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Research Article

**ASSOCIATION OF SERUM URIC ACID LEVELS WITH
BLOOD PRESSURE IN NORMOTENSIVE,
PREHYPERTENSIVE AND HYPERTENSIVE POPULATION**Dr. Marina Khan¹, Dr. Aneeqa Khalil², Dr. Ziarmal Khan³¹ WMO DHQ hospital Mianwali² DHQ Teaching Hospital Mirpur³ Federal Government Poly Clinic Hospital Islamabad

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Abstract:

Background: uric acid, a final metabolic product of purine breakdown, appears as an etiology in gout. Higher levels have also been associated with hypertension, cardiovascular morbidity and mortality. Few studies have been conducted, especially in India, to elucidate the relationship between uric acid and prehypertension.

Objective: In this study, the relationship between serum uric acid levels and blood pressure in the normotensive, prehypertensive and hypertensive population was evaluated. Also, it should be checked whether there is an incremental increase in serum uric acid with an increase in blood pressure.

Place and Duration: In the Medicine department of Holy Family Hospital Rawalpindi for one year duration from March 2019 to February 2020.

Material and methods: Two hundred OPD patients meeting the inclusion and exclusion criteria and were included in the study population. A venipuncture was measured to collect venous blood to measure the blood pressure of each participant and then serum uric acid. According to the classification of the National Joint Committee 7, the participants were divided into 4 groups such as Normal, Prehypertension, Hypertension - Stage 1, Hypertension Stage -2. The data were analyzed to determine and confirm serum uric acid levels from four categories. The relationship of uric acid with blood pressure.

Results and conclusion: A gradual increase in serum uric acid levels was observed with an increase in blood pressure. A strong positive linear correlation was observed between serum uric acid levels and mean arterial pressure (Pearson correlation coefficient $r = 0.74$; $p < 0.0001$). Uric acid was associated with blood pressure in the prehypertensive population ($r = 0.442$). Serum uric acid levels are associated with prehypertension and hypertension and are strong independent predictors of cardiovascular mortality.

Keywords: blood pressure, prehypertension, uric acid.

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INTRODUCTION:

Uric acid is the end product of the breakdown of purines in humans and is mainly excreted in the urine. Serum uric acid levels are regulated by dietary purine intake, endogenous purine metabolism, and urinary excretion rate. 15 million years ago, during the evolutionary process, two mutations caused uricase genes to not function in humans and large monkeys. As a result, uric acid is not converted into allantoin, a product that is easily soluble and easily excreted in water, resulting in higher serum uric acid levels in humans and large monkeys¹⁻². As early as 1848, Sir Alfred Garrod showed that gout, an inflammatory disease of the joints, was associated with hyperuricemia, i.e. high serum uric acid (> 7 mg / dl in men and > 6 mg / dl in women)³⁻⁴. Gout is a disease of the joints characterized by the accumulation of monosodium urate crystals that cause inflammation and pain in the joints. A few years later, in 1874, Frederick Mohamed first suggested "people with high blood pressure belong to gout families" and suggested a possible relationship between hyperuricemia and high blood pressure. Many researchers have described the relationship between elevated serum uric acid and hypertension⁵. At the end of the 19th century, many studies showed that uric acid was also associated with cardiovascular disease. However, the lack of a possible mechanism by which hypertension and uric acid binds has led to the conclusion that uric acid is not a real risk factor for cardiovascular disease. Among contradictory reports, Mohamed's hypothesis that uric acid plays a causal role in hypertension remains controversial even after more than 130 years⁶⁻⁷. Recent animal studies and clinical observations show the possible direct causal role of uric acid in the pathogenesis of hypertension by various mechanisms. Recently, more and more significant evidence has been gathered of the related and causal role of uric acid in hypertension and cardiovascular morbidity⁸⁻⁹. Studies to date have not assessed the relationship between serum uric acid levels and blood pressure, and have increased with increasing blood pressure in hypertensive patients. Therefore, in this study, we tried to assess the relationship between serum uric acid levels and blood pressure in participants with normotension, hypertension and hypertension. We also plan to check the incremental increase in serum uric acid concentration with increasing blood pressure.

MATERIALS AND METHODS:

Our study was conducted in the Medicine department of Holy Family Hospital Rawalpindi for one-year duration from March 2019 to February 2020. Prior to the study, the approval of the Corporate Ethics Committee was obtained. The prospective study was outpatient. The study group consisted of two hundred participants (103 men and

97 women) from the 20-60 age group. Persons meeting the inclusion and exclusion criteria listed below were informed and explained about the study and included in the study after obtaining their written consent.

Inclusion and exclusion criteria: pediatric and psychiatric patients, pregnant women, diagnosed secondary cases of hypertension, diuretics and antihypertensives were excluded from the study. Study participants were compulsory to sit comfortably in a chair for five minutes. Systolic and diastolic blood pressure were measured twice by auscultation with a mercury sphygmomanometer (cuff size, 12.5 x 40 cm) on the right shoulder. The first and fifth stages of Korotkoff's sounds are treated as criteria for SBP and DBP, respectively. The average of two consecutive readings was recorded and used for analysis. Mean systolic and diastolic blood pressure (SBP + DBP / 2) were calculated and observed as mean arterial pressure. According to the Joint National Committee (JNC) classification, participants were classified as normal if systolic blood pressure (SBP) <120 mm Hg and diastolic blood pressure (PAD) <80 mm Hg; SBP / DBP 120-139 / or 80-89 mm Hg is antihypertensive; Grade 1 is classified as hypertension if SBP / DBP 140-159 / or 90-99 mm Hg, and SBP / DBP is classified as grade 2 hypertension if ≥ 160 / or ≥ 100 mm Hg. Under aseptic conditions, a puncture was performed in the middle cubic vein and 2 ml of blood was collected into a sterile plastic tube, which was drained with a red cap without additives. Blood samples were allowed to clot for 30 minutes at room temperature. Samples were centrifuged for 15 minutes at 1500 g to remove serum. Serum uric acid levels were measured using the ERBA XL 300 fully automated analyzer. To guarantee quality, internal quality control samples were analyzed daily and the coefficient of variation (CV) was <5% overnight. The laboratory also had an external quality assurance program.

Statistical analysis: Statistical analysis of participant data was performed using the "IBM SPSS Statistics 20" software. Data were analyzed to measure age and sex distribution of participants and to classify participants with normal blood pressure and mean serum uric acid as normal, pre-hypertension, grade 1 hypertension and grade 2 hypertension. Pearson's correlation coefficient was calculated to explain the statistical relationship between serum uric acid levels and blood pressure.

RESULTS:

The demographic characteristics of the study population are summarized in Table 1. The study population consists of 200 participants, 103 of whom are men and 97 of them are women.

Table: 1. Age sex distribution of study population with mean blood pressure

Age (years)	Number of Males	Number of females	Blood pressure* (mm of Hg)
20 - 30	35	44	98.08 ± 9.09
31 - 40	14	14	101.96 ± 13.13
41 - 50	17	15	107.21 ± 14.27
51 - 60	37	24	112.23 ± 12.69

Statistically highly significant ($p < 0.0001$). A similar correlation was observed between serum uric acid and systolic blood pressure ($r = 0.746$) and diastolic blood pressure ($r = 0.609$). Strong correlation with blood pressure in the state antihypertensive population, formally related ($r = 0.442$), weak correlation in the normal population ($r = 0.113$), mean age of the studied population was 40.06 ± 13.8 years and age. The average male and female was 41.98 ± 13.48 years and 38.03 ± 13.91 years, respectively, and the average study population increased with age, the prevalence of undiagnosed hypertension in population was 22% ($n = 44$) and of undiagnosed prehypertension was 42% ($n = 84$), put together comprising nearly 65% of study population. A stepwise increase in serum uric acid levels was observed when study population was categorised into four groups namely, Normal, Prehypertension, Hypertension stage-1, Hypertension stage-2 based on the JNC 7 classification of blood pressure. Similar increasing trend in mean serum uric acid level was observed along with mean blood pressure of the study population. (Table-2)

Table: 2. Serum uric acid and blood pressure in normotensives, prehypertensives and hypertensives

JNC 7 BP classification ¹⁴ (SBP/DBP mm of Hg)	Males	Females	Serum Uric acid* (mg/dl)	Blood Pressure* (mm of Hg)
Normal (<120/ and <80)	30	42	5.09 ± 0.65	92.95 ± 4.7
Prehypertension (120-139/ or 80-89)	47	37	5.70 ± 0.73	104.08 ± 5.21
Hypertension Stage-1 (140-159/ or 90-99)	18	14	6.81 ± 0.77	119 ± 6.94
Hypertension Stage-2 (≥ 160 / or ≥ 100)	8	4	7.59 ± 0.57	136.41 ± 6.86

DISCUSSION:

Our prospective study with 200 participants showed that serum uric acid is associated with blood pressure in seemingly healthy people, undiagnosed people with hypertension and people with hypertension. This is the first study in Pakistan that has explained the relationship between serum uric acid levels and blood pressure in a hypertensive population. The population survey covers adults between 20 and 60 years old. The average age of the studied population is 40.06 ± 13.8 years and can be compared with other similar studies with an average age of 42.3 ± 0.2 years and 41.6 years. Although known hypertensive patients were excluded from the study, 22% ($n = 44$) participants had hypertension and 42% ($n = 84$) had hypertension⁹⁻¹⁰. Independent researchers have reported similar prehypertension (39%) among adults in India and the United States. It is noteworthy that a large percentage of the population at risk of hypertension (42%) who may develop cardiovascular disease and undiagnosed hypertensive patients (22%) have not been noticed. In our study, serum uric acid levels were positive ($r = 0.740$) and significantly (p

< 0.0001) related to blood pressure. Other researchers also observed similar statistically significant positive correlations¹¹⁻¹². When participants were classified as normal, hypertension, Grade 1 hypertension and Grade 2 hypertension according to the JNC7 classification, a gradual increase in serum uric acid was observed. Cross-sectional study in Japan. However, this study classified participants according to Japanese society guidelines JSH-2009 rather than JNC 7 classification. A similar relationship ($r = 0.15$; $p < 0.001$) was shown in the study in a large probable group of men. They also showed that serum uric acid is independently associated with congestive heart failure and stroke-related mortality. A positive association of serum uric acid with hypertension ($r = 0.32$) was observed independent of BMI smoking and other confounding factors. One study showed a significant correlation ($p < 0.0001$) between uric acid and antihypertensive status in adults, but it was also found that the relationship was not statistically significant in people over 65 years of age. A 9-year study showed a relationship between serum uric acid and hypertension and a stronger relationship

between black people. A PIUMA study with a cohort of 1,720 patients with a 12-year follow-up showed that people with higher uric acid levels had a higher risk of cardiovascular events (relative risk 1.73, 95% confidence interval)¹³. In a study of 125 children (age group 6-18 years) with primary hypertension, a relationship was found between serum uric acid and systolic blood pressure ($r = 0.80$) and diastolic blood pressure ($r = 0.66$). In another pediatric age study, a relationship was found between serum uric acid levels and ambulatory diastolic blood pressure ($r = 0.29$; $p = 0.0033$). Serum uric acid has long been associated with hypertension, the primary etiology of cardiovascular morbidity. Several large cohort studies have shown that serum uric acid predicts mortality from coronary heart disease in women. Few studies have shown that uric acid has an independent and significant association with the risk of cardiovascular mortality and myocardial infarction¹⁴⁻¹⁵. One study found that serum uric acid is a strong and independent predictor of cardiovascular mortality in middle-aged men. Increased serum uric acid levels are associated with high blood pressure as well as cardiovascular disease and mortality. However, the causal role of uric acid in hypertension and the pathogenesis of cardiovascular events are unclear. Recent studies have explained legitimate mechanisms explaining how high uric acid levels cause hypertension. Studies in animal models have shown that high levels of uric acid cause interstitial and renal blood vessel damage.

CONCLUSION:

Serum uric acid levels are associated with hypertension and are independent and strong predictors of cardiovascular mortality, myocardial infarction and coronary artery disease in both sexes of different ethnicities. So it cannot be an exaggeration to say that "Uric acid licks joints and bites hearing."

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