** The prevalence of hyperuricemia was found to be significantly greater in the hypertensive cohort as compared to the normotensive control cohort (31% vs. 6%, $p<0.001$). The results indicate that the hypertensive individuals had a significantly elevated serum uric acid level compared to the control group (mean±SD: 6.22±0.80 vs. 5.50±0.46 mg/dL, $p<0.001$). The results indicate that individuals with stage II hypertension exhibited elevated levels of serum uric acid in comparison to those with stage I hypertension (mean±SD: 6.55±0.72 vs. 5.81±0.67 mg/dL, $p<0.001$). The results indicate that within the hypertensive group, there were significant positive correlations observed between uric acid levels and both systolic and diastolic blood pressure. However, in the control group, a positive correlation between uric acid levels and systolic blood pressure was observed exclusively. **Conclusion:** The study found that individuals diagnosed with essential hypertension exhibited elevated levels of serum uric acid in comparison to normotensive controls. Furthermore, patients diagnosed with stage II hypertension demonstrated higher levels of uric acid in comparison to those diagnosed with stage I hypertension. The study found that there was a significant positive correlation between the serum uric acid level and both systolic and diastolic blood pressure in individuals with hypertension.

Keywords: hyperuricemia, serum uric, normotensive, hypertensive

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INTRODUCTION

Numerous epidemiological studies have established a correlation between uric acid and the onset of hypertension, as well as with occurrences of cardiovascular events. Several studies have indicated a disparity between the sexes in terms of cardiovascular events, wherein the unfavorable cardiovascular correlation of uric acid is observed solely in females.(6–8) Animal studies have provided compelling evidence that heightened levels of uric acid have an adverse impact on both blood pressure and renal function. The introduction of uric acid to rat models has been observed to lead to an increase in arterial blood pressure. Furthermore, prolonged exposure to elevated levels of uric acid has been linked to the development of hypertension that is sensitive to salt and irreversible damage to the kidneys, which is characterized by damage to both the arterioles and glomeruli.(9-10) In addition, it has been observed that the xanthine oxidase inhibitor, allopurinol, exhibits a reduction in blood pressure among adolescents who suffer from hypertension and hyperuricemia. Moreover, both allopurinol and the uricosuric drug, probenecid, have been found to lower blood pressure in obese adolescents who have prehypertension.(11-12) According to a recent meta-analysis, the administration of allopurinol in adults has been associated with a reduction of 3/2 mm Hg in blood pressure. However, this effect has not been evaluated in a prospective study specifically designed for this purpose. Notwithstanding these findings, there remains a contentious issue regarding the causative function of uric acid, and the cardiovascular advantages of allopurinol may be attributed to either the reduction of uric acid or alternate mechanisms, such as the reduction of superoxide anion.(13-14)

METHODS

The study population consisted of patients with essential hypertension who visited the Medicine OPD

of the hospital during the designated study period. This study comprised a sample of 100 individuals diagnosed with hypertension and 100 age and sex-matched healthy individuals with normal blood pressure, who were otherwise healthy.

The hypertensive group consisted of individuals of both sexes who were over 18 years of age and had essential hypertension, either newly diagnosed or receiving treatment, as per the criteria outlined in the seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7).Exclusion criteria for this study included 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. The sampling method employed in this study was consecutive convenient sampling.

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.[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.

BIOCHEMICAL ASSESSMENTS

The study participants underwent an overnight fast of 8-12 hours prior to the collection of venous blood samples. The collected blood samples were used to measure various parameters including plasma glucose, serum creatinine, serum uric acid, and lipid profile. The biochemical assays were examined using a semi-automated analyzer. The uricase method was utilized to measure the serum uric acid level, while the Jaffe method was employed to measure serum creatinine. Enzymatic method was used to measure triglyceride, total cholesterol, and HDL cholesterol. The Friedewald equation was employed to determine the LDL-cholesterol levels.The glucose oxidase method was utilized to measure glucose levels in venous blood samples that were collected in EDTA tubes. The Cockroft-Gault formula was utilized to compute the estimated glomerular filtration rate (eGFR).Hyperuricemia was characterized as a condition where serum uric acid (SUA) levels exceeded 7.0 mg/dL in males and 6.0 mg/dL in females.(18)

STATISTICAL ANALYSIS

The data underwent processing and analysis through the utilization of SPSS (Statistical Package for Social Sciences) Version 25.0. The mean and standard deviation (SD) were utilized to express the quantitative data, and the Student's t-test was employed to make comparisons. The study utilized qualitative data, which were presented in terms of frequency and percentage. The Chi-square test was employed to conduct comparisons. A p-value of less than or equal to 0.05 was deemed to be statistically significant.

RESULTS

Both the hypertensive and control groups exhibited no significant differences with respect to age, gender, smoking status, BMI, serum creatinine, total cholesterol, and LDL-Cholesterol levels. The hypertensive group exhibited elevated levels of systolic blood pressure, diastolic blood pressure, and fasting plasma glucose. The healthy control group exhibited higher levels of Estimated Glomerular Filtration Rate (GFR), High-Density Lipoprotein (HDL) Cholesterol, and Triglycerides (TG), as presented in Table 1. The study revealed that the average uric acid level among hypertensive individuals was notably greater in comparison to normotensive individuals. Additionally, the incidence of hyperuricemia was more frequent in the hypertensive cohort, as indicated in Table 2. The prevalence of hyperuricemia was found to be significantly greater in the hypertensive cohort as compared to the normotensive control group (31% vs. 6%, $p<0.001$). The study findings indicate that the mean serum uric acid level was significantly elevated in the hypertensive group compared to the control group (6.22±0.80 vs. 5.50±0.46 mg/dL, mean±SD, $p<0.001$). Among the hypertensive cohort, individuals diagnosed with stage II hypertension exhibited elevated levels of serum uric acid in comparison to those with stage I hypertension (mean±SD: 6.55±0.72 vs. 5.81±0.67 mg/dL, respectively), with statistical significance ($p<0.001$). Significant positive correlations were observed between uric acid level and both systolic and diastolic blood pressure in the hypertensive group. However, in the control group, such correlation was observed between uric acid and systolic blood pressure only.

Table 1: Characteristics of the study participants.

Variables	Subgroups	HTN group	Control group	p
Age (years)		51.63±5.62	49.96±5.82	0.13
	Male	58	55(55%)	
Gender	Female	42	45 (45%)	0.74
	Smoker	22	15 (15%)	
Smoking status	Non-smoker	78	85 (85%)	0.42
BMI (kg/m2)		24.59±1.24	24.44±1.14	0.21
SBP (mmHg)		157.58±8.33	122.20±6.70	0.001
DBP (mmHg)		96.13±5.26	79.40±5.55	0.001
S. creatinine (mg/dL)		0.85±0.11	0.83±0.08	0.18
eGFR (mL/min/1.73m2)		89.79±8.1	97.98±9.5	0.001
FPG (mmol/L)		98.45±12.19	94.12±12.38	0.04
Total Cholesterol (mg/dL)		176.55±21.58	178.98±13.98	0.46
LDL-Cholesterol (mg/dL)		103.60±11.09	102.51±6.97	0.52
HDL-Cholesterol (mg/dL)		43.38±7.87	45.97±4.08	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	Control group	P value
S. uric acid (mg/dL)	6.22±0.80	5.50±0.46	0.001
Hyperuricemia	31	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=100)		Normotensive subjects (n=100)	
	r	p	r	p
Age (year)	0.01	0.72	0.26	0.05
SBP (mmHg)	0.48	0.001	0.40	0.002
DBP (mmHg)	0.17	0.01	0.22	0.08
BMI (kg/m2)	0.11	0.11	-0.52	0.001
eGFR (mL/min/1.73m2)	0.02	0.64	0.19	0.15

Table 3 displays the associations between serum uric acid level and other variables. The study revealed a noteworthy positive association between the levels of serum uric acid and both systolic and diastolic blood pressure in patients diagnosed with hypertension. The control group exhibited a noteworthy affirmative association between the level of serum uric acid and systolic blood pressure, while no significant correlations were observed between uric acid and diastolic blood pressure. Additionally, a significant inverse correlation was observed between uric acid and BMI.

DISCUSSION

The present investigation exhibited an elevated incidence of hyperuricemia in individuals with essential hypertension as opposed to normotensive individuals. Additionally, the hypertensive participants displayed increased levels of serum uric acid in comparison to the control group. Furthermore, it was observed that individuals diagnosed with stage II hypertension exhibited elevated levels of serum uric acid in comparison to those diagnosed with stage I hypertension. In hypertensive patients, there was a significant positive correlation observed between the uric acid level and both systolic and diastolic blood pressure.

The independent association of serum uric acid with cardiovascular disease has been established.In contemporary times, there has been a surge in research interest regarding uric acid levels, primarily due to the rising incidence of hyperuricemia cases. Additionally, there is a growing body of evidence that suggests a positive correlation between hyperuricemia and the onset of hypertension, as well as suboptimal blood pressure management. The potential pathogenesis of hypertension in hyperuricemia involves several mechanisms, including: (a) the activation of the renin-angiotensin system and its impact on the glomerular apparatus induced by uric acid; (b) the development of insulin resistance and hyperinsulinemia, which leads to reduced excretion of uric acid, sodium, and potassium from renal tubules; and (c) the involvement of uric acid in the proliferation of vascular smooth muscle and endothelial dysfunction, which results in decreased nitric acid production.(21-27) The association between hyperuricemia and hypertension is

complicated by various confounding factors such as metabolic syndrome, diabetes mellitus, chronic kidney disease, obesity, alcohol consumption, salt intake, and fluid volume status.(28)

Numerous studies conducted globally have reported a greater prevalence of hyperuricemia among individuals with essential hypertension in comparison to those who are normotensive. However, there exists a significant range in the documented frequencies. Bauer et al. conducted a study in Australia which found that 31% of individuals with essential hypertension had hyperuricemia. Similar studies conducted in Egypt, Pakistan, Nepal, and India reported frequencies of 55.4%, 37.4%, 28.8%, 37%, and 46% respectively, of hypertensive subjects with hyperuricemia.(29-31) According to a study conducted in Bangladesh, the prevalence of hyperuricemia was observed to be 25.4% and 9.8% among hypertensive and normotensive subjects, respectively.(32) The current investigation revealed that hyperuricemia was detected in 31% of individuals with hypertension and 6% of normotensive controls, consistent with the findings of previous studies conducted in this geographic region. The study findings indicate that the hypertensive patients had a higher mean serum uric acid level compared to the normotensive controls. Prior scholars have made comparable findings.(32)

The present study revealed that hypertensive individuals diagnosed with stage II hypertension exhibited a statistically significant elevation in uric acid levels in comparison to those diagnosed with stage I hypertension. Steele TH et al. (33) have also reported an association between elevated levels of uric acid and advanced stages of hypertension. Additionally, the present study found significant positive associations between serum uric acid levels and both systolic and diastolic blood pressure among hypertensive individuals.

CONCLUSION

The study found that individuals diagnosed with essential hypertension exhibited elevated levels of serum uric acid in comparison to normotensive controls. Furthermore, patients diagnosed with stage II hypertension demonstrated higher levels of uric acid in comparison to those diagnosed with stage I hypertension. The study found that there was a significant positive correlation between the serum uric acid level and both systolic and diastolic blood pressure in individuals with hypertension. To determine the involvement of hyperuricemia in the development of essential hypertension, it is imperative to conduct extensive longitudinal studies on a significant scale.

REFERENCE

1. Mellen PB, Bleyer AJ, Erlinger TP, Evans GW, Nieto FJ, Wagenknecht LE, Wofford MR, Herrington DM. Serum uric acid predicts incident hypertension in a biethnic cohort: the atherosclerosis risk in communities study. Hypertension. 2006;48:1037–1042.
2. Forman JP, Choi H, Curhan GC. Plasma uric acid level and risk for inci- dent hypertension among men. J Am Soc Nephrol. 2007;18:287–292.
3. Masuo K, Kawaguchi H, Mikami H, Ogihara T, Tuck ML. Serum uric acid and plasma norepinephrine concentrations predict subsequent weight gain and blood pressure elevation. Hypertension. 2003;42:474–480.
4. Sundström J, Sullivan L, D'Agostino RB, Levy D, Kannel WB, Vasan RS. Relations of serum uric acid to longitudinal blood pressure tracking and hypertension incidence. Hypertension. 2005;45:28–33.
5. Dawson J, Quinn T, Walters M. Uric acid reduction: a new paradigm in the management of cardiovascular risk? Curr Med Chem. 2007;14:1879–1886.
6. Bos MJ, Koudstaal PJ, Hofman A, Witteman JC, Breteler MM. Uric acid is a risk factor for myocardial infarction and stroke: the Rotterdam study. Stroke. 2006;37:1503–1507.
7. Culleton BF, Larson MG, Kannel WB, Levy D. Serum uric acid and risk for cardiovascular disease and death: the Framingham Heart Study. Ann Intern Med. 1999;131:7–13.
8. Tuttle KR, Short RA, Johnson RJ. Sex differences in uric acid and risk factors for coronary artery disease. Am J Cardiol. 2001;87:1411–1414.
9. Mazzali M, Hughes J, Kim YG, Jefferson JA, Kang DH, Gordon KL, Lan HY, Kivlighn S, Johnson RJ. Elevated uric acid increases blood pres- sure in the rat by a novel crystal-independent mechanism. Hypertension. 2001;38:1101–1106.
10. Mazzali M, Kanellis J, Han L, Feng L, Xia YY, Chen Q, Kang DH, Gordon KL, Watanabe S, Nakagawa T, Lan HY, Johnson RJ. Hyperuricemia induces a primary renal arteriolopathy in rats by a blood pressure-inde- pendent mechanism. Am J Physiol Renal Physiol. 2002;282:F991–F997.
11. Feig DI, Soletsky B, Johnson RJ. Effect of allopurinol on blood pressure of adolescents with newly diagnosed essential hypertension: a random- ized trial. JAMA. 2008;300:924–932.
12. Soletsky B, Feig DI. Uric acid reduction rectifies prehypertension in obese adolescents. Hypertension. 2012;60:1148–1156.
13. Agarwal, V, Hans, N, Messerli, FH. Effect of Allopurinol on Blood Pressure: A Systematic Review and Meta-Analysis. J Clin Hypertension. Published online 20 August 2012.
14. George J, Carr E, Davies J, Belch JJ, Struthers A. High-dose allopurinol improves endothelial function by profoundly reducing vascular oxidative stress and not by lowering uric acid. Circulation. 2006;114:2508–2516
15. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Jones DW et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42(6):1206-52.
16. Bachorik PS, Ross JW. National cholesterol education program recommendations for measurement of low-density lipoprotein cholesterol: Executive summary. Clinical Chemistry. 1995;41(10):1414-20.
17. Kemperman FA, Krediet RT, Arisz L. Formula-derived prediction of the glomerular filtration rate from

plasma creatinine concentration. Nephron. 2002;91(4):547-58.
18. Schoenfeld MR. Serum cholesterol-uric acid correlation. Metabolism. 1963;12:714.
19. Verdecchia P, Schillaci G, Reboldi G, Santeusanio F, Porcellati C, Brunetti P. Relation between serum uric acid and risk of cardiovascular disease in essential hypertension. The PIUMA study. Hypertension. 2000;36(6):1072-8
20. Kim YH, Suh YD, Son SP, Shim YW, Shin YW, Shin YK. Observation of the serum uric acid in essential hypertension. Korean J Intern Med. 1986 Jan;1(1):14-20. doi: 10.3904/kjim.1986.1.1.14
21. Drum DE, Goldman PA, Jankowski CB. Elevation of serum uric acid as a clue to alcohol abuse. Arch Int Med. 1981;141:477.
22. Zhou X, Matavelli L, Frohlich ED. Uric acid: its relationship to renal hemodynamics and the renal renin-angiotensin system. Curr Hypertens Rep. 2006;8(2):120-4.
23. Babinska K, Kovacs L, Janko V, Dallos T, Feber J. Association between obesity and the severity of ambulatory hypertension in children and adolescents. J Am Soc Hypertens. 2012;6(5):356- 63.
24. Yoo TW, Sung KC, Shin HS, Kim BJ, Kim BS, Kang JH, et al. Relationship between serum uric acid concentration and insulin resistance and metabolic syndrome. Circ J. 2005;69(8):928-33.
25. Corry DB, Eslami P, Yamamoto K, Nyby MD, Makino H, Tuck ML. Uric acid stimulates vascular smooth muscle cell proliferation and oxidative stress via the vascular renin-angiotensin system. J Hypertens. 2008;26(2):269-75.
26. Higashi Y, Kihara Y, Noma K. Endothelial dysfunction and hypertension in aging. Hypertens Res. 2012;35(11):1039-47.
27. Kang DH, Park SK, Lee IK, Johnson RJ. Uric acid induced C-reactive protein expression: implication on cell proliferation and nitric oxide production of human vascular cells. J Am Soc Nephrol. 2005;16(12):3553-62
28. Drum DE, Goldman PA, Jankowski CB. Elevation of serum uric acid as a clue to alcohol abuse. Arch Int Med. 1981;141:477
29. Bauer RGEG, Ewan CE, Neale FC. Serum Uric Acid in Normal and Hypertensive Australian Subjects: From a Continuing Epidemiological Survey on Hypertension Commenced in 1955. Internal Med J. 1972;2(4):351-6.
30. Fessel WJ, Siegelaub AB, Johnson ES. Correlates and consequences of asymptomatic hyperuricemia. Arch Int Med. 1973;132:44.
31. Ahmed N, Anwar W, Waqas H. Obesity, hyperlipidemia and hyperuricemia in young and old hypertensive patients. J Ayub Med Coll Abbottabad. 2009;21(4):53-6
32. Kashem MA, Hossain MZ, Ayaz KM, Alam MB, Khan MH, Alam AB, et al. Relation of serum uric acid level and essential hypertension among patients without metabolic syndrome. J Dhaka Med Coll. 2011;20(1):5-8.
33. Steele TH. Asymptomatic hyperuricemia pathogenic or innocent bystander? Arch Int Med. 1979;139:24–25