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A study on association of serum uric acid and blood pressure in hypertensive patients at a tertiary hospital

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Abstract

Background: Hypertension is an increasing important medical and public health issue. Uric acid exerts a pro-inflammatory effect on endothelial cells which may be associated with MetS risk factors such as elevated triglyceride (TG) levels, hypertension and insulin resistance.[5] Present study was aimed to study of association of serum uric acid and blood pressure in hypertensive patients at a tertiary hospital.
Material and Methods: Present study was prospective, comparative, observational study, conducted among cases (Subjects of either gender, age >18 years, diagnosed as hypertensive (first time) were enrolled in this study during a regular routine health check-up at general medicine OPDs) & controls (Age & gender matched normotensives subjects at general medicine OPDs).
Results: In present study, 100 subjects each were studied in hypertensive as well as normotensive group. Mean levels of age, gender, BMI & co-morbidities among both groups were comparable & difference was not significant statistically. Mean pulse rate & respiratory rate were comparable among both groups & difference was not significant statistically. The mean levels of SBP and DBP were significantly more in the hypertensive subjects as compared to normotensive subjects ($p < 0.001$). In present study, prevalence of hyperuricemia was 9% (1% in normotensive and 8% in hypertensive subjects). Hypertensive subjects had increased mean levels of SUA than in the normotensive subjects ($p < 0.001$). In Pearson's correlation coefficient test, SUA levels were significantly related with SBP and DBP ($p < 0.001$). The average level of TG and HDL were also significantly different between the groups ($p < 0.05$).
Conclusion: A stronger co-relationship for higher levels of SUA concentration was noted with blood pressure hypertension and prehypertension in the participants.

Keywords: Serum uric acid, blood pressure, hypertension, hypertensive

Introduction

Hypertension is an increasing important medical and public health issue. Hypertension markedly increases the risk for myocardial infarction, stroke, congestive heart failure, peripheral vascular disease and end stage renal disease. Various risk factors for development of hypertension, both modifiable and non-modifiable, have been identified to aid in its

prevention and management. In recent years, various studies have shown serum uric acid (SUA) levels to be an independent predictor for developing hypertension [1].
Uric Acid (UA) is a heterocyclic compound whose concentration in the body depends upon the balance between purine breakdown and rate of urate excretion [2]. Plasma uric acid is a circulating marker of oxidative damage in a variety of pathological conditions such as ischemic liver injury, hyperlipidemia, chronic heart disease, atherosclerosis, ischemic reperfusion injury, and diabetes [3]. The serum uric level depends on gender, lifestyle, meals, and previous use of diuretics [4].
Uric acid exerts a pro-inflammatory effect on endothelial cells which may be associated with Mets risk factors such as elevated triglyceride (TG) levels, hypertension and insulin resistance [5]. Moreover, in recent years, elevated SUA levels in adults have been suggested as CVD risk factors in some studies [6, 7]. Present study was aimed to study of association of serum uric acid and blood pressure in hypertensive patients at a tertiary hospital.

Material and Methods

Present study was prospective, comparative, observational study, conducted under department of physiology, at XXX medical college & hospital, XXX, India. Study duration was of 6 months (July 2021 to December 2021). Study was approved by institutional ethical committee.

Inclusion criteria

- **Cases:** Subjects of either gender, age >18 years, diagnosed as hypertensive (first time) were enrolled in this study during a regular routine health check-up at general medicine OPDs.
- **Controls:** Age & gender matched normotensives subjects at general medicine OPDs.

Exclusion criteria

- Individuals having pre-existing hypertension.
- Individuals having a known history of gout and cardiac or severe renal diseases.
- Subjects who were already under medication for anti-hyperuricemic.
- Subjects who were not willing to participate.
- Study protocol was informed to all subjects and written informed consent was obtained from them prior to enrolment in the study. General information such as name, age, gender, previous medical history was noted in CRF. General & systemic examination findings along with Body mass index (BMI) [body weight in kgs divided by (height in m) ^{2}] was noted in CRF.

Blood pressure (BP) was measured by trained professionals using a digital BP machine (Philips) on the left arm in a sitting position after at least 10 minutes of rest. Three recordings of blood pressure as systolic and diastolic blood pressure (SBP and DBP) has been taken after a minimum of 5 minutes of rest to avoid any possible effects of anxiety and with an interval of 5 minutes.
Hypertension was defined as per JNC-7 classification of hypertension [8].

Table 1: JNC-7 classification of hypertension [8]

Blood Pressure Staging	Systolic BP (mm Hg)	Diastolic BP (mm Hg)
Normal	<120	And <80
Prehypertension	120-139	Or 80-89
Stage 1 Hypertension	140-159	0r 90-99

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Stage 2 Hypertension	>160	Or>100
Isolated Systolic Hypertension	>140	And <89

The venous blood samples were obtained after an overnight fasting (≥12hrs) for estimation of complete blood counts, renal function tests (Serum Urea, Serum Creatinine & Serum uric acid), Thyroid-stimulating hormone (TSH), random blood sugar and serum lipids: total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C), The values were determined calorimetrically using commercially available diagnostic kits (Human Diagnostic, Germany), using an auto-analyser (Humalyzer 3000, USA). Hyperuricemia was defined as SUA levels >416.4_mol/L (7.0 mg/dL) in men and >356.9_mol/L (6.0 mg/dL) in women.
Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Pearson's correlation coefficient test was performed to assess the interrelationships between baseline variables and SUA concentrations. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

Results

In present study, 100 subjects each were studied in hypertensive as well as normotensive group. Mean levels of age, gender, BMI & co-morbidities among both groups were comparable & difference was not significant statistically.

Table 2: General characteristics

Variables	Hypertensive (n=100) [mean ± SD/n (%)]	Normotensive (n=100) [mean ± SD/n (%)]	Total (n=200) [mean ± SD/n (%)]	P value
Age (years)	54.75 ± 9.74	53.38 ± 11.23	54.22 ±10.75	0.073
Gender				0.085
Male	69 (69 %)	71 (71 %)	140 (70 %)	
Female	31 (31 %)	29 (29 %)	60 (30 %)	
BMI (kg/m2)	22.51 ± 2.56	22.94 ± 2.16	22.71 ± 2.23	0.067
Co-morbidity				
Smoking,	19 (19 %)	15 (15 %)	34 (17 %)	0.052
Alcohol,	19 (31 %)	16 (16 %)	35 (35 %)	0.055
Tobacco chewing	16 (16 %)	15 (15 %)	31 (31 %)	0.082
Diabetes Mellites	11 (11 %)	14 (14 %)	25 (12.5 %)	0.059

Mean pulse rate & respiratory rate were comparable among both groups & difference was not significant statistically. The mean levels of SBP and DBP were significantly more in the hypertensive subjects as compared to normotensive subjects ($p < 0.001$).

Table 3: Examination findings

Variables	Hypertensive (mean ± SD)	Normotensive (mean ± SD)	Total (mean ± SD)	P value
Pulse rate (/min)	81.35 ± 11.54	80.61 ± 10.97	80.98 ± 11.15	0.089
Respiratory rate (/min)	18.96 ± 3.01	19.09 ± 2.91	19.07 ± 2.95	0.086
SBP (mm Hg)	155.35 ± 18.51	131.38 ± 14.91	145.39 ± 17.62	<0.0001
DBP (mm Hg)	96.12 ± 7.11	83.92 ± 6.01	91.46 ± 6.57	<0.0001

In present study, prevalence of hyperuricemia was 9% (1 % in normotensive and 8% in

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hypertensive subjects). Hypertensive subjects had increased mean levels of SUA than in the normotensive subjects ($p < 0.001$). In Pearson's correlation coefficient test, SUA levels were significantly related with SBP and DBP ($p < 0.001$). The average level of TG and HDL were also significantly different between the groups ($p < 0.05$). Other parameters such as Hemoglobin, Total Count, Platelet Count, Serum Urea, Serum Creatinine (mg/dL), Fasting Blood Sugar, TSH, Total Cholesterol & LDL were comparable among both groups & difference was not significant statistically.

Table 4: Hematological characteristics

Variables	Hypertensive (mean ± SD)	Normotensive (mean ± SD)	P value
Hemoglobin (g %)	11.64 ± 2.49	11.17 ± 2.47	0.082
Total Count (/mm^3)	7757.1 ± 3563.8	7855.5 ± 3921	0.069
Platelet Count (/mm^3)	218.06 ± 85.76	230.47 ± 91.95	0.081
Serum Urea (mg/dL)	27.81 ± 8.97	26.19 ± 9.01	0.055
Serum Creatinine (mg/dL)	0.81 ± 0.41	0.69 ± 0.24	0.068
Serum uric acid (mg/dL)	6.43 ± 2.11	6.01 ± 1.93	<0.0001
Fasting Blood Sugar (mg/dL)	109.69 ± 17.89	102.61 ± 23.13	0.074
TSH (mIU/mL)	2.24 ± 0.82	2.19 ± 0.78	0.075
Total Cholesterol (mg/dL)	213.78 ± 38.74	213.19 ± 42.29	0.064
LDL (mg/dL)	109.46 ± 22.98	109.7 ± 24.86	0.056
HDL (mg/dL)	52.28 ± 15.78	43.34 ± 15.2	0.045
TG (mg/dL)	103.71 ± 39.74	139.63 ± 43.72	0. 041

Discussion

Being a powerful antioxidant, uric acid has been proposed to be protective against cardiovascular disease as well as some cancers. But although it may seem to possess antioxidant activity in the extracellular compartment, its effects are quite detrimental once it enters cells such as vascular smooth muscle cells. These adverse effects include initiation of platelet aggregation, pro-inflammatory actions and an inhibitory effect on the production of nitric oxide [5, 7].

Experimental, clinical, and epidemiologic data suggest that individuals with elevated serum uric acid (SUA) levels are at increased risk of CVD and kidney dysfunction [9, 10, 11]. The mechanistic basis is partly due to the dual role of SUA as an antioxidant (intracellular) and a pro-oxidant (extracellular) to oxidative stress, depending on its localization [12].

Hyperuricemia affects 25-40% of patients with untreated hypertension. A much lower prevalence has been reported in normotensives or in the general population [13]. In addition to serving as an independent risk factor for incident hypertension in the general population, hyperuricemia may have important differential effects in age, gender, and racial subgroups [14].

In study by Chanchal S *et al*., [15] mean serum uric acid level in group A (Essential Hypertension) was significantly higher than group B (normotensive cases) (6.56 ± 0.76, 4.91 ± 0.97 mg/dl, $p<0.001$ respectively). 37.33% of patients had hyperuricaemia in group A as compared to 14% in group B ($p<0.01$, OR=3.66) indicating that a hyperuricaemic individual has 3.66 times more risk of developing Essential Hypertension as compared to the one with lower value of serum uric acid. Serum uric acid could be useful as a potential indicator for early risk detection of development of EHT.

Samozai MN *et al*., [16] studied 245 subjects, mean age of the participants was 42.4 8.4 years (Range 18-70 years). There was no significant difference in the mean levels of Height, Weight and BMI between the two groups. Mean levels of WC, HC were significantly different between two group ($p < 0.05$) subjects. The mean levels of SBP and DBP were also significantly more in the hypertensive subjects ($p < 0.001$). In Pearson's correlation

coefficient test, SUA levels were significantly related with SBP and DBP. They observed a stronger relationship for SUA concentration with hypertension and prehypertension in the participants.

Ghali R *et al*., [17] noted a strong correlation between SUA level with systolic blood pressure (SBP) in patients with primary HTN ($r = 0.5046$; $P < 0.0001$) was observed. The mean SBP (163.89 ± 9.99 mmHg) was significantly high ($P < 0.001$) in hyperuricemic patients and raised SUA was noted in 38% of the cohort. Stage II hypertensive subjects of the 58-66 years age group were found to be a particularly vulnerable group (odds ratio of 32). History of diabetes mellitus, tobacco, and alcohol consumption showed a significant association with elevated SUA levels in males ($P < 0.05$).

Sujeet Raina *et al*., [18] studied 50 newly diagnosed cases of essential hypertension and 50 age and sex matched normotensive healthy volunteer. Prevalence of hyperuricemia was 24% among the cases and 6% among the controls ($P<0.05$). Odds ratio was 4.9 (CI=1.3 to 18.8). The mean SUA was significantly higher in the cases (5.5±1.7 mg/dl) than in the controls (4.9±1.1 mg/dl; $P<0.05$). Odds ratio in male hyperuricemic hypertensive versus hyperuricemic normotensive was 6 (CI=1.0 to 33.2) and 4.46 (CI=0.4 to 42.5) among female hyperuricemic hypertensive versus hyperuricemic normotensives.

In study by Bawazier LA *et al*., [19] about 31.1% of 733 subjects with prehypertension became hypertensive after 10 years, 24.6% returned to normal tension and the rest of it remained in prehypertensive state. Mean (SD) of SUA levels in 2017 was significantly higher in men than in women (5.78 (1.25) mg/dL vs 4.52 (1.10) mg/dL, $p<0.001$). Furthermore, men tended to have high-normal (5-7 mg/dL) or high SUA levels (≥7 mg/dL) compared with women ($p<0.001$, Relative Risk (RR) = 2.60). High-normal and high SUA levels in population with a history of prehypertension were significantly associated with current prehypertension and hypertension only in women ($p=0.001$, RR=1.21). Age and body mass index was found to be significantly associated with both systolic and diastolic BP in men, but only with systolic BP in women. Fasting blood glucose and SUA levels were significantly associated with systolic and diastolic BP only in women.

Despite the clinical and epidemiological evidence, many authorities do not consider an elevated uric acid to be a true cardiovascular risk factor, because patients with hyperuricemia often have other well-established risk factors for cardiovascular disease, such as hypertension, renal disease, obesity, dyslipidemia, and insulin resistance.

At the tissue level, chronic exposure to increased UA promotes vascular changes leading to renal ischemia and stimulation of renin-angiotensin system and development of insulin resistance, hypertriglyceridemia, and hepatic steatosis through pro-oxidative mechanisms. Therefore, early screening of UA levels is advisable to prevent and manage complications of elevated levels of SUA [20].

Present study limitations were a cross-sectional study, did not permit us to make any inference on the causal relationship between uric acid and hypertension. Secondly, the limited sample size also limited the power of the analysis. A further study designed as a prospective randomized follow up study with a larger sample size would be required to substantiate the results of the present study.

Conclusion

A stronger co-relationship for higher levels of SUA concentration was noted with blood pressure hypertension and prehypertension in the participants. Hence, estimation of SUA levels is advisable at the diagnosis of hypertension in order to diagnose, prevent and manage complications of elevated levels of hypertension

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