How to Cite:
Bhosale, A., Khedkar, S., Khade, S. K., & Reddy, M. M. (2022). Study of serum uric acid levels in essential hypertension. *International Journal of Health Sciences, 6*(S7), 3528–3536.
https://doi.org/10.53730/ijhs.v6nS7.12511

Study of serum uric acid levels in essential hypertension

Anita Bhosale
Assistant Professor, Department of Medicine, MIMER Medical College Talegaon Dt Pune, Maharashtra India

Sudam Khedkar
Professor Department of Medicine, MIMER Medical College Talegaon Dt Pune, Maharashtra India

Sachinkumar K Khade
Assistant Professor, Department of Medicine, MIMER Medical College Talegaon Dt Pune, Maharashtra India

Dr. Musuku Manisha Reddy*
Senior Resident Department of Medicine, MIMER Medical College Talegaon Dt Pune, Maharashtra India and House number 3-7-337, Ramana Neuro Centre, Vavilalapally, Karimnagar, Telangana 505001, 9665630026
*Corresponding author email: manishareddymusuku@gmail.com

***Abstract*---**Background: Hypertension is a major public health problem in developed and developing countries. Objective: to determine the prevalence and association of hyperuricemia with diagnosed cases of essential hypertension. Material and Methods: A hospital based cross sectional study was conducted at Department of General Medicine in a Medical College. Results: Out of the total 235 cases with hypertension, 83.8% were in stage I hypertension while 16.2% were in stage II hypertension. Prevalence of hyperuricemia was seen as 27.7% among cases with hypertension. Prevalence of hyperuricemia was 23.4% in cases with stage I hypertension while it was 50% in cases with stage II hypertension ($p<0.01$). Mean Systolic (153.2 vs 149.8 mmHg) and diastolic (99.8 vs 96.9 mm Hg) blood pressure was significantly more in cases with hyperuricemia ($p<0.01$). A significant correlation was observed between serum uric acid levels and systolic and diastolic blood pressure i.e. serum uric acid levels increases with increase in blood pressure ($p<0.01$). Conclusion: Prevalence of hyperuricemia was significantly higher in diagnosed subjects with essential hypertension, affecting every one out of four individual. Mean serum uric acid levels were significantly associated with increase in systolic and diastolic blood pressure.

Manuscript submitted: 9 April 2022, Manuscript revised: 18 June 2022, Accepted for publication: 27 July 2022

Keywords---Prevalence, Hyperuricemia, Essential hypertension.

Introduction

Hypertension and dyslipidemia are associated with oxidative stress and are major causes of cardiovascular disease amounting to 30% of global death rate. Urban subjects had a higher prevalence of hypertension 37% while for rural prevalence was significantly lower at 33%. Hypertension which is defined as blood pressure of equal to or greater than 140/90 mmHg[1] has been recognized as the most common cardiovascular disorder[2] and leading cause of morbidity and mortality in both developed and developing countries[3]

Hypertension is a major independent risk factor for the development of CAD, stroke and renal failure. Hypertension is defined as systolic blood pressure (SBP) level higher than 140 mm Hg and/or a diastolic blood pressure (DBP) higher than 90mm Hg. Blood pressure is optimal if the systolic blood pressure (SBP) is lower than120 mm Hg and diastolic blood pressure (DBP) is less than 80mmg Hypertension has been recognized as one of leading reported causes of death with about 4% of such deaths due to hypertensive complications[4] Although defined as "an elevation of blood pressure" alone, hypertension is characterized by abnormalities of cardiac output, systemic vascular resistance, and arterial compliance.

Depending on methods of patient ascertainment, ~80–95% of hypertensive patients are diagnosed as having "essential" hypertension (Primary Hypertension). In the remaining 5–20% of hypertensive patients, a specific underlying disorder causing the elevation of blood pressure can be identified (secondary hypertension). Essential hypertension has been appropriately called the silent killer because it is usually asymptomatic and undetected. [5]

Uric acid is a final enzymatic product in the degradation of purine nucleosides and it has the ability to scavenge oxygen radicals and protect the erythrocyte membrane from lipid oxidation. Hyperuricemia or elevated serum uric acid levels (SUA) is a biochemical entity that is gaining increasing importance as it is found by some researchers to be not only a cardiovascular risk factor but also plays a role in development of renal and metabolic diseases. [6]

The relationship between uric acid (UA) and blood pressure (BP) is certainly not new and has been recognized for over a century[7] Multiple studies have demonstrated an independent association between hyperuricemia and hypertension, although the issue of direct causality is still debated.

Uric acid is thought to play a pathogenic role in hypertension mediated by several mechanisms such as inflammation, vascular smooth muscle cell proliferation in renal microcirculation, endothelial dysfunction and activation of renin-angiotensin-aldosterone system. [8, 9]

There are few studies that explored the relationship between SUA levels and hypertension in the general healthy population. The present study thus aimed to

determine the prevalence and association of hyperuricemia with diagnosed cases of essential hypertension.

Material and Methods

This Hospital Based Cross-sectional Study was conducted among cases of essential hypertension attending the medicine OPD and also admitted under Department of General Medicine, in a Medical College. Duration of study was 18 months. Permission for the study was obtained from the College authorities prior to commencement

Sample Size Calculation:

The sample size was calculated using following formulae:

$n = (Z\alpha/2)\ 2 * (P * 1\text{-}P) / L2$

where;

n- Sample size

$Z\alpha/2$ – Z value at 5% error (1.96)

P– Prevalence of hyperurecemia in hypertension is approx. 29%

L – allowable error (taken as 20% of P)

$n – (1.96)2 * (0.29 * 0.71)$
$(0.058)2$

n- 235 (approx.)

Inclusion Criteria

1. Stage1 and stage 2 hypertension.

2. Age >30 years and < 70 years.

3. Either Gender

Exclusion Criteria

1. Diabetes Mellitus - type1 & type2 and metabolic syndrome
2. Patients with chronic kidney disease
3. Hypertensive patients with known cerebrovascular disease
4. Hypertensive patients with coronary artery disease-Myocardial ischemia or infarction

5. Patients with long term drug intake like thiazide diuretics, steroids, antitubercular drugs, antimetabolites or chemotherapy
6. Patients who regularly consume alcohol
7. Patients having chronic liver disease and metabolic disorder
8. Hypothyroid patients
9. Psoriasis patients
10. Patients in whom BMI >30
11. Patients having myeloproliferative or lymphoproliferative disorder
12. Malignant hypertension / hypertensive crisis.
13. All causes of secondary hypertension

Methodology

Hypertensive patients were selected from a tertiary care hospital. Written informed consent was taken from the participants after providing them all the information about the study. The patient were asked to fast for 12 hours and to avoid smoking and heavy physical exercise for more than 2 hours before the examination. After a 5 minutes rest in a quiet room systolic and diastolic blood pressures will be measured in a sitting position with back supported, legs uncrossed with feet flat on the floor and arm supported with BP cuff at heart level using correct cuff size on bare arm. Readings were taken twice at an interval of five minutes on the right arm with a validated and standard mercury sphygmomanometer on three separate occasions. Average of three readings were considered.

Hypertension was defined according to the JNC VIII (Joint National Committee VIII)

Uric Acid Estimation

Principle: The principle for the determination of Serum Uric Levels is with a modified Trinder peroxidase method using TBHB.

Uric acid + O2 + H2O uricase. Allantoin + CO2 + H2O2.

H2O2 + 4- AAP + TBHB Peroxidase Quinoneimine + H2O

The intensity of chromogen (Quinoneimine) formed is proportional to the uric acid concentration in the sample when measured at 510 nm (510 -550nm). Hyperuricemia is defined as serum uric acid level ≥7 mg/dl (in men) or ≥6.0 mg/dl (in women). [10]

Statistical Analysis

All the data was noted down in a pre-designed study proforma. Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed by Chi-Square test. Quantitative data was represented using Mean ± SD. Analysis of Quantitative data between the two groups was done using unpaired t-test if data passed 'Normality test' and by Mann-Whitney Test if data failed 'Normality test'. A p-value < 0.05 was taken as level of significance. Results were graphically represented where deemed necessary. SPSS Version 21.0 was used for most analysis and Microsoft Excel 2010 for graphical representation

Results

Mean age of the cases with hypertension was 55.02 years with 28.9% cases being above 60 years of age. Out of the total 235 cases, 57.9% were males while 42.1% were females. Out of the total 235 cases with hypertension, 83.8% were in stage I hypertension while 16.2% were in stage II hypertension. Prevalence of hyperuricemia was seen as 27.7% among cases with hypertension. Table 1

Table 1.
Distribution of study groups as per prevalence of hyperuricemia

Hyperuricemia	N	%
No	170	72.3%
Yes	65	27.7%
Total	235	100.0%

Mean age was comparable among cases with and without hyperuricemia (54.85 vs 55.09 years; p-0.84). table 2

Table 2
Mean age comparison among cases with and without hyperuricemia

Variables	Hyperuricemia	N	Mean	SD	p- value
Age	**Yes**	65	54.85	8.08	**0.84**
	No	170	55.09	9.14	

Gender distribution was comparable among cases with and without hyperuricemi (p- 0.63). Table 3

Table 3. Gender comparison among cases with and without hyperuricemia

Gender	Hyperuricemia		Total
	No	Yes	
Female	70	29	99
	70.7%	29.3%	100.0%
Male	100	36	136
	73.5%	26.5%	100.0%
Total	170	65	235
	72.3%	27.7%	100.0%
p- value - 0.63			

Both the cases with and without hyperuricemia were comparable with regard to anthropometric parameters (p>0.05). Table 4

Table 4. Mean anthropometry comparison among cases with and without hyperuricemia

Anthropometry	Hyperuricemia	N	Mean	SD	p- value
Height	**Yes**	65	169.03	8.04	**0.18**
	No	170	167.27	9.52	
Weight	**Yes**	65	73.40	15.51	**0.25**
	No	170	70.48	18.09	
BMI	**Yes**	65	25.66	5.06	**0.42**
	No	170	25.05	5.42	

Prevalence of hyperuricemia was 23.4% in cases with stage I hypertension while it was 50% in cases with stage II hypertension (p<0.01). Table 5

Table 5
Stage of hypertension comparison among cases with and without hyperuricemia

Stage of Hypertension	Hyperuricemia		Total
	No	Yes	
I	151	46	197
	76.6%	23.4%	100.0%
II	19	19	38
	50.0%	50.0%	100.0%
Total	170	65	235
	72.3%	27.7%	100.0%
p- value <0.01			

Mean Systolic (153.2 vs 149.8 mmHg) and diastolic (99.8 vs 96.9 mm Hg) blood pressure was significantly more in cases with hyperuricemia ($p<0.01$).

A significant correlation was observed between serum uric acid levels and systolic and diastolic blood pressure i.e. serum uric acid levels increases with increase in blood pressure ($p<0.01$).

Discussion

Hypertension is a major independent risk factor for the development of CAD, stroke and renal failure. The relationship between uric acid (UA) and blood pressure (BP) is certainly not new and has been recognized for over a century. [9] In present study, we aimed to determine the prevalence and association of hyperuricemia with diagnosed cases of essential hypertension. Study included 235 cases of essential hypertension.

Mean age of the cases with hypertension was 55.02 years with 28.9% cases being above 60 years of age. Out of the total 235 cases, 57.9% were males while 42.1% were females. Mishra A et al. in their study observed the mean age of the study cases with hypertension as 51.9 years with 58% males to 42% females. Lin CS et al observed mean age as 56.7 years with 60% males to 40% females. Ali N et al observed that out of 255 subjects, 140 were male, and 115 were female subjects. Mean age of the participants was 52.7 ± 13.8 years (range 18–80 years). Ansari RN et al. observed that maximum number of patients were in 41-55 years with

mean age of 51.2 years. Incidence of HTN is higher in men (51%) than in female (49%).

Out of the total 235 cases with hypertension in present study, 83.8% were in stage I hypertension while 16.2% were in stage II hypertension. Lin CS et al in their study observed 87% cases in stage I and 13% in stage II. Ali N et al in a similar study, observed that 83% cases were hypertension stage I while 17% were stage II. Ansari RN et al observed 72% cases in stage I while 28% in stage II.
Over the past few decades, there has been an increasing appreciation that hyperuricemia is a strong independent predictor of hypertension and may indeed be causative.

In present study, prevalence of hyperuricemia was seen as 27.7% among cases with hypertension. Prevalence of hyperuricemia was 23.4% in cases with stage I hypertension while it was 50% in cases with stage II hypertension ($p<0.01$). Mean Systolic (153.2 vs 149.8 mmHg) and diastolic (99.8 vs 96.9 mm Hg) blood pressure was significantly more in cases with hyperuricemia ($p<0.01$). A significant correlation was observed between serum uric acid levels and systolic (r-0.51; $p<0.01$) and diastolic blood pressure (r- 0.56; $p<0.01$) i.e. serum uric acid levels increases with increase in blood pressure.

Mishra A et al[11] in their study observed the prevalence of hyperuricemic in hypertensive cases as 26%. Serum uric acid was significantly associated with systolic blood pressure (r = +0.367) and diastolic blood pressure (r = +0.302). These associations were statistically significant (p value<0.05). Ansari RN et al[12] observed that among 100 patients, 65% of patients having high SUA level. The study showed that the SUA levels were significantly increased in patient with stage 2 hypertension in comparison with those with stage 1 hypertension, showing that the severity of hypertension also related to the SUA levels. Garrick et al[13] observed that 31% of their study patients had hyperuricemia along with hypertension. Kinsey et al[14] in his study with 400 hypertensive patients reported a 46% incidence of hyperuricemia in hypertensives. Kolbe et al[15] in his study of 46 hypertensive patients found 26 to be having increased SUA levels (56%). In a study by Bulpitt CJ et al 48 % male hypertensives and 40 % female hypertensives had their SUA level in the hyperuricemic range.

Conclusion

Prevalence of hyperuricemia was significantly higher in diagnosed subjects with essential hypertension, affecting every one out of four individual. Mean serum uric acid levels were significantly associated with increase in systolic and diastolic blood pressure. Since elevated serum uric acid levels are not only a cardiovascular risk factor but also plays a role in development of renal and metabolic diseases along with hypertension, the early diagnosis and management of the same should be a priority to improve the prognosis of hypertensive cases

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