



Serum Uric Acid Level In Recently Detected Primary Hypertension

KEYWORDS

Hypertension, Hyperuricemia, BMI, Metabolic syndrome

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ABSTRACT Hypertension markedly increases the risk for myocardial infarction, stroke, peripheral vascular disease and end stage renal disease. Hyperuricemia is common among adults with prehypertension. So, this study is conducted to find the association between hyperuricemia and hypertension and other cardiovascular risk factors. A total of 100 patients and 100 age and sex matched controls were studied for Serum uric acid levels. The study showed a significant difference in Serum uric acid levels between the hypertensive subjects and the normotensive controls and also the association between metabolic syndrome and serum uric acid. An elevated or high – normal serum uric acid value > 5.5mg/dl in an adult being evaluated for hypertension strongly supports the presence of primary hypertension. Hyperuricemia is associated with metabolic syndrome, as evidenced by other studies.

INTRODUCTION

Hypertension is an increasing important medical and public health issue. Hypertension markedly increases the risk for myocardial infarction, stroke, congestive heart failure, peripheral vascular disease and end stage renal disease.

Approximately 30% of adults are still unaware of their hypertension, more than 40% of individuals are not on treatment, and two thirds of hypertensive patients are not being controlled to BP levels less than 140/90 mmHg.⁽¹⁾

Hyperuricemia is also common among adults with prehypertension, especially when microalbuminuria is present. The observation that hyperuricemia precedes the development of hypertension indicates that it is not simply a result of hypertension per se.⁽²⁾

Uric acid is a purine metabolite that in most mammals is degraded by the hepatic enzymes uricase to allantoin. However, mutations in the uricase gene occurred during primate development, with the consequence that human have relatively higher levels of serum uric acid.

An elevation in serum uric acid has been associated with an increased risk for the development of hypertension,^(3,4) and 25% to 50% of hypertensive individuals are hyperuricemic. Hyperuricemia also confers increased risk for cardiovascular mortality, especially in women^(4,5) Despite the clinical and epidemiological evidence, many authorities do not consider an elevated uric acid to be a true cardiovascular risk factor, because patients with hyperuricemia often have other well – established risk factors for cardiovascular disease, such as hypertension, renal disease, obesity, Dyslipidemia, and insulin resistance.

Several studies have found that an elevated uric acid level is an independent risk factor for cardiovascular disease after controlling for the contribution of established risk factors by multivariate analyses.

AIMS OF THE STUDY

1. To find the association of hyperuricemia in recently detected hypertensive patients.
2. To find the association of serum uric acid in hypertensive patients who have metabolic syndrome.

Materials and methods

Study setting

Mahatma Gandhi Memorial Government Hospital and K.A.P.Viswanatham Government Medical College, Trichy.

Study design

Analytical study

Period study

October 2014 to September 2015

Patient population

Cases

One hundred adults aged between 20-50 years were selected for the study and referred consecutively to the Hypertension OPD of Mahatma Gandhi Memorial, Government Hospital, Trichy. They were studied for Serum uric acid levels.

Controls

Normotensive controls (n=100) were selected for the study and evaluated for clinical and laboratory data.

Both males and females were included for the study. All subjects and controls had normal renal function (Renal bio-

chemistry, USG Abdomen)

Inclusion Criteria

1. Hypertension patient, who are recently detected (<1yr) without any target end organ damage.
2. Age group between 20 to 50 years
3. Both sexes were included
4. Stage 1 and 2 Hypertension according to JNC – VIII.

Exclusion Criteria

- 1 Hypertensive patients with target end organ damage
- 1 Hypertensive Heart Disease as evidenced by left ventricular hypertrophy – ECG – voltage criteria.
- 2 Hypertensive Nephropathy
- 3 Hypertension Retinopathy
- 2 Diabetic Mellitus Type 1 & Type 2
- 3 Metabolic syndrome, after enrolment
- 4 Patient with chronic kidney disease
- 5 Hypertensive patients with known cerebrovascular disease
- 6 Hypertensive patients with coronary Artery disease Myocardial ischemia or infarction
- 7 Patients with long term drug intake like steroids anti tuberculous treatment (ATT), diuretics, antimetabolite or chemotherapy drugs .
- 8 Patients who were regularly consuming alcohol – Alcohol dependence subjects – Evidence by History, liver function tests and USG Abdomen
- 9 Patients of Myeloproliferative/lymphoproliferative disorders.
- 10 Patients who had chronic liver disease and metabolic disorders
- 11 Endocrine Disorder – Hypothyroid patient
- 12 Psoriasis patients
- 13 Patients in whom BMI > 30
- 14 Hypertensive crisis / Malignant Hypertension

Consent

The study group identified by the above criteria (inclusion and exclusion) were first informed about the nature of the study. Participants willing for the study were selected after getting an informed and written consent from them. Thus, a total of 100 patients were taken up for study who satisfied the inclusive and exclusion criteria similarly, 100 age and sex matched subjects were kept as control.

Urinary excretion and urate clearance were not done, only serum uric acid levels were analysed.

Evaluation of subject and controls

Laboratory analyses, performed in Biochemical laboratory at the MGM Government Hospital, Trichy included blood tests for the evaluation of renal parameters, fasting blood sugar, serum electrolytes, uric acid, lipid profile, thyroid function tests.

- Complete urine analysis were performed by the pathological faculty.
- ECG was taken for all the subjects and control to rule out coronary artery diseases and left ventricular hypertrophy.
- Fundus examination was done for all subjects.

Definition used in the present study

1 Hypertension

Hypertension is defined as systolic blood pressure of ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg. (Blood pressure classification: By JNC VIII)

2 Hyperuricemia

Hyperuricemia is defined as serum uric acid level more than > 7.0 mg/dl in Indian men and > 6.0 mg/dl in Indian women.

3 Metabolic syndrome - NCEP : ATP III 2001

Three or more of the following

1. Central obesity: Waist circumference > 102 cm (M), > 88 cm(F)
2. Hypertriglyceridemia: Triglycerides ≥ 150 mg/dl or specific medication
3. Low HDL cholesterol : < 40 mg/dl(M) and < 50 mg/dl(F) or specific medication
4. Hypertension: Blood pressure ≥ 130 mmHg systolic BP or ≥ 85 mm Hg diastolic BP or specific medication.
5. Fasting plasma glucose ≥ 100 mg/dl or specific medication or previously diagnosed type 2 Diabetes.

Statistical Analysis

Data was analysed statistically using standard software. Significance testing of the difference between means was done by unpaired 2 – tailed student't'test and correlations were assessed by Pearson coefficient.

RESULTS

The total number of subjects included in this study was 200. Of these 100 were study cases (Hypertension without target end organ damage) and other 100 were controls (Non – Hypertensive).

Both the cases and controls selected were adjusted for age distribution, sex, BMI, selected cardio vascular risk factor like smoking, family history.

At the end of the study, 30 subjects in study group were found to have metabolic syndrome according to NCEP-ATP III Criteria. Similarly 10 of the 100 controls satisfied the criteria for metabolic syndrome.

Both the cases and controls who met the criteria for metabolic syndrome were excluded from the study .Thus, subjects selected for the study after excluding metabolic syndrome were; cases – 70; controls – 90

Distribution of socio – demographic and clinical profile in cases and controls

Table 1

S.no		Cases	Control
1	Total	70	90
2	Gender	M=43, F-27	M=52, F-38
3	Mean age	37.34	37.21
4	BMI	20.96 TO 30.00	20.59 TO 29.38
5	Mean BMI	25.07	24.99
6	Waist circumference	82-106cm	80-106cm
7	Blood pressure	155.85	113.00
8	Mean SBP(mmHg)	101.92	74.12
9	Mean DBP(mmHg)	3.0-8.2	3.0-7.2
	Uric acid (mg/dl)	5.71	3.87
	Mean uric acid		

The age of the subjects in both groups ranges from 20-50 years. The mean and standard deviation for age of the cases and controls are 37.34 ± 2.7 and 37.21 ± 2.6 respectively, there is no significant difference among the cases and controls with reference to the age ($p=0.35$, not significant)

In 70 cases the subjects involved in this study are 43 males and 27 females. In 90 controls, there are 52 males and 39 females.

The sex distribution of the study group and control group does not differ. The study subjects whose BMI > 30 are excluded from the study as BMI > 30 has a strong association with hyperuricemia. The mean and standard deviation of BMI for the cases and controls are 25.06±2.88 respectively the details are shown in table 5 given below. There is no significant difference among cases and control with regard to BMI.

Distribution of blood pressure in cases and controls

The mean and standard deviation of systolic blood pressure in cases and controls are 155 ± 12.7 and 113.00 ± 7.41 respectively.

Similarly, the mean and standard deviation of diastolic blood pressure in cases and controls are 101 ± 17.35 and 74 ± 8.39 respectively.

Table – 2
Cases and controls in relation to blood pressure

Blood pressure	Cases *		Controls	
	Mean	S.D.	Mean	S.D.
Systolic	155	12.73	111	7.41
Diastolic	101	17.35	74	8.39

Analysis of serum uric acid in study and control groups

Serum uric acid in the study population and control varied from 3.0 to 8.2 mg/dl and 3.0 to 7.2 mg/dl respectively. The mean and standard deviation of uric acid among cases is 5.71 ± 1.06, while in control it is 3.87 ± 0.84 respectively. P=0.021 (Significant)

Table – 3

Serum uric acid	Cases		Controls	
	Mean	S.D.	Mean	S.D.
	5.71	1.07	3.87	0.84

Table – 4

Hyper uricemia in cases and controls

Hyper-uricemia	Cases				Controls			
	No	%	Mean	SD	No	%	Mean	SD
Present	21	30.0	6.98	0.69	04	04.4	7.12	0.39
Absent	49	70.0	5.18	0.70	86	95.6	3.72	0.50

Discussion

In this study, the relation of serum uric to BP in recently detected hypertensive adults without any target end organ damage was examined. The study was based on strong epidemiologic data that have linked serum uric acid to hypertension in human^(6,7) and experimental animal data, which suggest that hyperuricemia contributes to hypertension.^(8,9)

The experimental studies further demonstrated that hyperuricemia caused preglomerular vascular disease via a BP – independent pathway⁽⁹⁾ and once vascular changes were established, the hypertension was driven by the kidney, and lowering uric acid levels was no longer protective⁽⁹⁾. It is therefore hypothesized that if serum uric acid were important in the genesis of primary hypertension, then the relation would be greatest in the new and recent onset hypertensive subjects.

To test this hypothesis, 70 adults of which 43 males and 27 females referred for hypertension were evaluated. Both the cases and controls selected were matched for age, sex and BMI. The subjects in our sample included both young and old (20 to 50 years), but most of the studies included only

younger subjects. The mean age of the study population was 37.3 and 37.2 in both cases and controls respectively.

Blood pressure in both controls and cases were measured and the mean blood pressure in cases was 155/ 101 and in controls it was 113/74 respectively.

Uric acid was normally distributed among both subjects and was examined as continuous variable. The mean plasma uric acid in cases was 5.7 mg/dl ± 1.0 (range 3.0 to 8.2) and the mean plasma uric acid in control was 3.8 mg/dl ± 0.86 (range 3.0 to 7.2). The association between uric acid and hypertension was analysed using Student 't' test and statistical difference was assessed by Pearson coefficient.

The study showed a significant difference between the hypertensive subjects and the normotensive controls (p value = 0.021)

If uric acid was simply a marker, then a similar degree of hyperuricemia in the control subjects would be expected, and this was not observed.

Though mean uric acid was higher in subjects with BMI ≥ 25 (5.86) than those subjects with BMI < 25 (5.50) The relationship between uric acid and BMI did not show a statistical difference in this study, but Nakanishi et al. found a stronger association among those with lower BMI.

The study also examined a relation between metabolic syndrome and uric acid. There is a future perspective that hypertension can be treated by lowering uric acid levels particularly in recently detected hypertension. Once microvascular lesion develops, lowering uric acid levels will not be useful, as the late stage hypertension is uric acid independent and salt sensitive.

Daniel feig et al⁽¹⁰⁾ showed lowering uric acid levels in adolescent hypertension resulted in BP reduction. The results represent a new potential therapeutic approach, although not a fully developed therapeutic strategy due to potential adverse effects. These preliminary findings require confirmation in larger clinical trials.

Conclusion

Serum uric acid is strongly associated with BP in recently detected primary hypertension.

An elevated or high – normal serum uric acid value > 5.5mg/dl^(7,12,13)(mean uric acid – 5.7 in this study) in an adult being evaluated for hypertension strongly supports the presence of primary hypertension.

Though mean uric acid is higher in study subjects whose BMI > 25 than those subjects with BMI<25, the association is not significant

Hyperuricemia is associated with metabolic syndrome, as evidenced by other studies

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