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Indian Journal of Clinical Anatomy and Physiology

Journal homepage: <https://www.ijcap.org/>

Original Research Article

A study on association of serum uric acid and blood pressure in hypertensives at a tertiary care centre

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ARTICLE INFO

Article history:

Received 19-10-2021

Accepted 13-11-2021

Available online 07-12-2021

Keywords:

Hypertension
Serum uric acid
Uricemia
SBP
DBP
BMI

ABSTRACT

Hypertension (HTN) is the most common and significant cardiovascular disease because of its prevalence and severity of the damage to the mankind globally. Hyperuricemia, a condition of increased levels of Serum Uric acid (UA) has been proposed to have an association with hypertension in various studies. In certain studies, serum uric acid levels has been found to be an independent predictor for developing hypertension. On the basis of the above observations, we have proposed to the present study to compare the relationship between serum UA and hypertension in a single cohort with adjustment of all possible confounding factors.

A total of 245 subjects were enrolled in this study during a regular routine health checkup. All subjects were informed about the study aims. Individuals having a known history of gout and cardiac or severe renal diseases and patients who are already under medication for anti-hyperuricemic were excluded from the study. General information like Name, Age, Sex, Occupation, Address along with history of any drug intake and anthropometric indices - body weight (BW), body height (BH), hip circumference (HC), waist circumference (WC), and lifestyle information have been obtained. The data has been arranged in tables with mean \pm SD for further analysis. The data is analyzed using IBM SPSS version 23. The difference between the groups for baseline variables was done by independent sample t-test (two-tailed). Pearson's correlation coefficient test was performed to assess the interrelationships between baseline variables and SUA concentrations. The differences for the variables among the groups was determined by using One-way ANOVA.

Of the 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. In this study, we have observed comparatively a stronger relationship for SUA concentration with hypertension and prehypertension in the participants.

The extended mechanism for the effect of SUA on hypertension is yet to be elucidated. There are some hypotheses partly explain the association between SUA and high blood pressure. One of the possible mechanism might be uric acid deposition on the blood vessels walls activates the renin-angiotensin system, suppress the liberate of carbon monoxide, enhance inflammation, and leads to vasoconstriction on later stage, which consequently leads to hyperplasia and incidence of hypertension. Another possibility involving oxidative stress and endothelial dysfunction associated with high SUA levels may contribute to high blood pressure.

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1. Introduction

Hypertension (HTN) is the most common and significant cardiovascular disease because of its prevalence and severity of the damage to the mankind globally. In India also, the prevalence and occurrence of HTN is increasing regularly and also found to be associated with certain age, sex, occupation, life style etc., resulting in increase of morbidity and mortality. These effects of HTN are known to be relate with incidence of myocardial infarction, heart failure, stroke, and renal failure.¹⁻⁴

Hyperuricemia, a condition of increased levels of Serum Uric acid (UA) has been proposed to have an association with hypertension in various studies. In certain studies, serum uric acid levels has been found to be an independent predictor for developing hypertension.⁵⁻⁷ Irrespective of the different ethnic origins & regions, a certain association between serum UA and blood pressure (BP) has been seen in African-Americans and whites^{8,9} as well as in the Asians^{7,10} including Koreans.¹¹⁻¹³ In the study of causal role of serum UA in the development of hypertension, Mazzali et al.¹⁴ observed an elevation in the levels of serum UA followed by an increase in BP via a crystal-independent mechanism in rat models. Further it has also been found that reduction of serum UA was associated with a decrease in BP through the regulation of renin-angiotensin and nitric oxide system.¹⁵

On the basis of the above observations, we have proposed to the present study to compare the relationship between serum UA and hypertension in a single cohort with adjustment of all possible confounding factors. This study is focused on the association between serum UA and hypertension.

2. Materials and Methods

A total of 245 subjects (123 hypertensives and 122 normotensives; age >18 years) were enrolled in this study during a regular routine health checkup. All subjects were informed about the study aims and written informed consent was obtained from them prior to enrollment in the study. Individuals having a known history of gout and cardiac or severe renal diseases and patients who are already under medication for anti-hyperuricemic were excluded from the study. Ethical Clearance was obtained from the Institutional Ethical Committee, Dr. Patnam Mahender Reddy Institute of Medical Sciences, Chevella, Telangana. The procedure and the methods used in the present study were in accordance with the institutional guidelines and regulations.

General information like Name, Age, Sex, Occupation, Address along with history of any drug intake and anthropometric indices - body weight (BW), body height (BH), hip circumference (HC), waist circumference (WC),

and lifestyle information have been obtained. BW was measured to the nearest 0.1 kg using a calibrated digital weighing machine and BH was recorded to the nearest 0.1 cm using a height measuring tape. Body mass index (BMI) was calculated as the weight in kg divided by height in meter square. WC was measured by placing the tape horizontally midway between the iliac crest on the mid-axillary line and the ribs lowest border. HC was measured at the largest circumference of the buttocks. Blood pressure (BP) was measured by trained professionals using a digital BP machine (Omron M10, Omron Corporation, Tokyo, Japan) on the left arm in a sitting position after atleast 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. The venous blood samples were obtained after an overnight fasting (≥ 12 hrs). The blood sample was centrifuged and serum was stored at -20°C for further analysis. The concentration of SUA, and serum lipids: total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), were determined calorimetrically using commercially available diagnostic kits (Human Diagnostic, Germany). All the biochemical tests were measured using a auto-analyzer (Humalyzer 3000, USA). Hypertension was defined as SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg and prehypertension as when SBP 120–139 mm Hg; and/or DBP 80–89 mm Hg.¹⁶ Hyperuricemia was defined as SUA levels >416.4 $\mu\text{mol/L}$ (7.0 mg/dL) in men and >356.9 $\mu\text{mol/L}$ (6.0 mg/dL) in women.^{17,18} The participants were divided into groups – Normotensives and hypertensives and the prevalence of Uremia in correlation with hypertension was studied in each group.

The data has been arranged in tables with mean \pm SD for further analysis. The data is analyzed using IBM SPSS version 23. The difference between the groups for baseline variables was done by independent sample t-test (two-tailed). Pearson's correlation coefficient test was performed to assess the interrelationships between baseline variables and SUA concentrations. The differences for the variables among the groups was determined by using One-way ANOVA analysis. The relationship between SUA and hypertension was evaluated by logistic regression modeling. A p-value < 0.05 was considered to be statistically significant.

3. Results

In our present study, increased Serum Uric Acid levels is significantly related to incidence of hypertension.

The baseline characteristics of all the subjects are presented in Table 1. Of the 245 subjects, mean age of the participants was 42.4 ± 8.4 years (range 18–70 years).

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Table 1: Baseline characteristics of each group by age

Variables	Total	Normotensives	Hypertensives
	Mean±SD	Mean±SD	Mean±SD
Age (years)	42.4±8.4	32.4±4.5	58.1±4.6
Height (cms)	164.4±5.1	166.4±5.4	160±1.2
Weight (kgs)	65.4±11.5	66.1±19.4	60.5±15.6
Waist circumference (cms)	69.4±34.4	62.4±35.4	78.4±27.8
Hip circumference (cms)	94.5±4.6	94.4±5.4	98.5±4.5
BMI (Kg/m ²)	22.6±4.6	23.4±2.4	22.4±1.5
SBP (mmHg)	138.5±15.6	120.4±15.4	154.5±17.5
DBP (mmHg)	82.4±5.6	86.1±5.2	90.4±4.6
Serum UA (mg/dl)	7.3±1.2	6.1±1.4	8.1±1.1
Total Cholesterol (mg/dl)	185.4±26.4	188.5±34.5	194.5±25.4
HDL (mg/dl)	51.3±15.2	50.6±21.6	58.1±19.5
Tg (mg/dl)	106±64.4	126.4±45.6	146.1±41.6
LDL (mg/dl)	104±45.5	155.4±56.4	156±40.4

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 ($p < 0.001$). Hypertensives have been found to have increased mean levels of SUA than in the normotensive subjects ($p < 0.001$). The average level of TG and HDL-C were also significantly different between the groups ($p < 0.001$). Overall, hyperuricemia prevalence was 9.7% with 0.9% in normotensive and 9.3% in hypertensive subjects.

4. Discussion

The present study reveals a positive association between elevated SUA levels and hypertension in a general adult cohort. This association was persisted after adjustment for age, sex, BMI, and lipid profile. An increasing trend for the incidence of prehypertension and hypertension was found with elevated levels of SUA in the quartiles. Some studies have demonstrated the relationship between hyperuricemia and hypertension in adult population.^{19–24} A study of Japanese adults has showed that hypertension OR was 1.20 for each 1 mg/dL increase in SUA concentration.¹⁹ Another cross-sectional study in US observed elevated SUA levels were positively associated with prehypertension, and the multivariate OR comparing highest quartile of SUA (>356.9 $\mu\text{mol/L}$) with the lowest quartile (<237.9 $\mu\text{mol/L}$) was 1.96 (1.38–2.79).²³ Another study conducted of non-hypertensives in US reported multivariate relative risk was 1.65 when compared to the highest quartile with the lowest quartile.²² Framingham Heart Study, after examining the participants for 4 years, have reported increased SUA levels by each standard deviation was related with an OR of 1.17 for developing hypertension.²⁵ Similar to our findings, in some recent studies, a positive association between SUA

and hypertension was found in adult cohorts of China and Korea.^{26–29}

In this study, we have observed comparatively a stronger relationship for SUA concentration with hypertension and prehypertension in the participants. It is known that hypertensives with uricemia are more vulnerable to hypertension.³⁰ The extended mechanism for the effect of SUA on hypertension is yet to be elucidated. There are some hypotheses partly explain the association between SUA and high blood pressure. One of the possible mechanism might be uric acid deposition on the blood vessels walls activates the renin-angiotensin system, suppress the liberate of carbon monoxide, enhance inflammation, and leads to vasoconstriction on later stage, which consequently leads to hyperplasia and incidence of hypertension.^{31–34} Another possibility involving oxidative stress and endothelial dysfunction associated with high SUA levels may contribute to high blood pressure.³⁵

Our study had a few limitations. First, the cross-sectional design of this study may preclude the cause-effect relationships between SUA concentrations and hypertension being assumed. Second, the sample size of this study was relatively small; therefore, the findings may not represent for the whole population. Third, we did not have individual information on family history of hypertension and physical activity which may affect the incidence of high blood pressure. Moreover, all participants of this study were apparently healthy adults; whether our finding is similar in other ethnic populations needs to be further studied. However, this study findings are worthy as a reference for future investigations. Further studies are required to establish the potential mechanism between SUA and hypertension in humans.

5. Conclusions

Increased levels of SUA were positively associated with hypertension among general adults. The SUA quartiles

also showed significant correlation with SBP and DBP. Our study findings suggest an independent relationship of elevated SUA with hypertension and indicate the significance of maintaining normal SUA concentration to prevent hypertension. Early and proper management of SUA levels, as well as blood pressure, may be useful in preventing the development of future CVDs.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare no conflict of interest.

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Cite this article: Samoza MN, Devarapalli R, Babu KR. A study on association of serum uric acid and blood pressure in hypertensives at a tertiary care centre. *Indian J Clin Anat Physiol* 2021;8(4):264-268.