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RELATIONSHIP BETWEEN SERUM URIC ACID LEVELS AND BLOOD PRESSURE ACROSS DIFFERENT AGE GROUPS

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ABSTRACT

To determine the frequency of hyperuricemia and its association with blood pressure across different age groups in patients attending outpatient clinics for general health check-ups at a tertiary care hospital. Place and Duration of Study: Department of Internal Medicine, Fazaia Ruth Pfau Medical College, PAF Faisal Base, Karachi, from November 18, 2024, to February 20, 2025. Following ethical approval, 200 participants were recruited, including 100 newly diagnosed hypertensive patients (Group A) and 100 age-matched normotensive controls (Group B). Serum uric acid levels were measured, and hyperuricemia was defined based on standard clinical criteria. The primary outcome was the prevalence of hyperuricemia among hypertensive versus normotensive individuals. Secondary outcomes included assessment of serum uric acid levels across different age groups. Statistical analysis was conducted using chi-square tests and comparison of means, with $p < 0.05$ considered significant. Hyperuricemia was observed in 64% of hypertensive patients compared to 21% of controls ($p < 0.001$). Mean serum uric acid levels were 5.58 ± 1.95 mg/dL in adolescents and 8.6 ± 1.76 mg/dL in geriatric patients, with no significant age-related correlation. Hyperuricemia is strongly associated with elevated blood pressure, independent of age, highlighting its potential role as a modifiable risk factor in hypertension management.

INTRODUCTION

Blood pressure is one of most important modifiable risk factors which can be leading cause of death and a major health burden worldwide if left uncontrolled and untreated (Cheng et al., 2017). Its prevalence is mounting in many countries at an alarming rate. Recently, a large community-based epidemiological survey conducted simultaneously in all four provinces of Pakistan comprising ten thousand patients revealed that the prevalence of hypertension in Pakistan was 46 percent. Serum uric acid and blood pressure were found to be continuously correlated in African Americans and Whites, as well as in Asians, including Koreans, regardless of their diverse ethnic backgrounds. Despite high prevalence of hypertension in Pakistan, its association with high serum uric acid levels, has not been established in local studies. The lack of awareness of this important etiology can extend the list of modifiable risk factors for hypertension (Mirzaei et al., 2020).

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Over the past three years, findings from multiple large-scale, longitudinal studies on cardiovascular health have demonstrated that elevated serum uric acid levels can be predictor of both the onset and progression of blood pressure over time (Afroza et al., 2023. Notably, pediatric studies have revealed that more than 90% of children have essential hypertension with associated serum uric acid levels exceeding 5 grams per deciliter, suggesting a potential link between hyperuricemia, hypertension and age.[4] Experimental studies using animal models, particularly rats, have shown that elevated uric acid levels can induce hypertension through several pathways. Therefore, preventative and control measures can be devised to prevent hypertension and cardiovascular illnesses (Ouyang et al., 2022). It is proposed by some authors that controlling serum uric acid levels can delay onset of hypertension.[4] Nonetheless, previous research has produced inconsistent results.[5] Whether or not, the aging process affects serum uric acid in hypertensive patients, is not established yet. Therefore, it is of the utmost important to explore the relationship between serum uric acid and elevated blood pressures for different age groups to identify vulnerable cohort of individuals (Qiu et al., 2013).
Considering these facts, we designed the present study to find the frequency of hyperuricemia in patients who were un-diagnosed with hypertension before and compare serum uric acid levels among them to find for any significant relation to age.

Methodology:
After seeking ethical committee authorization Ref. No: FRPMC-IRB-2024-69, this quasi-experimental study was performed in out-patient clinics of internal medicine at Fazia Ruth Pfau Medical College. Study was performed after obtaining ethical permission. Patients visiting outpatient clinics for mild complaints like fever, flu or sore throat were enrolled into the study with their written informed consent. Study participants were approached by the consultant in their clinic, and they were invited to participate in study. All participants were explained study purpose. The sample size was calculated with help of WHO sample size calculator keeping significance level 5%, power of test 80 percent, the frequency of hyperuricemia to be 74%[6] percent in hypertensives and 25%[6] in non-hypertensives. The sample size came out to be 20. The sample was collected based on the following criteria: **Inclusion Criteria:** Patients with an age range between 18-85 years presenting to medical outpatient department with common cold and mild complaints like fever, flu and sore throat with no history of any chronic disease.

Exclusion criteria: Participants with a history of using antihypertensive drugs or medications that might influence serum uric acid (UA) levels were excluded from the study. Patients with obesity (BMI>30), chronic kidney disease, Gout, inflammatory joint diseases and Diabetes mellitus were also excluded.
Written informed consent was taken from all participants. The blood pressure of patients was measured by manual method at reception. All patients were approached by the consultant in their clinic, and they were invited to participate in study. The patients who had higher blood pressure were advised to take rest for thirty minutes and then blood pressure was re-checked with non-invasive blood pressure monitor (Life Scope, BSM-2500, Nihon Kohden). The average of three readings taken from NIBP monitor 15 minutes apart was taken as final reading to label a patient hypertensive. Hypertension was outlined as a systolic pressure of greater than equal to 140 mmHg or a diastolic pressure of greater than equal to 85mmHg. All participants were explained study purpose. Serum uric acid samples were taken from all patients who consented to participate. The blood samples were processed in the hospital laboratory for blood and uric acid analysis. Anthropometric measures including weight in kilograms and height in centimeters were recorded to calculate body mass index (weight in kilograms / height in meters^2). Hyperuricemia was termed as a serum uric acid level exceeding 7 milligram per deciliter in males and 6.0 milligram per deciliter in females. The primary outcome was the frequency of hyperuricemia in hypertensives compared to controls with normal blood pressure. The secondary outcome was a comparison of uric acid levels among hypertensives. Age was divided into five categories, Adolescents (18-21 years), young (22-35 years), early middle-age (36-55

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years), Late middle-age (56-65 years), Old age (66-80), Geriatric (>80 years). Another parameter recorded was the gender of patients. The study flow involved the following stages: Assessment of eligibility, Enrollment, Follow-Up and Analysis. (Figure-1)

The data was collected and analyzed using SPSS software version 26. Variables were categorized as either quantitative or qualitative. For qualitative variables that did not exhibit a normal distribution, the median and interquartile range were calculated. Quantitative variables were summarized using the mean ± standard deviation (SD), while frequencies and percentages were used to describe qualitative variables. To compare frequency of hyperuricemia between the two groups, a chi-square test was performed and to compare uric acid levels among hypertensives, one sample chi-square test was used. The significance was evaluated using a p-value. A p-value below 0.05 was considered statistically significant.

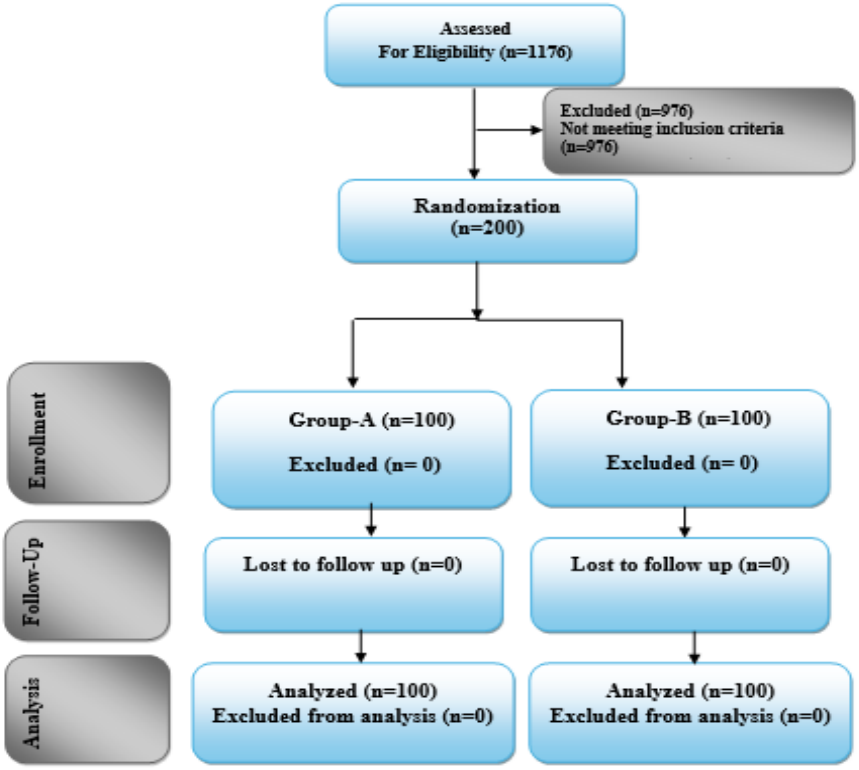

Figure-1: Consort flow diagram of study

Results:

A sample of 0f 200 patients was collected from the medical OPD after scrutiny of 1176 patients based on inclusion and exclusion criteria. One hundred patients with high blood pressure were recruited and 100 aged-matched, non-hypertensive controls were also enrolled. The primary outcome was the frequency of hyperuricemia in both hypertensive and non-hypertensives. There were 9(9.0%) adolescents, 22(22.0%) young and early middle-aged patients, 29 (29.0%) older Middle-Aged, 15 (15.0%) old aged and 3(3.0%) geriatric patients in the study group A. In study group-B there were 12 (12.0%) adolescents, 18 (18.0%) young, 24(24.0%) early middle-aged patients, 24 (24.0%) Older Middle-Aged, 12 (12.0%) old aged 5 (5.0%) geriatric patients in study group B and there was no noteworthy age-related variation with p value of 0.783. The weight, height and BMI had non-normal distribution. The median weight of group-A patients was 68.0Kg with an interquartile range of 65.0-74 Kg and the median weight of group-B patients was 68.0Kg with IQR of 65.0-74.0Kg. The rest of the anthropometric measures also had similar distribution between both study sets with p value of

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Volume 3, Issue 2, 2026

greater than 0.05. There were 56 (56.0%) males and 44 (44.0%) females in group-A and there were 57(57.0%) males and 43 (43.0%) females in study group-B. The demographics have been displayed in Table-I.

The primary outcome was frequency of hyperuricemia in both groups. Sixty-four (64.0%) patients in group-A had hyperuricemia and 36 (36.0) patients had normal uric acid levels. Twenty-one (21.0%) patients in group-B had high serum uric acid levels and 79 (79.0%) had normal serum uric acid levels with p value of <0.001. The mean serum uric acid levels in adolescents was 5.58±1.95 mg/dl and mean serum uric acid levels in geriatric patients was 8.6±1.76 mg/dl with no significant correlation with respect to age. The age-related statistics of all demographic groups are mentioned in Table-II.

Table-I: The demographic profiles of both study groups (n=200)

Parameters		Group-A n=100 Frequency (%)	Group-B n=100 Frequency (%)	p value
Age	Adolescents (18-21 Years)	9 (9.0%)	12 (12.0%)	0.783
	Young (22-35 Years)	22(22.0%)	18 (18.0%)	
	Early Middle-Aged (36-55 Years)	22(22.0%)	29 (29.0%)	
	Older Middle-Aged (56-65 Years	29 (29.0%)	24 (24.0%)	
	Old age (66-80)	15 (15.0%)	12 (12.0%)	
	Geriatric (>80 Years).	3(3.0)	5 (5.0%)	
Gender	Male	56 (56.0%)	57 (57.0%)	0.120
	Female	44 (44.0%)	43 (43.0%)	
		Median (IQR)	Median (IQR)	
Weight (Kg)		68.0 (65.0-74)	68.0 (65.0-74.0)	0.992
Height (cm)		159.0 (156.0-166.0)	159.0 (157.0-167.0)	0.926
BMI (Kg/m^2)		26.0 (24.9-29.3)	27.2 (25.4-29.2)	0.477

Table-II: Frequency of hyperuricemia in both study groups (n=200)

		Group-A n=100 Frequency (%)	Group-B n=100 Frequency (%)	p value
Hyperuricemia	Yes	64 (64.0)	21 (21.0)	<0.001
	No	36 (36.0)	79 (79.0)	

Table-III: The comparison of uric acid levels among different age categories in Group-A (n=100)

		Group-A Frequency (%)	P value
Mean serum uric acid mg/dl)	Adolescents (18-21 Years)	5.58±1.95	0.998
	Young (22-35 Years)	5.9±2.38	1.000
	Early Middle-Aged (36-55 Years)	7.6±2.1	0.966
	Older Middle-Aged (56-65 Years	7.75±2.1	1.000
	Old age (66-80)	6.95±2.49	1.000
	Geriatric (>80 Years).	8.6±1.76	1.000

Discussion:

Our study showed that a significant association existed between hypertension and hyperuricemia. The concealed co-existence of both problems in patients not only implied their explicit association but also exhibited that elevated uric acid levels are raised before the high blood pressure manifests as disease in individuals (Kim et al., 2021). The patients recruited were oblivious to the development of hypertension. Thus, we extrapolate that hyperuricemia can be linked to pathophysiology of hypertension. Sixty-four percent of patients had

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hyperuricemia and hypertension in our study, which cannot be a mere coincidence. With reference to a cross-sectional analysis by Miguel A et al, twenty percent of hypertensive patients with un-treated hypertension had 1mg per deciliter increase in uric acid levels (Cortez et al., 2023). Another cross-sectional research conducted in Nigerians evaluated uric acid in blood of hypertensive individuals and reported a prevalence of fifty nine percent in males and sixty-two percent in females This high prevalence could have been accredited to the low cutoff for uric acid concentration used in their study, which was >5.5 mg/dl for both male and female participants. In contrast, our study applied a cutoff of greater than six milligrams for females and greater seven milligrams for males Daka et al., 2024.

Ning Ding et al, 2022) in their study revealed a linear relationship amongst uric acid levels and blood pressure in the group receiving hypertension treatment. As uric acid levels increased, both systolic & diastolic pressures gradually decreased. Conversely, in the group not receiving treatment for hypertension, the relationship followed an inverted U-shape. They advocated that their study was first to investigate the relationship between uric acid and pressure both systolic and diastolic, in treated & untreated hypertensives. Their study awas done on Chinese population, and we cannot generalize it on Pakistani population. The major difference being difference in salt intake of both populations. The Salt consumption in Chinese population has remained consistently high, with recent data from 24-hour urinary sodium excretion showing an average intake of 11 g/day.[15] This level is more than double the maximum recommended intake of 5 g/day set by the WHO. In Pakistan the average salt intake is 8.7 grams per day (Feig & Johnson, 2003).

Cheng et al[17] indicated that the connection between hyperuricemia and hypertension is primarily observed in younger individuals within a healthy Chinese population with normal blood pressure, serum kidney function and lipid profiles. The association was particularly identified with participants aged 41 to 50 years but was not evident in those aged 51 to 70 years. A similar link relating uric acid to hypertension was highlighted by Woohyeun Kim et in their study. They also notified an association between uric acid and high blood pressure based on age and sex, with younger women being the most susceptible to uric acid-related hypertension. There were no significant age-related and gender related differences in uric acid levels between study groups in our study. According to Roxana Buzas et al younger hypertensives exhibited significantly lower serum uric acid levels compared to elderly hypertensives regardless of glomerular filtration rate. Additionally, younger adults had notably lower intima-media thickness levels in comparison to elderly individuals. According to them, the impact of age on hypertension management was still a topic of debate. Their study was cross-sectional study conducted on American population, and we performed quasi-experimental study on Pakistani population (Elahi et al., 2023).

Sasaki et al performed a retrospective cohort study involving six thousand participants who were normotensive and normoglycemic with an average age of 64.6 years had serum uric acid levels up to 5 grams per deciliter. Almost 2000 patients developed hypertension in six years follow-up. They suggested that these patients might have been benefit from targeted interventions aimed at managing serum uric acid levels as a preventive strategy. This means addressing elevated serum uric acid level's role in reducing the likelihood of hypertension onset and improving long-term cardiovascular in this group could play a crucial health outcome.

According to systematic review performed by Yang Wang et al, high uric acid levels are strongly correlated to the development of hypertension in adolescents and to prehypertension. Additionally, the use of urate-lowering medications has been shown to be effective in treating preliminary hypertension. According to them, salt sensitivity of blood pressure was affected by uric acid levels of blood and a two-phase process mediated it. Initially, stimulation of the local renin-angiotensin-aldosterone pathway triggered renal damage, followed by disruptions in sodium regulation, which increases salt sensitivity (Zhou et al., 2024).

We performed a prospective, quasi-experimental study which showed that hypertension has high prevalence, and it is linked to high serum uric acid concentration and this combination was found in patients who were oblivious to their presence.

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Volume 3, Issue 2, 2026

Recommendation of study: Monitoring uric acid levels can help identify potential contributors to hypertension and guide early interventions, such as lifestyle modifications or targeted therapies, to improve blood pressure control and reduce the risk of associated complications

Limitations of study: We only performed serum uric acid levels in patients who had high blood pressure in OPD. We advised follow-up to patients who had high serum uric acid levels, but did not include that detailed work-up in our study as main objective was to measure serum uric acid levels as preliminary investigation. There is need for detailed trials on the subject.

Conclusion: We concluded that hyperuricemia has a strong association with high blood pressure but there are no statistically significant age-related differences.

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