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A Study of Association of Hyperuricemia with Hypertension

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Abstract
Background: Hypertension is a known public health issue in India. Several studies have suggested that hyperuricemia and hypertension are related. Serum uric acid (UA), a standalone predictor for the development of hypertension. The onset of hypertension is frequently predicted by an elevated uric acid level. This present study was a hospital-based case control study carried out in the Department of Medicine at Teerthanker Mahaveer Medical College and Research Centre, Moradabad (U.P.) to study the association of hyperuricemia with hypertension. **Material and Methods:** This study included an equal number of age and sex matched cases and controls. Subjects were divided into - Group 1 and Group 2.Group 1 comprised of cases of Primary hypertension. Group 2 comprised of normotensive subjects. Inclusion Criteria- Group 1 (Cases): Cases of Hypertension as per JNC VII guidelines. Group 2 (Controls): Subjects who were normotensive. Exclusion Criteria-Known cases of hyperuricemia/ gout, diabetes mellitus, renal failure, metabolic disorders, fluid volume disturbances and endocrinal disorders, Smokers and chronic alcoholics, H/O recent intake of ATT {in last 6 months}, Chemotherapy/Radiotherapy. **Results:** Majority of study subjects (66%) of study subjects were above 30 years of age. 50% were males while 50% were females. 34% cases in hypertensive Group 1 had past history of hypertension,7% cases in hypertensive Group 1 had history of chest pain 7% cases had breathlessness 5% cases had sweating associated with chest pain. 37% were in Stage 1 as per JNC VII guidelines while 11% in Stage 2 and 2% in prehypertension category. Raised uric acid levels were seen in 27% of cases of which 19% were in hypertensive Group I and 8% in normotensive Group II. This difference was found to be statistically significant ($p<0.05$). **Conclusion:** The findings of the current investigation suggest that hyperuricemia may also be an independent risk factor for the onset of hypertension in addition to being a marker of CVDs.
Keywords: Uric Acid, Serum Uric Acid, Cardiovascular Disease, NADPH.

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Introduction

Both developed and developing nations experience a serious public health issue with hypertension.By 2025, it is predicted to impact more than 1.5 billion people.[1,2]Since it increases the risk of cardiovascular diseases, hypertension is a known public health issue in India.[3,4] A growing number of contributing factors have come to light in recent decades, contributing to the multifaceted and complex etiology of primary hypertension.[5]

Several studies have suggested that hyperuricemia and hypertension are related. Serum uric acid (UA), a standalone predictor for the development of hypertension has been proved in previous study.[6] Frederick Mohamed discovered the link between serum uric acid (SUA) and primary hypertension in 1870.[7] Alcohol use, a high-fructose diet, eating meat or shellfish, several drugs, particularly ACE, diuretics, as well as hypertension and obesity have all been linked to HUA.[8,9] According to a serum UA >7 mg/dL definition, HUA is present in 13% of the general population in the USA and 21% of males and females, respectively.[10] Due to estrogen's inhibition of urate reabsorption, menopausal females have as higher prevalence of HUA. Among lifestyle disorders, hypertension has proven to be the main source of morbidity. Although many modifiable & known risk factors for hypertension have been thoroughly examined, but it is urgent to find new therapeutic risk factors that are very prevalent in the general population, easily detected and changeable. Hyperuricemia may be a risk factor for hypertension that can be managed and treated, thereby lowering its prevalence. Baseline levels of uric acid in serum serve as a reliable indicator of hypertension risk. The onset of hypertension is frequently predicted by an elevated uric acid level. In hypertensive individuals, lowering serum uric acid levels may result in better blood pressure management, which in turn will prevent the development of atherosclerosis and renal failure. Additionally, it is believed that hyperuricemia enhances oxidative stress and accelerates production of free radicals, which may eventually serve as the nidus for developing cardiovascular disease (CVD).[11] This present study was a hospital based case control study carried out in the Department of Medicine at Teerthanker Mahaveer

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Medical College and Research Centre, Moradabad (U.P.) to study the association of hyperuricemia with hypertension.

JNC-VII GUIDELINES FOR HYPERTENSION:[12]

Blood Pressure Classification	Systolic (mm Hg)	Diastolic (mm Hg)
Normal	<120	And <80
Prehypertension	120-139	or 80-89
Stage I Hypertension	140-159	or 90-99
Stage II Hypertension	>160	or >100
Isolated Systolic Hypertension	>140	and <90

SERUM URIC ACID cut-off point

Hyperuricemia was defined as a serum uric acid concentration > 6.0mg/dl in females and >7.0mg/dl in males.[13,14,15]

AIM

- To study the association of Hyperuricemia with Hypertension.

OBJECTIVES

- To identify patients of Hypertension
- To measure Serum Uric Acid in these patients

To study association of serum uric acid with hypertension

Methodology

Study Population

- This study included an equal number of age and sex matched cases and controls.
- Subjects were divided into - Group 1 and Group 2
- Group 1 comprised of cases of Primary hypertension admitted to the IPD of Department of Medicine.
- Group 2 comprised of normotensive subjects who presented to the OPD/IPD of Department of Medicine.

Inclusion Criteria

Group 1 (Cases): Subjects who were diagnosed cases of Hypertension as per JNC VII guidelines.

Group 2 (Controls): Subjects who were normotensive and have never been on any treatment for Hypertension were taken as control.

Exclusion Criteria

1. Known cases of hyperuricemia/ gout
2. Patients on long term diuretics
3. Known cases of diabetes mellitus
4. Known cases of patients with renal failure
5. Known cases of metabolic disorders, fluid volume disturbances and endocrinal disorders

- Smokers and chronic alcoholics
- Patients with H/O recent intake of ATT {in last 6 months}
- Patients with malignancy on Chemotherapy/Radiotherapy.

RESULTS

Table 1: Distribution of study participants according to Gender

Gender	Group 1 (n=50)	Group 2 (n=50)	Total (n=100)
Female	20	30	50
Male	30	20	50

Out of 100 cases, 50% were males while 50% were females.

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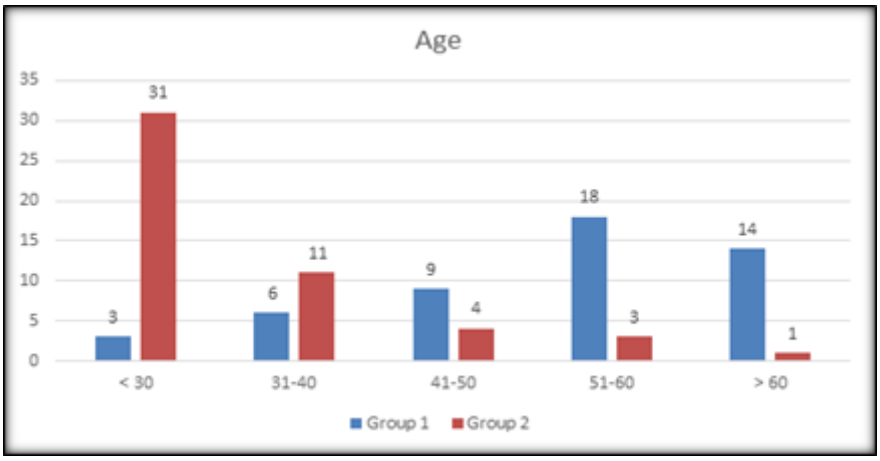

Figure 1: Graphical representation of study participants according to Age

Majority of study subjects (66%) of study subjects were above 30 years of age.

Table 2: Distribution of study participants according to Past History of Hypertension

Past History of Hypertension	Group 1 (n=50)	Group 2 (n=50)	Total (n=100)
No	16	50	66
Yes	34	0	34

Out of 100 cases, 34% cases in hypertensive Group 1 had past history of hypertension.

Table 3: Distribution of study participants according to Chest Pain, Breathlessness & Sweating

Chest Pain	Group 1 (n=50)	Group 2 (n=50)	Total (n=100)
Yes	7	0	7
No	43	50	93
Breathlessness			
Yes	6	1	7
No	44	49	93
Sweating			
Yes	5	0	5
No	45	50	95

Out of 100 cases, only 7% cases in hypertensive Group 1 had history of chest pain. Out of 100 cases, only 7% cases had history of breathlessness as shown in Table. Out of 100 cases, only 5% cases in hypertensive Group 1 had history of sweating associated with chest pain.

Table 4: Distribution of study participants according to Stage of Hypertension (JNC VII)

Stage of Hypertension (As Per JNC VII)	Group 1 (n=50)	Group 2 (n=50)	Total (n=100)
Normal	0	50	50
Prehypertension	2	0	2
Stage 1	37	0	37
Stage 2	11	0	11

[Table 4] shows that 37% of study subjects in Group 1 were in Stage 1 as per JNC VII guidelines while 11% were in Stage 2 and 2% were in prehypertension category.

Table 5: Distribution of study participants according to Uric Acid

Uric Acid	Group 1 (n=50)	Group 2 (n=50)	Total (n=100)	p-value
Normal	31	42	73	0.012
Raised	19	8	27	

Out of 100 cases, raised uric acid levels were seen in 27% of cases of which 19% were in hypertensive Group I and 8% in normotensive Group II. This difference was found to be statistically significant ($p<0.05$)

DISCUSSION

The present study was a hospital-based case control study carried out in the Department of Medicine at Teerthanker Mahaveer Medical College and Research Centre, Moradabad (U.P.). Subjects were divided into two

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Groups. Group 1 comprised of cases of Primary hypertension admitted to the IPD of Department of Medicine. Group 2 comprised of normotensive subjects who presented to the OPD/IPD of Department of Medicine. According to the current study's findings, hyperuricemia increases the likelihood of developing hypertension and is more common in those with hypertension than it is in those without.

Majority of study subjects (66%) of study subjects were above 30 years of age. Out of 100 cases, 50% were males while 50% were females. It is well known that estrogen encourages the UA excretion. Given that estrogen is a uricosuric substance, the gender differences in the relationship between HUA and HTN are explainable. Higher plasma estrogen levels and lower tuber urate post-secretory reabsorption were the causes of the higher renal clearance of urate in women, according to a study by Anton et al.[16] 54% were vegetarians while 46% were having mixed diet. Only 7% cases in hypertensive Group 1 had history of chest pain, 7% cases had history of breathlessness, 5% cases had history of sweating associated with chest pain and pallor was seen in 17% of cases. Out of 100 cases, 34% cases in hypertensive Group 1 had past history of hypertension. 37% of study subjects in Group 1 were in Stage 1 as per JNC VII guidelines while 11% were in Stage 2 and 2% were in prehypertension category. There was a statistically significant difference between Group 1 and Group 2 in systolic and diastolic blood pressure, TLC, total cholesterol, LDL, HDL, serum globulin and serum uric acid levels. In a study with 80 patients, Silva et al. examined the relationship between hyperuricemia, cardiometabolic risk factors and metabolic syndrome. They found that hyperuricemia was more prevalent in people with the people with hypertension, metabolic syndrome, women with obesity, men with abdominal obesity and people with lower HDL levels ($p<0.05$).[17]

Out of 100 cases, raised uric acid levels were seen in 27% of cases of which 19% were in hypertensive Group I and 8% in normotensive Group II. This difference was found to be statistically significant ($p<0.05$). Raised uric acid levels were seen in 19% of cases of which 8% were females and 11% were males in hypertensive Group. This was no gender difference found which was statistically significant ($p<0.05$). The primary conclusion of the current study is the association between HUA and HTN which is statistically significant. There are currently conflicting findings relating HUA with development of HTN. Despite the fact that certain studies have indicated that hyperuricemia is an independent risk factor in the development of HTN, other studies have not discovered a connection between the two.[18,19] The correlation between hyperuricemia and the likelihood of developing hypertension is positive, which has a number of possible explanations. First off, a HUA can cause vasoconstriction in kidneys by lowering circulating NO and activating RAAS, which raises blood pressure.[20] Second, numerous studies have shown that hyperuricemia can affect endothelial function by inhibiting the formation of nitric oxide, having antiproliferative effects, and that xanthine oxidase-produced oxygen radicals play a role in the development of HTN.[21] Thirdly, hyperuricemia may reach smooth muscle in vessels, activating a number of molecules such COX-2 and growth factor derived from platelets that promote the smooth muscle cell proliferation in vessel wall and thus cause secondary arteriolosclerosis.[22]

Limitation of the Study

However, some restrictions must be taken into account while interpreting our results. First off, one cannot deduce causality from this study. Our findings must therefore be verified in a subsequent prospective study. Second, in the present study data related to risk factors for hyperuricemia was available with certain limitations. As a result, there may be varying degrees of accuracy and completeness in our findings. Last but not the least, our study had a small sample size. Studies that examined the relationship between HUA and HTN with smaller sample size than ours were also studied by us. We ensured our case-control study with a design and sample volume was optimal for addressing the clinical query posed.

CONCLUSION

This is the first study in the area to show a connection between hyperuricemia and the likelihood that people may become hypertensive. The result of our study adds to the existing knowledge in this field by proving that hyperuricemia and the risk of hypertension are linked. Establishing a causal relationship between HUA and HTN has been difficult in various previous studies. This is due to inability of distinction of hyperuricemia as an independent risk factor for systemic arterial hypertension which typically coexists with a variety of cardiovascular risk factors. The findings of the current investigation, however, suggest that hyperuricemia may also be an independent risk factor for the onset of hypertension in addition to being a marker of CVDs.

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