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# HYPERURICEMIA;
## A RISK FACTOR FOR DEVELOPMENT OF HYPERTENSION IN PAKISTANI COMMUNITY.

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**ABSTRACT… Objectives:** To determine the association of hyperuricemia with hypertension. **Study Design:** Case-control study. **Place and Duration of Study:** Out-patient department of Fuji foundation hospital, Rawalpindi. The study conducted over a period of six months from 1st February 2012 till 31st July 2012. **Methodology:** 268 patient were selected for study and divided into two groups on the basis of presence or absence of hypertension (group 1 comprised of newly diagnosed hypertensive patients and group 2 comprised normotensive individuals). Each group comprised 134 patients fulfilling inclusion/ exclusion criteria. Serum uric acid levels were checked and compared in both groups. **Results:** In hypertensive group, the minimum age was 20 years and the maximum age was 100 years with a mean age of 50.76. Minimum uric acid level was 193/literμmol and maximum uric acid level was 608 μmol/L with a mean of 316.87. In non-hypertensive group, minimum age was 20 years and the maximum age was 80 years with a mean age of 47.84. The minimum uric acid level was 125μmol /L and the maximum was 404μmol/L with a mean of 273.24. The P-value was 0.000 which means that the difference between the two groups was statistically significant. **Conclusion:** There is statistically significant association of hyperuricemia with hypertension. More studies are recommended to establish this fact.

**Key words:** Hypertension, Uric Acid, Blood Pressure, Metabolic Syndrome.

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## INTRODUCTION

Hyperuricemia is a part of metabolic syndrome and a common health problem. Two third patients of hyperuricemia remain a symptomatic.[1] It clinically presents in two forms. First Uric acid Crystal deposition in the form of Gout[2], and second in raised serum uric acid levels which present in associations with Hypertension, insulin resistance, chronic kidney disease, cardiovascular disease and obesity.[3] Hypertension share a major health burden all other the world. Though exact cause of hypertension is not known but is considered as multifactorial and raised serum uric acid concentration is considered as an independent risk factor for that. A number of mechanism have been considered leading to development of hypertension in hyperuricemic individuals. One of these mechanism includes uric acid induced vascular injury of pre renal vessels through stimulation of rennin angiotensin system.[4] This hypothesis is gaining more attention by a study performed on rodents in which uric acid associated hypertension and arteriopathy was observed. This idea was further strengthen by a randomized clinical trial performed on 30 adolescents. All the study population was hypertensive and hyperuricemic at a time. One group received uric acid lowering agents (Allopurinol) and significant reduction in hypertension was noted in that group.[5] While no such change was noted in a group where no such interventions were performed. However it is yet to establish whether any of such interventions lower hypertension in adults or not who share a large burden of hypertension.[6] Though a number of studies have established the fact that hyperuricemia is a risk factor for hypertension but it is to check weather all hypertensive patients have preexisting hyperuricemic or not. It is also observed that hyperuricemia is more associated with diastolic hypertension as compare to systolic hypertension. Dietary practices has

also a role in rising trends in uric acid levels in general population. Urbanization, frequent use of artificial sweeteners, table sugars, and other forms of fructose consumption in modern human diets may have played a role in hyperuricemia. It is said that fructose rapidly depletes ATP and thus cause rise in serum uric acid levels. This was further studied in rats by Nakagawa. Fructose was given to all rats and one group was given uric acid lowering agent (Allopurinol) others group did not. Group who was not given Allopurinol they develop hypertension, weight gain, insulin resistance and hypertriglyceridemia while the group who received allopurinol did not develop such presentation. Association of hypertension and hyperuroicemia is also noticed in low birth weight babies. Hyperuricemia also cause renal damage including both renal vasculature and interstitial, this may be the other mechanism of development of hypertension via chronic renal injury in hyperuricemic individuals.[7] In our study we are trying to observe the association between hyperuricemia and hypertension in local population, in case of establishment of association, we can improve the control of hypertension via uric acid lowering agents and avoid the future risk of cardiovascular damage mediated by hypertension and hyperuricemia, both.

## METHODOLOGY

After approval of ethical review board of institution, 268 patients were selected for the study. Study designed as case control study, conducted at outpatient department of fauji foundation hospital, Rawalpindi. Study conducted over a period of six months from 1st February 2012 to 31st July 2012. Sampling technique used was Consecutive non-probability sampling. Sample size calculated by using WHO calculator for sample size. Sample comprised of total 268 patients, divided into 2 groups, each group consisted of 134. Power of test was 80%, Level of significance: 5%, anticipated population proportion 1: 25% and anticipated population proportion 2:13.10%. study population included both genders, of age 20 years and above Patients who were newly diagnosed as having essential hypertension distributed in study group while non-hypertensive patients were included in control group while Patients who had diabetes, diagnosed case of secondary hypertension, diagnosed case of chronic kidney disease or those taking uric acid lowering drugs excluded from the study. Informed consent was taken from all the patients included in this study. Group 1" included subjects who were newly diagnosed with hypertension (criteria for hypertension was taken as per American heart association i-e systolic blood pressure 140 mmHg or more while diastolic blood pressure 90 mmHg or more at two or more than 2 occasions) and "Group 2" included subjects without hypertension or any other condition which affects uric acid levels who met the laid down inclusion/ exclusion criteria were enrolled in study. Blood pressure was recorded on the same day on two separate occasions at least 2 hours apart, by standardized mercury sphygmomanometer. Mean BP was recorded. 2 ml of blood sample was drawn for serum uric acid levels and were send to pathology lab Serum uric acid was measured by micro lab 200 analyzer using end point method. Results had been verified by a consultant pathologist. The study variables were recorded on a proforma. Data analysis was performed on SPSS version 17. Mean and standard deviation was calculated for numerical variable like serum uric acid level in both groups. Frequency and percentages were presented for categorical variable like gender and hyperuricemia in each group. Odds ratio was calculated. Chi square test was used to determine the difference in hyperuricemia in two groups. P value $< 0.05$ was considered significant.

## RESULTS

A total of 268 patients were included in the study. These patients divided into 2 groups, each group comprised 134 individuals. (134 hypertensive and 134 non-hypertensive).

In hypertensive group, there were 134 patients, 30 were males and 104 were females. In hypertensive patients, the minimum age was 20 years and the maximum age was 100 years. (Figure-3)The minimum uric acid level was 193 micromoles/litre and the maximum uric acid level was 608 micromoles/liter. In non-hypertensive group, there were 134 patients in all. 30 were

males and 104 were females. The minimum age was 20 years and the maximum age was 80 years. (Figure-3) The minimum uric acid level was 125 micromoles/litre and the maximum uric acid level was 404 micromoles/liter. Table-III shows that by applying the Chi-square tests to compare hyperuricemia between the two groups the P-value was found out to be 0.000, whichis statistically significant (Table-III).

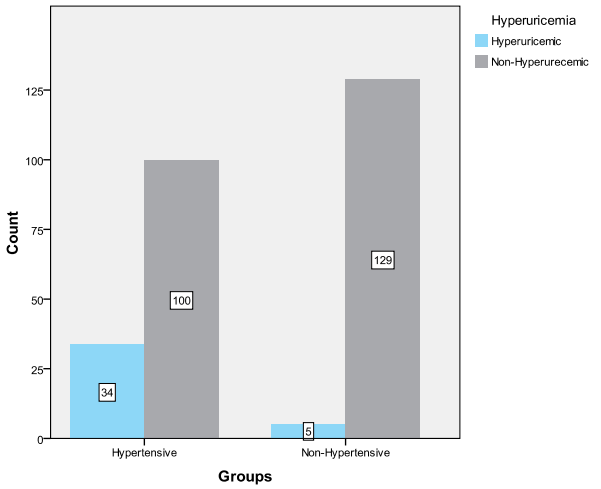


**Figure-1. Total number of hyperuricemic and non-hyperuricemic patients in both groups.**

## DISCUSSION

Hypertension shares major health burden and constant cause of morbidity especially in elderly. Sufficient data is available to consider an association between hyperuricemia and hypertension but still there is a controversy that whether uric acid has an independent causative role or just a mediator.

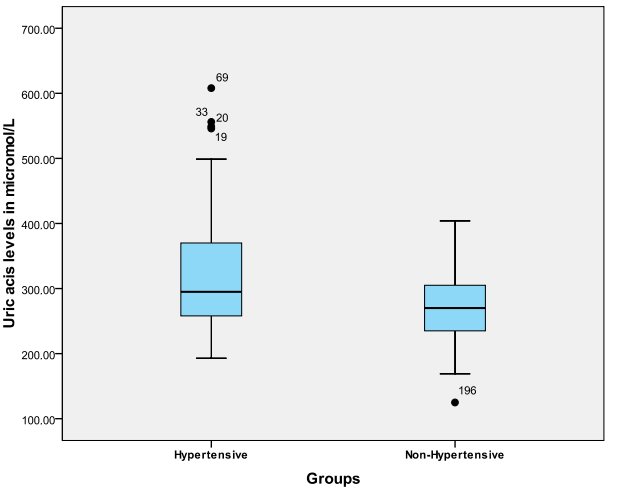


**Figure-2. Boxplot showing distribution of uric acid level between hypertensive and non hypertensive group**

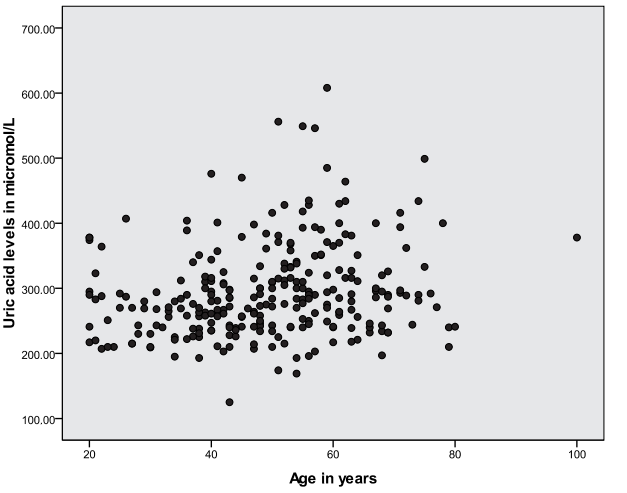


**Figure-3. Scatter diagram showing distribution of uric acid level according to age in study population.**

| Hyperuricemia * Groups Crosstabulation | | | | | |
|---|---|---|---|---|---|
| | | | Groups | | |
| | | | Hypertensive | Non-hypertenisve | Total |
| Hyperuricemia | Hyperuricemic | Count<br>% within Hyperuricemia | 7<br>100.0% | 0<br>.0% | 7<br>100.0% |
| | Non-hyperurecemic | Count<br>% within Hyperuricemia | 23<br>43.4% | 30<br>56.6% | 53<br>100.0% |
| Total | | Count<br>% within Hyperuricemia | 30<br>50.0% | 30<br>50.0% | 60<br>100.0% |

**Table-I. Hyperuricemia-groups cross tabulation in male population**
a. Gender = Male

| Hyperuricemia * Groups Crosstabulation | | | | | |
|---|---|---|---|---|---|
| | | | Groups | | |
| | | | Hypertensive | Non-hypertenisve | Total |
| Hyperuricemia | Hyperuricemic | Count<br>% within Hyperuricemia | 27<br>84.4% | 5<br>15.6% | 32<br>100.0% |
| | Non-hyperurecemic | Count<br>% within Hyperuricemia | 77<br>43.8% | 99<br>56.3% | 176<br>100.0% |
| Total | | Count<br>% within Hyperuricemia | 104<br>50.0% | 104<br>50.0% | 208<br>100.0% |

**Table-II. Hyperuricemia-groups cross tabulation in Female population**
a. Gender = Female

| | Value | df | Asymp. Sig. (2-sided) | Exact Sig. (2-sided) | Exact Sig. (1-sided) |
|---|---|---|---|---|---|
| Pearson Chi-Square | 25.237(b) | 1 | .000 | | |
| Continuity Correction(a) | 23.526 | 1 | .000 | | |
| Likelihood Ratio | 27.877 | 1 | .000 | | |
| Fisher's Exact Test | | | | .000 | .000 |
| Linear-by-Linear Association | 25.142 | 1 | .000 | | |
| N of Valid Cases | 268 | | | | |

**Table-III. Association of hyperurecemia with Hypertension**
a. Computed only for a 2x2 table
b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 19.50.

Proposed mechanisms based on animal studies suggests few basic mechanisms for uric acid that are responsible for damage to vascular endothelium, inflammation of blood vessels and activation of rennin angiotensin aldosterone axis. As renal injury is a common association of both hypertension and hyperuricemia and few other common mediators also play a role that's why it is complicated and difficult to identify exactly the mechanisms involved. However there are certain studies which conclude that if we treat hyperuricemia in hypertensive individuals via uric acid lowering agents not only it reduced serum uric acid levels but, marked reduction in hypertension as well this intervention further strengthen the association between hypertension and hyperuricemia.[8] Through this study we have tried to examine the association between uric acid level and elevated blood pressure. The hypothesis of this study was that there is association of hyperuricemia with hypertension. Our study supported this hypothesis as the test of association Chi-square shows value 0.001 which is statistically significant (Table-III) and the difference in hyperuricemia of age and gender matched hypertensive and non-hypertensive patients were alsosignificant. In our study there were 134 patients each in hypertensive and non-hypertensive group. In hypertensive group 34 patients were hyperuricemic and 100 patients were non hyperuricemic. Whereas in non hypertensive group only 5 patients were hyperuricemic (Figure-1). Our study revealed that in the hypertensive group the minimum uric acid level was 193 micromoles/liter and the maximum uric acid level was 608 micromoles/liter with a mean of 316.87 micromoles/liter and a standard deviation of 81.99 in this group. (Figure-2 shows box plot distribution of uric acid levels in both hypertensive and normotensive groups). The mean uric acid level was 348.13 micromoles/liter in men and 307.86 micromoles/liter in female hypertensive patients. The overall prevalence of hyperuricemia was 14.6 %. Hyperuricemia in males was 11.7 % while in females it was 15.4 %. In males all hyperuricemics were hypertensive (100%) while in females 84.4% hyperuricemics were hypertensive (Table-I and Table-II). Table-III shows that by applying the Chi-square tests to compare hyperuricemia between the two groups the P-value was found out to be 0.000 which means that the difference between the two

groups was statistically significant.

If compared with another study conducted by Li-yingchen[9] et al the overall prevalence of hyperuricemia was 13.10% which is comparable to my study. The condition was more common in men than in women (19.07% vs. 3.42%). The mean uric acid level was 5.77 mg/dl (micromoles/liter) in men and 3.67 mg/dl (micromoles/liter) in female hypertensive patients. In that study in men hypertensive hyperuricemics percentage was 37.5 while female hypertensive hyperuricemic patient's percentage was 32.26 which is considerably less than my study. One of the reasons of this variability may be the difference of ethnicity among study populations.

In another study conducted on US adolescents by Lauren F. Loeffler et al,[10] to check the association between hyperuricemia and hypertension. In this study mean age was 14.5 years and the mean uric acid level in normotensive group was 5 mg/dl and 5.6 mg/dl in hypertensive group. 6% of males and 9% of females had high uric acid level. This means that the prevalence of hyperuricemia in females was more than males. This is comparable to my study in which the prevalence of hyperuricemia is more in females than males. By stratification, analysis in above study; showed that the odds ratio was 1.45 (95% CI, 1.17-1.80) in male for rise in blood pressure for each 0.1 mg/dL increase in uric acid levelswhile in female it was 1.17 (95% CI, 0.84-1.61). Similarly the corresponding odds ratios of elevated blood pressure) were 2.23 (95% CI, 1.16-4.31) in males and 1.73 (95% CI, 0.95-3.13) in females for uric acid level ≥5.5 mg/dL (59.485*5.5). This study concluded that increasing levels of serum uric acid levels were associated with high blood pressure in healthy U.S adolescents. Adolescentswere chosen for this study because of relatively healthy status and less presence of comorbidities which are relatively more commonly present in elderly subjects. In another study, done by D conen et al[11] the prevalence of a high serum uric acid in men was 35.2% while in women it was 8.7% which is again different from results of my study. But uric acid association with hypertension was still significant in aforementioned study which is comparable to result of my study. The mean serum uric acid level in men was 408.7 micromoles/litre while in women it was 264.3 micromoles/litre. In that study they measured those hypertensive patients whose blood pressure was above 160/100 and who were hyperuricemics .In men this percentage was 35.9% and in women it was 40.2%.

In my study, the mean age of participants was 49.3 whereas in above mentioned study it was 44.7 in men and 44.5 in women. This difference in age as well as different population group may explain the prevalence of higher uric acid level in women in my study which is opposed to above mentioned study.

The limitations of our study include:

1. The male population was less as compared to female population in my study because in our hospital setting mostly families of army personal are entitled.
2. This study did not include the children and adolescents.
3. Relatively low sample size.

The implications of my study include:

1. It leads to the requirement of further studies to be carried out on a large number of Pakistani population.
2. This may help to screen people for hyperuricemia by which we can identify individuals at risk of developing hypertension. Measures could be then taken to reduce serum uric acid levels so that we can eliminate an important risk factor which can latter lead to HTN.

## CONCLUSION

From our study we concluded that there is statistically significant association of hyperuricemia with hypertension. Therefore it is recommended to screen the population for higher uric acid levels and those who are hyperuricemics should be strictly followed for development of hypertension. Every possible measure should be taken to reduce uric acid levels. Further similar studies are recommended in our population to establish the effect of hyperuricemia as a causative factor in development of hypertension.

It is also recommended that studies should be carried out on hypertensive hyperuricemics.



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*you'll be waiting the rest of your life.*

**– Unknown –**

## AUTHORSHIP AND CONTRIBUTION DECLARATION

| Sr. # | Author-s Full Name | Contribution to the paper | Author=s Signature |
|---|---|---|---|
| 1 | M. Saqib Habib | Concept, Study design, Data collection. | |
| 2 | Shafat Khatoon | Intellectual concept, Data analysis, discussion. | |
| 3 | Aijaz Ahmed Sand | Study design, Data collection. | |