

FREQUENCY OF HYPERURICEMIA IN HYPERTENSIVE PATIENTS AND ITS ASSOCIATION WITH AGE OF PATIENT

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ABSTRACT

Objective: To determine the frequency of hyperuricemia in hypertensive patients and its association with the age of patients.

Study Design: Cross sectional analytical study.

Place and Duration of Study: Combined Military Hospital Abbottabad, from Sep 2016 to Feb 2017.

Methodology: All patients of 18-70 years of age with either gender presenting in and out patient departments with hypertension were enrolled. Serum uric acid was measured. Analysis of serum uric was done with Selectra XL chemical analyzer having normal references range of 2.52-6.97 mg/dl for males and 1.51-6.0 mg/dl for females. Reports were verified by Pathologist.

Results: A total of 137 patients were selected for the study. Mean age of the patients was 56.09 ± 09.36 years. There were 76 (55.50%) patients with >55 years of age while 61 (44.50%) patients were presented with ≤ 55 years of the patients. Male preponderance was higher 83 (61%) as compared to females 54 (39%). Mean weight, height and Body Mass Index of the patients was 67.99 ± 6.91 kilograms, 1.63 ± 0.08 meters and 25.32 ± 2.15 kg/m² respectively. Mean systolic blood pressure of the patients was 166.71 ± 13.67 mmHg. Mean Diastolic blood pressure was 100.15 ± 8.84 mmHg. Mean serum uric acid level was 6.96 ± 0.82 mg/dl. Frequency of hyperuricemia was found in 102 (74.45%) while normouricemia in 35 (25.55%) patients.

Conclusion: Frequency of hyperuricemia was found higher in hypertensive patients and it was not associated with the age of patients.

Keywords: Hypertension, Hyperuricemia, Serum uric acid level.

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INTRODUCTION

One of the leading causes of death and disability across the globe is hypertension with 3.4 million deaths taking place worldwide in 2010¹. In Pakistan, hypertension frequency was 16.2% in the rural and 21.6% in the urban population².

Hyperuricemia is a condition in which there is abnormally higher level of uric acid is found in the blood or plasma. Nucleic acid metabolizes to give rise to uric acid as the final and last product. Although purine can be taken orally but it contributes much less fraction of body purines as larger amount of purines is biosynthesized than taken orally³. The presence of uric acid-binding proteins increases the physiological solubility of uric acid to 7.0 mg/dl from normal value of 6. This causes crystallization of uric acid in human

body.

The value of serum uric acid can vary and depends on geographical location, gender, dietary habits and medications⁴. Adenosine Tri Phosphate is the major energy molecule in human body and its metabolism produces uric acid which is further increased in cases of anaerobic respiration and conditions like hypertension. Xanthine Oxidase inhibitors (i.e., allopurinol and febuxostat) are effective in treatment of hyperuricemia due to excessive uric acid production⁵.

The prevalence of hypertension is around 21.6% in males and 8.6% in females in normal population. Previous local literature indicated that in Pakistani population the prevalence of Hyperuricemia in Hypertensive patients was 65% which was considerably higher than the expected rate⁶. Hypertension is also a major risk factor for cardiovascular mortality which is the leading cause of death worldwide with about 17.4 million

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annually⁷. Studies have shown that a blood pressure of 160 mm Hg or higher in absence of target organ damage and diabetes or cardiovascular disease is independently associated with poorer mortality⁸.

Hypertension is also a major contributing risk factor for Cerebrovascular accidents such as hemorrhagic infarct, subarachnoid hemorrhage and other intra and extra cerebral bleeds⁹. Blood pressure control amongst patients of type 2 Diabetes has also shown to reduce both micro and macro vascular complications^{10,11}.

Hyperuricemia not only increase the risk of development of hypertension but also found to be increased in established hypertension. It was found that an increase in serum uric levels by 1 mg/dl increased the prevalence of hypertension by 1.2-fold. Lowering the levels of uric acid has shown to reduce the blood pressure in young obese individuals¹². Uncontrolled Blood Pressure related to high serum uric acid levels can present even without other features of metabolic syndrome so Uric acid levels need to be taken into considerations in strategies for BP management¹³.

Our study is aimed at delineating an association between essential hypertension and hyperuricemia in the absence of other confounding factors. Also studied during our research was the effect of age on uric acid levels in hypertensive patients. In our population, such an association could be helpful in the development of future anti-hypertensive strategies and better management of blood pressure.

METHODOLOGY

It was a cross sectional analytical study, that was carried out at Combined Military Hospital, Abbottabad, from September 2016 to February 2017. Sample size (n) was 137 and was calculated using WHO sample size calculator with margin of error 5%, confidence interval 95%, anticipated population proportion 65% and absolute precision required 0.08. Hypertension was defined as blood pressure of $\geq 140/90$ mmHg on two occasions, measured as per parameters, described in JNC-8 guidelines. Hyperuricemia was labeled as

serum uric acid level greater than 6.97 mg/dl for males and more than 6.0mg/dl for Females.

Non-probability consecutive sampling technique was employed. Having taken approval from hospital Research Ethics Committee and informed consent, patients from both genders, having age between 18 to 70 years, presenting in and out patient departments with hypertension, according to operational definition, were enrolled in the study. People with secondary hypertension, gout, diabetes mellitus, chronic kidney disease, psoriasis, BMI >30 and using thiazide diuretics were excluded from data collection. Serum uric acid levels were measured using Selectra XL chemical analyzer having normal references range of 2.52-6.97 mg/dl for males and 1.51-6.0 mg/dl for females. Tests were carried out at Combined Military Hospital Abbottabad laboratory. All the reports were verified by Pathologist.

Data was entered and analyzed using SPSS version 20. For quantitative variables like age, serum uric acid levels, blood pressure and BMI, mean \pm SD was calculated. For qualitative variables like gender, normouricemia and hyperuricemia frequency and percentage was calculated. Post-stratification chi-square test was applied and *p*-value ≤ 0.05 was taken as significant.

RESULTS

A total of 137 patients were enrolled in the study. Among them, 83 (61%) were male while 54 (39%) were female. Mean age of the patients was 56.09 ± 09.36 years with minimum age 37 and maximum 70 years. Seventy six (55.50%) patients had age greater than 55 while 61 (44.50%) patients were younger than or equal to the age of 55. Mean weight, height and BMI of the patients were 67.99 ± 6.91 kg (ranging from 54 to 84 kg), 1.63 ± 0.08 m (ranging from 1.44 to 1.83 m) and 25.32 ± 2.15 kg/m² (ranging from 20.4 to 29.9 kg/m²) respectively. Maximum systolic blood pressure was 193 mmHg and minimum was 143 with mean of 166.71 ± 13.67 mmHg. Similarly, maximum diastolic blood pressure was 121 mm Hg and minimum was 90 mmHg with mean of 100.15 ± 8.84 mmHg. Mean serum uric acid level

was 6.96 ± 0.82 mg/dl with range of 8.44 to 4.93 mg/dl. Frequency of hyperuricemia was found in 102 (74.45%) while Normouricemia in 35 (25.55%) patients as shown in figure.

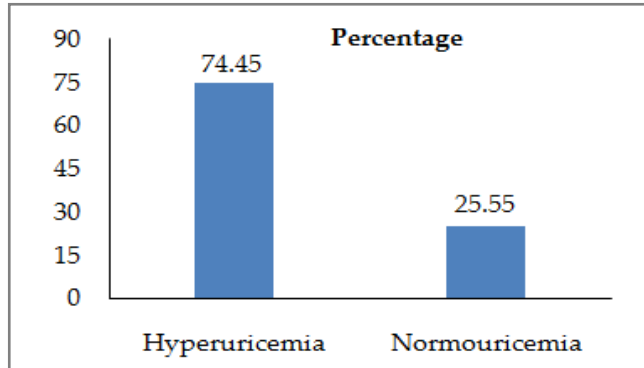


Figure: status of hyperuricemia (n=137).

Table-I: Comparison of uricemia status with age of female patients.

Age (years)	Status of Uricemia		p-value
	Hyperuricemia	Normouricemia	
≤55	23 (85.18%)	4 (14.81%)	0.033
>55	16 (59.25%)	11 (40.74%)	

Table-II: Comparison of uricemia status with age of male patients.

Age (years)	Status of Uricemia		p-value
	Hyperuricemia	Normouricemia	
≤55	23 (67.65%)	11 (32.35%)	0.143
>55	40 (81.63%)	9 (18.37%)	

Table-III: Comparison of uricemia status with gender of the patients.

Gender	Status of Uricemia		p-value
	Hyperuricemia	Normouricemia	
Male	63 (75.9%)	20 (24.1%)	0.629
Female	39 (72.22%)	15 (27.8%)	

DISCUSSION

The relationship between high serum uric acid levels and development and progression of hypertension has been a topic of interest for researchers over the last few years. This is because of the morbidity and mortality associated with hypertension and its consequences. Hyperuricemia in itself has detrimental effects on human physiology and a further association with hypertension would only compound the harmful nature of this by-product. Our study results showed that there was an increased incidence of hyperuricemia in patients of hypertension. Conversely,

our study results also showed that age did not have any significant effect on the uric acid levels in hypertensive patients. When we compared the results of our study with those of other studies conducted with similar parameters in different parts of the world, following comparisons and similarities were drawn which will be elaborated further in subsequent discussion.

In one study carried out by Tanaguchi *et al* in Osaka, Japan, it was observed in male population, that patients with hyperuricemia were more likely to develop hypertension than those with normal uric acid levels¹⁴. This is in consonance with the conclusions drawn in our study.

In one of the studies carried out by Dasti *et al* in 2015 in a rural setting within Pakistan, the frequency of hyperuricemia was found to be 65% in hypertensive patients, having a mean value of serum uric acid level of 13.74. This was also found to be statistically significant with reference to age ($p < 0.01$) and gender ($p < 0.05$)⁶. This varies from our study in that whereas we did find a positive association between hyperuricemia and hypertension, no such association was seen in terms of age.

In another study carried out within Pakistan, Bilal *et al* found that hyperuricemia was found to be present in approximately 42% of hypertensive patients. This was less than the previously quoted study. Similar to our study, Bilal *et al* did not find any significant association between age and hyperuricemia in these patients, having p -value of 0.380. Age group 30 to 55 years showed hyperuricemia was present in 44% of patients and above 55 years it was found in 45% of hypertensive patients¹⁵.

A study carried out in Sub Himalayan India by Raina *et al* revealed that the prevalence of hyperuricemia was higher in hypertensive patients than normotensive patients ($p < 0.05$). This study also elaborated on the effect of gender on uric acid levels in both hypertensive and normotensive patients and showed that not only was the prevalence of hyperuricemia higher in male patients as compared to female hypertensive pati-

ents but mean serum uric acid level was also higher in male patients as compared to females¹⁶.

Mazza *et al* concluded in their study carried out in 2017 that hypertensive patients with raised uric acid levels were at a higher risk of developing resistant hypertension i.e. hypertension not controlled with at least 3 first line anti-hypertensive medicine than normouricemic patients. This further substantiates the effects of hyperuricemia on hypertension¹⁷.

Adejumo *et al* conducted a study in Nigeria in 2017 in which they studied the effects of hyperuricemia on patients of pre dialysis Chronic Kidney Disease patients. In their study they also observed that patients with normal uric acid levels were more likely to have a better controlled blood pressure and were more likely to survive longer without the requirement of dialysis than those with raised uric acid levels¹⁸. Similar results were also seen in an Indian study conducted by Sircar *et al* where they observed that controlling hyperuricemia by using Febuxostat in Chronic Kidney Disease patients not only improved glomerular filtration rate but also improved blood pressure control¹⁹. Both these studies high light the role of uric acid in progression of disease in hypertensive patients.

Finally in a Chinese study carried out by Wang *et al* in 2016, it was observed that hyperuricemia was more frequent in hypertensive patients that in normotensive patient with other features of metabolic syndrome. There was also an association seen between obesity and higher uric acid levels in this study, however our study did not focus on this variable²⁰.

In our study, frequency of hyperuricemia was found in 74.45% of hypertensive patients; however it is not associated with age of the patients. In male patients hyperuricemia was present in 67.65% patients aged 55 years or less and in 81.63% of patients with age over 55 years with a *p*-value of 0.193. In female patients, hyperuricemia was present in 85.18% of patients aged less than 55 years and in 59.25% in patients aged over 55 years with a *p*-value of 0.033.

It was therefore recommended that more studies should be done on the subject to enhance the epidemiological basis and more diverse parameters may be studied independently to further clarify the role of each variable in the development of hypertensive complications. Studies should also be carried out to find out the effects of treating raised uric acid levels on the development and progression of hypertension and other cardiovascular risk factors in our population.

CONCLUSION

There was association between uric acid level and hypertension. Frequency of hyperuricemia was found higher in hypertensive patients and there was no association between hyperuricemia and age of patient.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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