

Original Research Article

Hyperuricemia among hypertensive and normotensive individuals: a case control study

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ABSTRACT

Background: The depth of association between hypertension and serum uric acid remains a mystery. In order to know the exact association between hypertension and serum uric acid, authors intended to investigate the serum uric acid levels among hypertensive and non-hypertensive patients and, authors assessed whether hyperuricemia increases with increasing duration of hypertension and severity of hypertension.

Methods: This case control study was conducted among hypertensive (Cases) and non-hypertensive patients (Controls) attending outpatient and inpatient department of general medicine in Sri Muthukumaran Medical College and Research Institute during January 2019 to March 2019. A total of hundred patients were included in this study with fifty cases and control each. Data was conducted using a proforma, covering particulars related to hypertension and the levels of serum uric acid were also noted in the same. Data analysis was done using SPSS.

Results: Hyperuricemia among cases and control was found to be statistically significant association with odds ratio of 3.7. Also, the study showed that the serum uric acid levels were significantly increased in patients with Stage 2 hypertension compared to stage 1 hypertension. Also, cases with longer duration of hypertension had significantly raised serum uric acid levels compared to cases with lesser duration of hypertension.

Conclusion: Assessment of serum uric acid may be recommended for all the hypertensive cases.

Key words: Hyperuricemia, Hypertension, Normotensive individuals, Serum uric acid

INTRODUCTION

Hypertension is one of the most challenging issues for public health. Its complications contribute to 9.4 million deaths among 17 million deaths from cardiovascular disease annually worldwide.¹ The concept that uric acid might be associated with the development of hypertension is not a new one. Even in the earliest discussions of hypertension as a disease entity, uric acid was considered. In the 1870s, Frederick Mahomed postulated that the problem of hypertension resulted from a circulating toxin that caused an increase in blood pressure (BP) and subsequently damaged the vasculature of the heart and kidneys.² A few years later, Alexander

Haig also linked uric acid with elevated BP and went so far as to write a textbook that suggested a diet that would lower uric acid and control BP in the general population.³ Henri Huchard, a renowned cardiologist, hypothesized that arteriole sclerosis, the vascular lesion associated with hypertension, had three causes: uric acid, lead, and intake of fatty meats, the latter of which also yield increased uric acid.⁴

The investigation of a link between uric acid and hypertension made relatively little progress through much of the 20th century. While some of the cardiovascular risk trials measured uric acid and suggested an association between uric acid and hypertension, or

cardiovascular disease, the lack of plausible mechanistic evidence linking the two led most investigators to conclude that uric acid was an associated surrogate marker for more important risk factors such as obesity, diabetes, and chronic kidney disease (CKD).⁵

In the 1980s, uric acid was removed from some of the common laboratory panels, markedly reducing the available epidemiologic data on uric acid in otherwise healthy patients and those with cardiovascular disease. The move was made after the majority of serious side effects from the urate-lowering drug, allopurinol, were observed in patients with asymptomatic hyperuricemia, not gout⁶. The shift to minimize inadvertent diagnosis of hyperuricemia was thought to reduce risk of unnecessary medication side effects and reduced the awareness of the prevalence of hyperuricemia in the absence of symptomatic gout.

In order to know the exact association between hypertension and serum uric acid, authors intended to investigate the serum uric acid levels among hypertensive and non-hypertensive patients and, authors assessed whether hyperuricemia increases with increasing duration of hypertension and severity of hypertension.

Objectives of this study to compare the levels of serum uric acid levels among hypertensive and non-hypertensive patients.

METHODS

This case control study was conducted among hypertensive (Cases) and non-hypertensive patients (Controls) attending outpatient and inpatient department of general medicine in Sri Muthukumaran Medical College and Research Institute during January 2019 to March 2019.

Patients aged more than 18 years of age in both the sexes with hypertension were included as cases and normotensives were included as controls. Patients with diabetes mellitus, ischaemic heart disease, secondary hypertension, obesity, alcohol abuse, renal disease and gout were excluded from both case and control group. A total of hundred patients were included in this study with fifty known hypertensive patients, who were considered as cases and another fifty non hypertensive patients, who were included as controls.

Ethical committee approval was obtained before the commencement of the study. The principal investigator explained the purpose of the study to each participant and a written consent was obtained from the participants prior to the commencement of the study. The participants were also informed that their participation was voluntary and that they could withdraw from the interview at any time without consequences. Every effort was made, to be sure that all information collected from the participants, remain confidential.

Two milliliters of venous blood were collected from all the study participants and sent for analysis of levels of serum Uric acid. The study was conducted using a proforma, covering particulars related to hypertension and the levels of serum uric acid was also noted in the same. Data was entered in Microsoft excel and data analysis was done using Statistical Package for Social Sciences (SPSS) version 17.

RESULTS

Among essential hypertension cases, 2 were less than 30 years of age in cases and 1 in controls. In the age group of 31-40 years there were 8 cases and 7 controls. 13 and 15 patients were reported in the age group of 41-50 years from cases and controls respectively. In the age group of 51-60 years 15 essential hypertension cases were reported and 16 controls. In the age group Of 61- 70 years 7 cases and 6 controls were there. Above 70 years of age there were 5 patients in each cases and control group. The mean age was found to be 50.18 and standard deviation (SD) 12.31 in the essential hypertension group and 51.42±11.24 in the control group.

In this present study, 34 males and 16 females were seen with essential hypertension whereas in control group there were 35 males and 15 females (Table 1).

Table 1: Age Group of the participants.

Variables	Cases	Controls	Total
Age group			
< 30 years	02	01	03
31-40 years	08	07	15
41-50 years	13	15	28
51-60 years	15	16	31
61-70 years	07	06	13
71-80 years	05	05	10
Total	50	50	100
Mean	50.18±	51.42±	51.4±
Age±SD	12.31	11.24	11.4
Sex			
Male	34	35	69
Female	16	15	31
Total	50	50	100

Among 50 cases of essential hypertension, majority of the patients 35 (70%) were in Stage II hypertension and 15(30%) cases were in Stage I hypertension. Also, there were 28 (56%) essential hypertension cases with duration of more than 5 years and 22 (44%) cases with less than 5 years duration of the disease (Figure 1).

Serum uric acid mean among cases was found to be 6.4 with Standard Deviation (SD) of 1.5 and in the control group the mean and SD was 5.2 and 1.3, respectively. This difference in serum uric acid between the cases and the controls were found to be statistically significant.

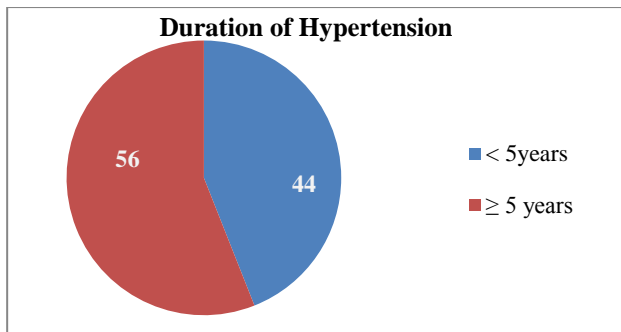


Figure 1: Proportion of cases with different duration of hypertension.

The mean and SD of serum uric acid level among Stage I essential hypertension cases was found to be 5.3 ± 1.0 and in Stage II essential hypertension cases it was 6.5 ± 1.4 . This difference in serum uric acid between patients in stage I and stage II hypertension were found to be highly statistically significant.

Based on the duration of hypertension, the mean and SD of serum uric acid was found to be 5.2 ± 0.8 and 6.1 ± 1.2 among patients with less than 5 years and more than or equal to 5 years, duration of essential hypertension respectively. The difference in serum uric acid between the patients with less than and more than (or equal to) 5

years of hypertension was found to be statistically significant (Table 2).

Table 2: Mean and SD of serum uric acid in each group.

Variables	Serum Uric acid	t value	p value
Group			
Cases	6.4±1.5	4.275	0.000*
Controls	5.2±1.3		
Stages of hypertension			
Stage I	5.3±1.0	4.932	0.000*
Stage II	6.5±1.4		
Duration of hypertension			
<5years	5.2±0.8	4.413	0.000*
≥5 years	6.1±1.2		

*Significant

In this study the number of hypertensive patients with hyperuricemia was found to be 19 whereas in the control group the number of patients with hyperuricemia was found to be 7. Also, there were 31 and 43 patients without hyperuricemia in the case and control groups, respectively. Odds ratio was found to be 3.76 and the association was found to be statistically significant (Table 3).

Table 3: Proportion of cases with Hyperuricemia among cases and controls.

Hyperuricemia	Cases	Control	Odds Ratio	95% CI	p value
Present	19	7	3.76	1.4-10.1	0.0081*
Absent	31	43			

*Significant

DISCUSSION

In the present study the incidence of hyperuricemia in controls was 14% and the incidence of hyperuricemia in cases was 38%. Various other studies have also shown that increased SUA levels were seen in hypertensive patients. Kinsey et al conducted a study among 400 hypertensive patients and reported 46% incidence of hyperuricemia among them.⁷ Kolbe et al in their study among 46 hypertensive patients found 26 to be having increased SUA levels (56%).⁸

Breckenridge et al reported that in their study, 58% of hypertensive participant and 27% of healthy participants had hyperuricemia.⁹ In a study conducted by Bulpitt et al, 48% male hypertensive patients and 40% female hypertensive patients had their SUA level in the hyperuricemic range.¹⁰ Ramsay et al reported that among 73 men with untreated hypertension, 18 had raised serum uric acid levels (25%).¹¹ Messerli et al reported an

incidence of 72% raised SUA in their study conducted among hypertensive patients.¹²

Serum uric acid mean among cases was found to be 6.4 with Standard Deviation (SD) of 1.5 and in the control group the mean and SD was 5.2 and 1.3, respectively. This difference in serum uric acid between the cases and the controls were found to be statistically significant. These reports were consistent with the reports of Turak et al, who reported hypertensive cases had significantly higher serum UA levels than the controls.¹³

Messerli et al hypothesized that the frequent presence of hyperuricemia in hypertensive patients reflects underlying renal dysfunction or reduced renal perfusion.¹² It is certainly possible that uric acid may be an earlier and more sensitive marker of decreased renal blood flow than serum creatinine. It has been recently suggested that since uric acid may play a role in the formation of free radicals and oxidative stress, the increased risk of hypertension in

subjects with raised serum uric acid levels might be associated with this increased generation of free radicals.

In a study by Tykarski et al, they reported that SUA concentration and the prevalence of hyperuricemia were significantly higher in hypertensive patients.¹⁴ They further demonstrated that tubular secretion of uric acid was significantly lower in hypertensive patients in comparison with normotensive subjects. There was no difference in pre and post secretory re-absorption of uric acid. They concluded that high prevalence of hyperuricemia in essential hypertension was caused by impaired renal excretion of uric acid. Goldstein et al showed in an adolescent population that, with age, weight, height and sexual maturity controlled, SUA significantly predicted blood pressure even in adolescents.¹⁵

Fessel et al showed no appreciable loss of renal function in 112 patients with gout as compared to normal subjects followed up for 12 years.¹⁶ In a study by Ramsay et al there was no evidence that hyperuricemia had a deleterious effect on renal function.¹¹ Canon et al considered that an impairment of renal function will raise the SUA levels more commonly than an increased SUA will cause renal damage.¹⁷

Hence it is unlikely that hypertension arises as a result of raised SUA levels, but the possibility that uric acid which plays a role in the formation of free radicals and oxidative stress, the increased risk of hypertension in subjects with raised serum uric acid levels might be associated with this increased generation of free radicals. Thus, the fact that raised SUA levels can lead to Hypertension cannot be entirely ruled out.

In our study authors found that there is definite relation in SUA levels between hypertensive patients and normotensive patients and there is a directly proportional relation in the levels of SUA in relation to the duration and severity of hypertension. Hence the possibility of serum uric acid acting by the production of free radicals and causing oxidative stress leading to hypertension and whether the duration and severity of hypertension lead to renal dysfunction in the form of nephrosclerosis leading to higher levels of serum uric acid has to be considered as various other studies have also show to have a positive relation in the SUA levels and hypertension.

CONCLUSION

Based on the findings of this study, authors found association between hyperuricemia and hypertension. Also, the study showed that the serum uric acid levels were significantly increased in patients with Stage 2 hypertension in comparison with those with stage 1 hypertension, showing that the severity of hypertension also related to the serum uric acid levels. This study also demonstrates that the duration of hypertension had a significant impact on the serum uric acid levels that those

participants with a longer duration of hypertension had significantly raised serum uric acid levels when compared with those of a lesser duration. Hence assessment of serum uric acid may be recommended for all the hypertensive cases.

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