



## RESEARCH ARTICLE

# HYPERURICEMIA AND HYPERTENSION: AN EMERGING ASSOCIATION, A CASE-CONTROL STUDY

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### ABSTRACT

**Aim:** To show association between Hyperuricemia and Hypertension. **Introduction:** Hyperuricemia has recently emerged as an independent risk factor in the development of hypertension. The various mechanisms has shown association between hypertension and hyperuricemia. That includes uric acid induced activation of renin-angiotensin system and action on glomerular apparatus, increased insulin resistance and hyperinsulinemia, causing decreased excretion of uric acid and uric acid induced proliferation of vascular smooth muscle, endothelial dysfunction with decreased nitric acid production. Various clinical trials shown potential role of uric acid lowering agents in management of hypertension. However, there are numerous confounding factors that is associated with hypertension and hyperuricemia like diabetes mellitus, smoking and alcohol intake. **Materials and Method:** Case control study done in Noida International Institute of Medical Science, Greater Noida on 120 patients in the department of medicine on both outpatient and inpatient patients, from January 2023 to December 2023. Studies include 60 cases with history of hypertension and 60 normotensive controls. Uric acid value determined in all patients and association established between hypertension and hyperuricemia. **Results:** Among 60 cases of essential hypertension, majority of the patients 33 (55%) were in Stage II hypertension and 12(20%) cases were in Stage I hypertension. Also, there were 18 (30%) essential hypertension cases with duration of more than 5 years and 30 (50%) cases with less than 5 years duration of the disease. Serum uric acid mean among cases was found to be 6.4 and in the control group was 5.2 . This difference in serum uric acid between the cases and the controls were found to be statistically significant. **Conclusion:** It can be concluded that hyperuricemia is significantly associated with hypertension and hyperuricemia-hypertension risk relationship is present in patients irrespective of metabolic syndrome.

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## INTRODUCTION

Hypertension is an important public health challenges which affect different age group with risk factors that involves multiple environmental and pathophysiological factors that affect multiple systems, as well as genetic predisposition<sup>1</sup>.

Hypertension (HT) is the most common risk factor for cardiovascular morbidity and mortality. This positive relationship between blood pressure (BP) and cardiovascular risk exists in both individuals with hypertension and prehypertension<sup>2</sup>.

Uric acid is the final oxidation product of purine metabolism in circulation and has been associated with the occurrence of gout and kidney stones. Hyperuricemia has recently emerged as an independent risk factor in the development of hypertension. The various mechanisms has shown association between hypertension and hyperuricemia<sup>3</sup>. That includes uric acid induced activation of renin-angiotensin system and action on glomerular apparatus, increased insulin resistance and hyperinsulinemia, causing decreased excretion of uric acid and uric acid induced proliferation of vascular smooth muscle, endothelial dysfunction with decreased nitric acid production. Various clinical trials shown potential role of uric acid lowering agents in management of hypertension. However, there are numerous confounding factors that is associated with hypertension and hyperuricemia like diabetes mellitus, smoking and alcohol intake<sup>4</sup>. So larger randomized controlled trials are therefore needed to establish the role of uric acid and hypertension and effect of uric acid lowering agent in the management of hypertension<sup>5</sup>. Present study is done to show the relationship between hyperuricemia and hypertension in Indian population.

**METHODS**

Case control study done in Noida International Institute of Medical Science, Greater Noida on 120 patients in the department of medicine on both outpatient and inpatient patients, from January 2023 to December 2023.

**Inclusion criteria**

All the subjects were divided into two groups.

- Any age groups
- Gender – both male and female
- Control group: 50 subjects with normal blood pressure (SBP= 90-119 mmHg, DBP= 60-79 mmHg) and
- Case group- 50 cases of hypertension as defined by JNC 7 criteria.

**Exclusion criteria**

- Pregnancy
- Secondary hypertension due to any cause
- Diabetes mellitus
- Smokers
- Alcoholics
- Patient taking antihypertensive, lipid lowering agents and hypouricemic agents.

After obtaining a written voluntary informed consent from all the subjects, physical examinations done, Blood Pressure measured and data was collected. Blood sample (3 ml) was drawn and serum was used to determine participant's serum uric acid. Other investigations done to rule out associated comorbidities.

**RESULTS**

**Table 1. Distribution of study participants according to Gender**

TOTAL=120	CASE (n= 60)	CONTROL (n=60)
MALE	32	38
FEMALE	28	22

**Table 2. Distribution of study participants according to Uric Acid**

TOTAL=120	CASE (n= 60)	CONTROL (n=60)
RAISED	28	11
NORMAL	32	49

Among 60 cases of essential hypertension, majority of the patients 33(55%) were in Stage II hypertension and 12(20%) cases were in Stage I hypertension. Also, there were 18 (30%) essential hypertension cases with duration of more than 5 years and 30(50%) cases with less than 5 years duration of the disease. Serum uric acid mean among cases was found to be 6.4 and in the control group was 5.2. This difference in serum uric acid between the cases and the controls were found to be statistically significant. In this study the number of hypertensive patients with hyperuricemia was found to be 28(46%) whereas in the control group the number of patients with hyperuricemia was found to be 11 (18%). Also, there were 32 and 49 patients without hyperuricemia in the case and control groups, respectively. Odds ratio is more than 1.

**DISCUSSION**

Uric acid is the final product of purine metabolism, and its increased serum levels have been directly involved in the pathogenesis and natural history of hypertension. The relationship between elevated uric acid and hypertension has been proven in both animals and humans, and its relevance is already evident in childhood and adolescent population. The mechanism responsible for blood pressure increase in hyperuricemic subjects is implicating both oxidative stress and intracellular urate activity with a primary involvement of XOR (xanthine-oxidoreductase activity).<sup>6</sup> An increase in the relative risk of hypertension has been confirmed by genetic data and by large meta-analyses of epidemiological data<sup>7</sup>. The effects of urate-lowering treatment on blood pressure control in patients with elevated serum uric acid has been investigated in a small number of reliable studies with a large heterogeneity of patient populations and study designs<sup>8</sup>. However, 2 large meta-analyses suggest a significant effect of urate-lowering treatment on blood pressure, thus confirming the significant relationship between high serum urate and blood pressure<sup>9</sup>.

The future research should be focused on a more appropriate identification of patients with cardiovascular hyperuricemia by considering the correct cardiovascular threshold of serum urate, the time-course of uricemia fluctuations, and the identification of reliable markers of urate overproduction that could significantly clarify the clinical and therapeutic implications of the interaction between serum uric acid and hypertension<sup>10</sup>. 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. Kolbe et al in their study among 46 hypertensive patients found 26 to be having increased SUA levels (56%). Breckenridge et al reported that in their study, 58% of hypertensive participant and 27% of healthy participants had hyperuricemia. 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. Ramsay et al reported that among 73 men with untreated hypertension, 18 had raised serum uric acid levels (25%).<sup>11</sup> Messerli et al reported an incidence of 72% raised SUA in their study conducted among hypertensive patients.<sup>12</sup> 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.<sup>11</sup> 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.

Messerli et al hypothesized that the frequent presence of hyperuricemia in hypertensive patients reflects underlying renal dysfunction or reduced renal perfusion<sup>12</sup>. It is certainly possible that uric acid may be an earlier and more sensitive maker 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. 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<sup>13</sup>. 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.

## CONCLUSION

It can be concluded that hyperuricemia is significantly associated with hypertension and hyperuricemia-hypertension risk relationship is present in patients irrespective of metabolic syndrome. Also, cases with longer duration of hypertension had significantly raised serum uric acid levels compared to cases with lesser duration of hypertension. So it is important to look for serum uric acid levels in any hypertensive patients and it is also important to treat uric acid level according to guidelines as it can be a cause for hypertension by different mechanism.

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