Influence of Serum Uric Acid on Mean Arterial Pressure in Females in Local Population

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Abstract

Objective: To find out the relationship and effect of hyperuricemia on mean arterial pressure in local population.

Material and Methods: The Study design was Cross sectional and the setting was in Lady Aitchison hospital Lahore. Duration of this this was March 2017- August 2017. Written informed consent was taken prior to data collection. Detailed history was asked. Mean arterial pressure was calculated by measuring systolic and diastolic blood pressures and putting them in the formula: MAP = diastolic pressure + 1/3 (pulse pressure). Uric acid was measured by uricase method after taking 1 ml venous blood under aseptic measures.

Result: A total of 60 patients with increased serum uric acid levels, with Mean Arterial Pressure ranging between 83.33 and 126.67 were considered. We use simple linear regression model and see the effect of Uric Acid on Mean Arterial Pressure. The model shows that for 1 mg/dl increase in Uric Acid, Mean Arterial Pressure increases by 14.89 at 5% level of significance. 72.74% of the variation in the Mean Arterial Pressure can be defined using the Uric Acid. Conclusion: Positive relationship has been seen between hyperuricemia and mean arterial pressure.

Keywords: Hyperuricemia, systolic blood pressure, diastolic blood pressure (DP), pulse pressure (PP) mean arterial pressure (MAP), hypertension.

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Introduction

Serum uric acid is the end product of purine metabolism.[1] Uric acid is produced both by exogenous and endogenous sources. Exogenous sources depend upon dietary intake of animal proteins, high fructose intake, alcohol consumption etc. while endogenous source is from liver, muscles, intestines, vascular endothelium and kidneys.[2] Its concentration in the serum is an important parameter regarding human well being. Normal level of uric acid in males is between 3.5 and 7.0 mg/dl and in females, between 2.5 and 5.7 mg/dl.[3] This level may be increased either due to increased production by liver or decreased excretion by intestines or kidneys. Clinical condition in which the level exceeds the normal range is called hyperuricemia, the prevalence of which is being increased gradually over the last 40 years. It has reached up to 21% in general population of United States and even double in South East Asia (52%).[4]

Hyperuricemia imparts great burden on health as documented by various researches which have confirmed direct or indirect correlation of hyperuricemia with a number of other diseases like gout, diabetes mellitus, hypertension, kidney diseases, and heart failure.[5] Besides, it is also a source of vascular diseases as it produces reactive oxygen species.

Hypertension, commonly known as high blood pressure, is a rapidly growing public health issue. According to 2017 guideline, a patient is considered to be hypertensive

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if his systolic BP ≥ 130 mmHg or a diastolic BP ≥ 806. It is also called silent killer as it is considered as one of the leading risk factors for various cardiovascular diseases, kidney disorders, brain and other diseases.[7] Globally prevalence of hypertension came out to be 31 - 56 %.[8] The ranking of hypertension has changed from fourth in 1990 to second and first in men and women respectively by 2017. It shares the mortality rate of millions of patients in the world. Worldwide around 7.5 million (12.8%) of the total deaths per year occur due to hypertension.[9] The number will reach 1.56 billion adults by 2025.

Mean arterial pressure is the average calculated blood pressure in one cardiac cycle, and is calculated by the formula: MAP = DP + 1/3(PP).[10] Normal value of MAP is considered between 70 and 100 mmHg. It has been observed through researches that, to predict adverse events of hypertension, high systolic blood pressure is more significant in patients of age greater than 50 years and high diastolic blood pressure in hypertensive individuals of age lesser than 50 years. So, probably due to different importance allocated to systolic and diastolic blood pressures, mean arterial pressure is considered to be used both for the purpose of diagnosis and statistical analysis of blood pressure as compared to systolic and diastolic blood pressure separately and hence as a better alternative predictive tool for assessment of adverse outcomes of hypertension.[11]

In addition to the above-mentioned causes of hyperuricemia, the subjects who have elevated levels of triglycerides, low-density lipoprotein, total cholesterol, apolipoprotein-B levels, ratio of triglycerides to high-density lipoprotein cholesterol in their serum are at more risk for its development. Moreover, a 4-fold or greater prevalence of hyperuricemia has been noted in patients with uncontrolled blood pressure[5] This is due to under excretion of uric acid through kidneys rather than its over-production. So, a bidirectional relationship is considered between hyperuricemia and hypertension.

Most of the studies done so far paid little attention to see the relationship of uric acid level and mean arterial pressure. So, this cross-sectional study has been conducted to assess the relationship of uric acid level on mean arterial pressure in local population of Lahore.

Materials And Methods

This cross sectional study was carried out after approval from hospital and ethical committee. 60 females (age ranging between 55 to 70 years) who fulfilled the criteria were taken from outpatient department of Lady Aitchison hospital Lahore. Written informed consent was taken prior to data collection. By using 5% level of significance, 95% confidence level, 90% power of test for expected percentage of uric acid level, participants were enrolled. Detailed history was taken from the patients. Participants' age and blood pressure were recorded. Serum uric acid between 2.5 and 5.7 mg/dl was considered as normal. Whereas, systolic blood pressure <130 mmHg and diastolic blood pressure <80 mmHg was taken as normal and mean arterial pressure was calculated by the above mentioned formula in each individual.

Blood sampling was done under aseptic measures. Centrifugation was done and serum samples were measured for serum uric acid by uricase method. Cups were numbered and stored in freezer at -70°C. Data was analyzed by R version 4.2.1 (2022-06-23 ucrt) – "Funny-Looking Kid". Pearson correlation coefficient was used to identify the strength of linear relationship between uric acid level and mean arterial pressure. p-value ≤ 0.05 was taken as significant.

Result

A total of 60 patients with increased serum uric acid levels along with mean arterial Pressure, ranging between 83.33 and 126.67 were considered. Furthermore, using a simple linear regression model, the effect of uric acid on mean arterial pressure was computed.

Firstly, to check the model assumptions, it was found that the distribution of the mean arterial pressure of patients in Normal using QQ Plot shown in Fig 1. Secondly, using pearson correlation coefficient it was found that there is a strong positive linear relationship between the two at 5% level of significance as shown in the Table 1. Fig 2 signifies that the computed model is homogeneous i.e., Variance of residuals are the same across the different values of the predictor. The model shows that for every one unit increase in uric acid (mg/dl), mean arterial pressure increases by 14.89 on average

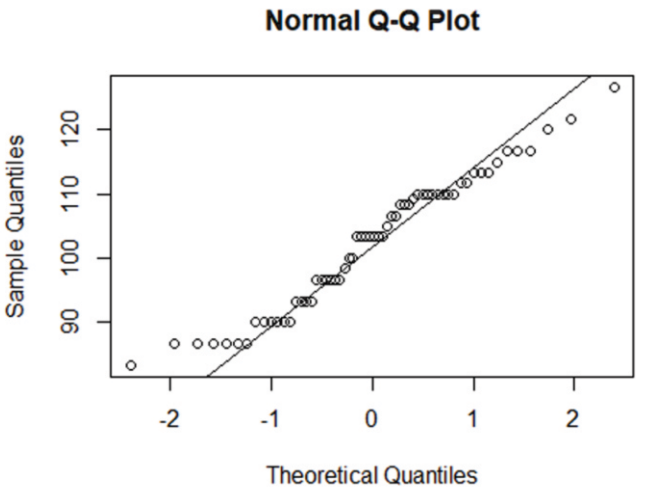
Table 1: *Correlation Coefficient*

Estimate	Statistic	p.value	parameter	conf. low	conf. high	method	alternative
0.8555772	12.58681	< 0.0001	58	0.7686415	0.9114807	Pearson's product-moment correlation	two. sided

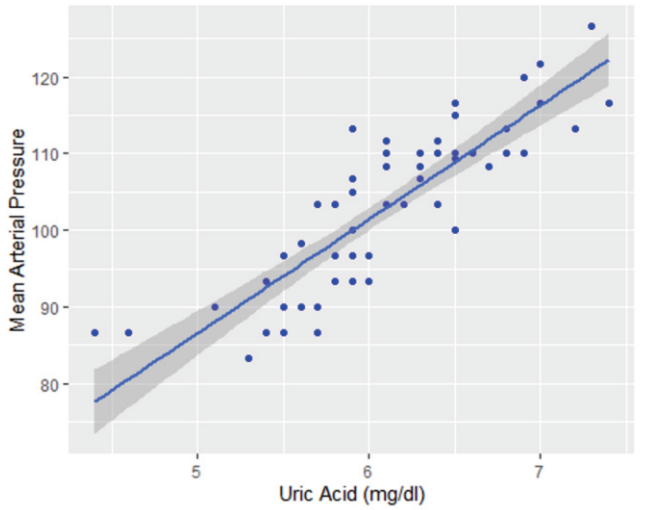
while keeping the other effects constant at 5% level of significance, shown in Table 2. Adjusted R-squared was found to be 0.7274 which means 72.74% of the variation in the mean arterial pressure can be defined using the uric acid.

Table 2: *Regression Coefficient*

	Estimate	Std. Error	t value	Pr (>|t|)
(Intercept)	12.12819	7.211900	1.681691	0.0980062
Uric Acid (mg/dl)	14.88595	1.182663	12.586811	0.0000000



Fitted Model



Discussion

Relationship between hypertension and hyperuricemia, being bidirectional, has long remained interested for the researchers. According to a cross-sectional study, an increase of 1mg/dL serum uric acid shares 20% rise in prevalence of hypertension in a general population of east Asia.[12] The possible pathophysiology behind this is, increased levels of uric acid cause renal artery disease, upregulation of renin-angiotensin-aldosterone system, oxidative stress, systemic inflammation and endothelial dysfunction.[2,13] On the other hand, hypertension may cause hyperuricemia and this may be attributed to renal under functioning due to high systolic and diastolic blood pressures.[4]

This cross-sectional study, which is consisted of 60 females with hyperuricemia, shows a strong positive linear relationship between uric acid and mean arterial pressure. Our results further demonstrate that for every one unit increase in serum uric acid (mg/dl), mean arterial pressure increases by 14.89 on average. In addition to it 72.74% of the variation in the mean arterial pressure is attributed to uric acid.

A study conducted in Japan documented odds ratio about 1.2 for every 1 mg/dl increase in serum uric acid. Males with hyperuricemia reported a greater risk of incident hypertension, as I mg/dl increase in serum uric acid caused 9% increase in the incident hypertension risk. Another study observed progressive increase in both systolic and diastolic blood pressures across the serum uric acid tertile, whereas confounders like age, gender, glomerular filtration rate and basal metabolic rate were kept adjusted.[14]

Results of most of the previous studies are consistent with our study. A cross sectional study from National Health and Nutrition Examination Survey (NHANES) observed a linear relationship between uric acid and blood pressure (both systolic and diastolic) in the group taking antihypertensives. Ning Ding et al. noticed a gradual decrease in systolic and diastolic blood pressures by increasing uric acid whereas the relationship between them was seem to be U shaped in the non-treatment group.[15]

In 2020, Jianga Y by cross lagged approach, observed a temporal relationship between hyperuricemia and hypertension and documented that hyperuricemia precedes hypertension.[16] A similar kind of statement has also been documented in a study that was done on 11488 subjects in 2022 by Xue Tian et al. According to them, increased initial serum uric acid as well as gradual rise over a period of time, both can predict the progression of hypertension from prehypertension.[17] Xue Tian and his companions conducted a study including 60,285 participants and concluded that hyperuricemia preceded hypertension, hence a temporal relationship was seen between hyperuricemia and hypertension.[18] It has also been revealed through different publications that progression from normal to low and moderate to high levels of serum uric

acid are associated with worst outcomes of new onset hypertension whereas opposite observations were seen in case of low or normal uric acid levels.[19]

Similar kind of findings have also been observed in childhood demonstrating that increased serum uric acid level in childhood is closely related to persistent childhood hypertension showing a key role played by childhood hyperuricemia in the development of hypertension.[20] Supporting this study, a survey by Korean National Health and Nutrition Examination showed 9.4% prevalence of hyperuricemia associated with high systolic blood pressure in school going subjects aged between 10-18 years.[21]

As far as the effect of urate lowering drugs in the treatment of high blood pressure is concerned, controversial results have been observed. Some of these drugs reduce the systolic blood pressure[22] whereas allopurinol fails to show such results.[23]

Almost all of the above mentioned studies favor our study that increase in serum uric acid results in increase in mean arterial pressure which is considered as a better diagnostic tool of hypertension. Yet, most of the literature commented the change in mean arterial pressure by 1 mg/dl increase in serum uric acid levels in their own areas and lacked information in our population, so our study filled that deficit. So, by keeping in control the uric acid level in serum, systolic and diastolic blood pressures can also be kept within normal level. However, our research focused only female population and thus further researches on both genders and wide range of ages are needed to estimate heterogenous effect.

Conclusion

Present study demonstrates a positive linear relation between serum uric acid and mean arterial pressure. Furthermore, simple linear regression model was used to see the influence of uric acid on mean arterial pressure and found that with 1 mg/dl increase in serum uric acid causes an increase of 14.89 in mean arterial pressure. Moreover, 72.74% of the variation in the mean arterial pressure is being defined by our proposed model.

Conflict of Interest: None

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Authors Contribution

RN, FN: Conceptualization of Project
RN: Data Collection
FN: Literature Search
AN: Statistical Analysis
MBM: Drafting, Revision
QM: Writing of Manuscript