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Original Research Article

Serum uric acid levels in essential hypertension and its correlation with the severity of hypertension

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ABSTRACT

Background: Serum uric acid has been closely linked and considered as an independent risk factor for development of hypertension. This study was carried out to assess the serum uric acid levels in essential hypertension and its correlation with the severity and known duration of hypertension.
Methods: The present observational case control study was conducted between November 2019 to February 2020 on total 100 out patients (30-65 years) of which 50 known cases of essential hypertension irrespective of treatment status and were graded into different stages of hypertension as per Joint National Committee VII (JNC VII) guidelines. Rest 50 patients who were age- sex matched and without any co-morbidity were included as control. Relevant clinical and laboratory data were recorded using proforma. Statistical analysis was done using Statistical package for social software (SPSS) software.
Results: Mean systolic/diastolic blood pressure (BP) was found significantly higher in cases 168/102 mmHg compare to control 114/74 mmHg. Among cases maximum patients were found in stage 2 hypertension which has significant difference in mean systolic/diastolic BP (186/112 mmHg, $p<0.001$) compare with stage 1 (146/94 mmHg) and isolated hypertensive patients (148/85 mmHg). Serum uric acid levels were significantly higher in stage 2 than other two hypertensive stages among cases and also compare to controls. Patients with >5 years of hypertension also has significant high serum uric acid level than <5 years of hypertension.
Conclusions: Serum uric acid can be used probably as an early biochemical marker to determine the severity of hypertension as stage 2 hypertensive had more elevation in serum uric acid levels as compared to other hypertensive patients.

Keywords: Hypertension, Hyperuricemia, JNC VII, Uric acid

INTRODUCTION

Hypertension (HTN) is a sustained elevation of systemic arterial pressure. Elevated blood pressure (BP) is defined as systolic blood pressure >l40 mmHg and/or diastolic blood pressure >90 mmHg. Hypertension is the third prominent killer disease in the world and is responsible for 1 in every 8 deaths. The prevalence of hypertension grows sophisticated with aging, resulting in higher morbidity and mortality through various events such as heart failure, myocardial infarction, stroke, and renal failure.[1]

Hypertension is a major public health problem in India and other countries as well. Lifetime risk of emerging hypertension is approximately 90% for male and female who are normotensive at 55-65 years old and lived to the age of 80-85 years.[2]

Hyperuricemia is defined as the serum uric acid (UA) >7.0 mg/dl in adult males, >6.0 mg/dl in adult females.[3] Study reveals that hyperuricemia decreases renal blood circulation apparently a reflection of nephrosclerosis. Compare to normotensive there is 5 times higher chance of occurring hypertensive in 25-50% of individuals having hyperuricemia with untreated primary hypertension.[4]

The mechanism(s) by which UA may endanger organ injury is still incompletely understood, but there is large evidence that endothelial dysfunction is a fundamental mechanism whereby this substance may affect cardiovascular and renal function and structure.[5]

The reasonable mechanism for the development of hypertension in hyperuricemia includes: (a) uric acid induced activation of renin-angiotensin system and action on glomerular apparatus (b) increased insulin resistance and hyperinsulinaemia, causing decrease in excretion of uric acid, sodium, potassium from renal tubules and (c) uric acid action in proliferation of vascular smooth muscle, endothelial dysfunction with decrease nitric acid production.[6-8] In order to know the correlation between hypertension and serum uric acid, present study has objectives to assess the serum uric acid levels in all stages of hypertension and its association with the duration of hypertension.

METHODS

The present study was an observational and case control study which was conducted conducted between November 2019 to February 2020 in GS Medical College and Hospital, Hapur. The study group comprised of hypertensive patients visiting the out-patient medicine department or admitted in the hospital. Age and sex marked controls were taken into study. A total of 100 patients were taken into the study with an equal proportion of cases and controls of 1:1. 50 patients were taken as cases who were known cases of essential hypertension irrespective of treatment status and were graded into different stages of hypertension as per JNC VII guidelines.[9] Rest 50 patients were taken as control who were age and sex matched without any co-morbidity. The protocol was reviewed and approved by institute ethics committee. The patients were included only after giving written informed consent after full explanation of nature and purpose of the study. Age between 30-65 years and known cases of essential hypertension were selected whether on or off treatment. The diagnosis of essential hypertension was established and the patients were categorized into various stages of hypertension according to JNC-VII report.

Excluded those patients who were beyond the age of <30 or >65 years, having history of secondary hypertension, diabetes, hypothyroidism, hyperparathyroidism, pregnancy induced hypertension, ischemic heart disease, congestive cardiac failure, obesity (body weight exceeding 25% of ideal weight), alcohol abuse, renal insufficiency, glomerulonephritis, pyelonephritis, hereditary nephropathy, gout, lymphoproliferative or myeloproliferative disorders etc. Patients on management with drugs altering uric acid levels such as thiazides, loop diuretics, pyrazinamide, allopurinol, levodopa, ethambutol, cytotoxic drugs etc. were also excluded from this study.

The demographic profile of all the patients was taken. Information was obtained from detailed history with special emphasis on duration and treatment of hypertension, any other coexistence disease. Vital signs, complete general physical examination including height and weight and systemic examination was recorded. Body mass index (BMI) was calculated manually using formulae weight (kg)/(height(meter))^2. Relevant laboratory investigations (blood fasting sugar, urea, creatinine, liver function test, lipid profile) were also recorded from the medical record.

Essential hypertension was diagnosed in the absence of an identifiable cause. The patients were categorized into the various stages of hypertension as per the JNC-VII report. Blood pressure was noted as the average of 2 or more readings at each of the 2 or more visits or on alternate days in admitted patients.

Hyperuricemia was defined as the serum uric acid >7.0 mg/dl in adult males, >6.0 mg/dl in adult females. Blood samples were taken in the early morning venous blood sample after the patient is kept fasting for 12 hours. Serum uric acid was measured by photometric method in clinical chemistry Medsource C Sense 100 automatic analyzer.

Statistical analysis

All the data obtained from the patients of the study group was put in Microsoft excel sheet. Data was summarized and analyzed using appropriate statistical techniques via Statistical package for social sciences (SPSS) software. Data were expressed in mean±standard deviation (SD). Parametric data were analyzed using student 't' test and analysis of variance. P value less than 0.05 were considered significant.

RESULTS

In this case control study, cases and controls were in the ratio of 1:1. Cases versus controls were closely matched as per their age, mean age in cases was (51.12) years whereas in controls it was (49.32) years (Table 1).

Table 1: Age distribution in two groups.

Age	Case (n=50)	Control (n=50)	P value
Age (years) (Mean±SD)	51.12±9.74	49.32±8.33	>0.05

Out of 50 cases, 24 (48%) were male patients and 26 (52%) were female patients. Among the controls, 27 (54%) were males whereas 23 (46%) were female patients. Gender distribution was equal among groups. Mean BMI in cases was 23.32 kg/m^2 whereas it was 23.47 kg/m^2 in case of controls which was comparable among the two groups.

Overall mean systolic BP in cases was 168 mmHg and mean diastolic BP was 102 mmHg. Among controls overall mean systolic BP was 114 mmHg and mean diastolic BP was 74 mmHg. Cases were further grouped into stages according to JNC VII criteria of BP staging.

Overall, 16 (32.0%) patients were grouped in stage 1. 27 (54.0%) patients in stage 2 and 7 (14.0%) patients in isolated systolic hypertension (ISH). Maximum patients were in stage 2 among both males (58.33%) and females (50.00%) (Table 2).

Table 2: Gender distribution in the three hypertensive stage as per JNC VII criteria.[9]

Stages of hypertension	Number of patients (%)		
	Males (n=24)	Females (n=26)	Total (n=50)
Stage 1	7 (29.17)	9 (34.62)	16 (32.0)
Stage 2	14 (58.33)	13 (50.0)	27 (54.0)
Isolated systolic	3 (12.50)	4 (15.38)	7 (14.0)

Mean systolic and diastolic blood pressure in stage 1 was 146.44 mmHg and 94.81 mmHg. In stage 2 it was 186.30 mmHg and 112.22 mmHg respectively. In ISH systolic BP was 148.57 mmHg and diastolic BP was 85.57 mmHg (Table 3).

Table 3: Mean blood pressure comparison between three hypertensive stage as per JNC VII criteria.[9]

Stages of hypertension	Mean±Standard Deviation	
	Systolic BP	Diastolic BP
Stage 1	146.44±6.20	94.81±3.10
Stage 2	186.30±11.49	112.22±5.06
Isolated systolic	148.57±11.07	85.57±2.88
P value	<0.0001	<0.0001

Among cases the range of serum uric acid level in males was 1.80-11.50 with mean value of 7.22 whereas in females range of serum uric acid level was 1.29-10.80 with mean value of 7.06. Overall mean value of cases was 7.14. Among controls the range of serum uric acid level in males was 2.30-5.20 with mean value of 4.47 whereas in females range of serum uric acid level was 1.60-6.20 with mean value of 4.11. Overall range in levels of serum uric acid in controls was 1.60-6.20 with a mean value of 4.31 (Table 4).

Overall mean serum uric acid levels in stage 1 hypertension was 6.45 mg/dl, in stage 2 it was 7.79 mg/dl and in ISH it was 6.19 mg/dl. Thus, the patients with higher value of blood pressure have higher levels of serum uric acid levels with stage 2 HTN having higher levels of uric acid than stage 1 HTN (Table 5).

Table 4: Gender based comparison of Serum uric acid level among cases and control group.

Groups	Cases		Control		P value
	Range	Mean±SD	Range	Mean±SD	
Males	1.80-11.50	7.22±2.55	2.30-5.20	4.47±0.76	<0.0001
Females	1.29-10.80	7.06±2.34	1.60-6.20	4.11±1.09	<0.0001
Total	1.29-11.50	7.14±2.42	1.60-6.20	4.31±0.94	<0.0001

Table 5: Comparison of mean serum uric acid level among three hypertensive stage as per JNC VII criteria.[9]

Stages of hypertension	Mean±Standard deviation		
	Males (n=24)	Females (n=26)	Total (n=50)
Stage 1	6.64±3.73	6.30±2.74	6.45±3.10
Stage 2	7.77±1.96	7.81±1.80	7.79±1.85
Isolated systolic	6.00±1.50	6.33±2.79	6.19±2.16
p value	0.445	0.272	0.113

Table 6: Comparison of mean serum uric acid level with duration of hypertension.

Stages of hypertension	Number of patients (%)		P value
	<5 years (n=10)	>5 years (n=40)	
Stage 1	6.32±3.97	6.51±2.84	0.862
Stage 2	6.57±2.02	7.94±1.81	0.042
Isolated systolic	5.35±1.20	6.52±2.48	0.156

Out of 50 cases, 10 patients had HTN of less than 5 years duration out of which 5 were included in stage 1, 3 in stage 2, and 2 in ISH. Remaining 40 patients had HTN of greater than 5 years duration, out of which 11 were included in stage 1, 24 in stage 2 and 5 in ISH.

Among patients with less than 5 years of duration of HTN, serum uric acid levels in stage 1 were 6.32 mg/dl, in stage 2 it was 6.57 mg/dl and in ISH the levels were 5.35 mg/dl. Among patients with greater than 5 years of duration of HTN, serum uric acid levels in stage 1 were 6.51 mg/dl, in stage 2 it was 7.94 mg/dl and in ISH the levels were 6.52 mg/dl.

Thus, the patients with more duration of HTN have higher levels of serum uric acid.

Levels of uric acid correlate with the duration and severity of blood pressure with stage 2 HTN having higher levels of uric acid than stage 1 (Table 6).

DISCUSSION

Hyperuricemia is commonly associated with hypertension. Serum uric acid has been closely linked to the development of hypertension and that it might be a marker of susceptibility or an intermediate step in the pathway leading to hypertension. Present study was carried out to assess the serum uric acid levels in essential hypertension and its correlation with the severity and known duration of hypertension.

In our study, mean age in cases was 51 years whereas in controls it was 49 years. Among the cases, 48% were male patients and 52% were female patients. Our study is closely matching as per age and gender distribution to the study of Reddy et al and Poudel et al.10,11 Mean age of our study patients was also similar to the study conducted by Eisen et al and Grayson et al.[12,13]

In our study, mean serum uric acid levels in cases was 7.14 mg/dl. Study conducted by Razak et al found the mean serum uric acid value of 8.03 mg/dl which was higher than our study. This difference is mainly due to majority of patients in their study were non-vegetarian by dietary habits while our state has mixed population who are both vegetarian and non-vegetarian by diet.[14] Study done by Vishnu et al on Kerala population found the serum uric acid levels lower than our study, this difference may be due to mainly non vegetarian and pulse diet habits in our community while south Indians are mostly vegetarian by diet.[15]

In our study, cases were further grouped into categories as per blood pressure according to JNC VII criteria of BP staging. Mean systolic blood pressures recorded in stage 1 hypertension, stage 2 hypertension and the isolated systolic hypertension in our study were in accordance with study of Vishnu et al and Ankit et al.[15,16] The patients with higher value of uric acid levels have higher blood pressure with stage 2 HTN having higher levels of uric acid than stage 1 HTN. The results were similar to the study done by Tykarski et al.[17] The patients with more known duration of HTN had higher levels of serum uric acid as in the studies conducted by Neki et al found significant increase in serum UA levels in patients with increased known duration of hypertension.[18]

It has been recently suggested that since uric acid may play a role in the formation of free radicals and oxidative stress which increase the risk of hypertension in subjects with raised serum uric acid levels. Besides, the longer duration and severity of hypertension lead to renal dysfunction in the form of nephrosclerosis leading to higher levels of serum uric acid.[19] Therefore increased uric acid levels could lead to increase in HTN and HTN in long term may lead to increased uric acid levels by renal dysfunction.

So serum uric acid may be a powerful tool to help identify patients at high risk of hypertensive diseases. It is therefore prudent to ponder serum uric acid along with other risk factors, such as obesity and hyperglycemia, in the assessment of overall hypertensive risk.

The remaining key questions, which need to be explored, are whether uric acid has a causal role in hypertension, whether a reduction of uric acid level could achieve prevention of hypertensive complications, cardiovascular, and whether uric acid could be reduced to an optimal level whereby it no longer imposes an increased risk for essential hypertension. Uric acid lowering drugs may have additional benefit in controlling HTN as has been shown in some studies (Assadi et al and Shibagaki et al).[20,21] Therefore the study of serum uric acid levels in HTN requires more further studies for better assessment of risk and control of HTN.

In limitations, our research was conducted on limited population, whether the results may be generalized to other populations with different cultural and dietary backgrounds requires further study. Study group was small. It was an observational one point study.

CONCLUSION

Thus, based on the present study, author concluded that the serum uric acid is significantly elevated in hypertensive as compared to normotensive individuals. Hyperuricemia was present equally among both gender in stage II hypertensive patients and were higher in patients with prolong hypertension. So, serum uric acid can be used probably as an early biochemical marker to determine the severity of hypertension as stage 2 hypertensive had more elevation in serum uric acid levels as compared to other hypertensive patients. The levels of uric acid in individuals would prompt clinician to check the blood pressure resulting in early diagnosis and necessary intervention to treat hypertension at an early stage and effect of lowering of serum uric acid level in treating hypertension need to be studied.

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