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Observation of Serum Uric Acid Levels in Hundred Cases of Essential Hypertension

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Abstract: ***Introduction:*** *An elevation in serum uric acid has been associated with an increased risk for the development of hypertension and 25% to 50% of hypertensive individuals are hyperuricemic.****Methods:****One hundred adults aged between 20-50 years were selected for the study and referred consecutively to the medical OPD of Sri VenkateswaraRamnarainRuia Government General Hospital, Tirupati.They were studied for Serum Uric acid levels.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 biochemistry, USG Abdomen).****Results:****In the present study , 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. Statistically significant higher values of serum uric acid were observed in study population compared to control group (p=0.02). Hyper uricemia was found in 30% (n=21) of the cases compared to only 4.4% (n=4) in controls and this difference was statistically significant (p=0.02).* ***Conclusion****: Serum uric acid is strongly associated with BP in new and recent onset primary hypertension. An elevated or high–normal serum uric acid value >5.5mg/dl (mean uric acid-5.7 in this study) in an adult being evaluated for hypertension strongly supports the presence of primary hypertension.*

Keywords*: serum uric acid, hypertension, association, Hyper uricemia*

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I. 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

Worldwide prevalence estimates for hypertension may be as much as 1 billion individuals, and approximately 7.5 million deaths per year may be attributable to hypertension[1]. The WHO reports that suboptimal blood pressure (>115 mm Hg Systolic BP) is responsible for 62% of cerebrovascular disease and 49% of ischemic heart disease, with little variation by sex. In addition, suboptimal blood pressure is the number one attributable risk for death throughout the world [1].

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 than140/90 mm Hg[1].

Studies of uric acid levels and the development of hypertension have generally been consistent, continuous, and of similar magnitude. Hyperuricemia is also common among adults with prehypertension, especially when microalbuminuria is present.1The 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 enzyme uricase to allantoin. However, mutations in the uricase gene occurred during primate development, with the consequence that humans 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[4]. 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. The lack of a mechanism by which uric acid can cause cardiovascular disease, coupled with the inconclusive clinical and epidemiological data, has left the issue unresolved.

Objectives of the present study were to find the association of hyperuricemia in new-onset and recent onset Hypertensive patients; to find the association of hyperuricemia in hypertensive patients with regard to gender and risk factors like smoking, central obesity and BMI and to find the association of serum uric acid in hypertensive patients who have metabolic syndrome.

II. Material & Methods:

Source of data:
One hundred adults aged between 20-50 years were selected for the study and referred consecutively to the medical OPD of Sri VenkateswaraRamnarainRuia Government General Hospital, Tirupati over a period from November 2017 to January 2019.
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 biochemistry, USG Abdomen).

Inclusion Criteria
Hypertensive patients (of stage 1 & stage 2), whom are of new-onset and recent onset (<1 yr) without any target end organ damage in the age group between 20 to 50 years.

Exclusion Criteria
1. Hypertensive patients with Target End Organ damage
   Hypertensive Heart disease as evidenced by Left Ventricular hypertrophy - ECG-voltage criteria, Hypertensive Nephropathy and Hypertensive Retinopathy
2. Diabetes Mellitus – Type 1 and Type 2 or metabolic syndrome
3. Patients with Chronic kidney disease.
4. Hypertensive Patients with known Cerebro vascular disease.
5. Hypertensive Patients with coronary Artery disease - Myocardial Ischemia or Infarction.
6. Patients with long term drug intake like steroids, Anti-Tuberculous Treatment (ATT), diuretics, antimetabolite or chemotherapy drugs.
7. Patients who were regularly consuming alcohol – Alcohol dependence subjects - Evidenced by History, liver function tests and USG Abdomen.
8. Patients of Lympho or Myelo proliferative disorders.
9. Patients who had chronic liver disease and metabolic disorders.
10. Endocrine disorder – Hypothyroid patients.
11. Psoriasis patients.
12. Patients in whom BMI >30.
13. Hypertensive crisis / Malignant Hypertension

Consent
The study groups 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.
There was no conflict of interest and financial support was Nil. Urinary excretion and urate clearance were not done, only serum uric acid levels were analysed.

Patient profile
Selected socio-demographic, clinical and laboratory data were collected from the cases and controls and recorded in proforma.

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

i) Complete urinalyses were performed by the pathological faculty.
ii)ECG was taken for all the subjects and controls to rule out coronary artery disease and left ventricular hypertrophy.
iii)Fundus examination was done for all subjects.

Statistical Analysis

Data was entered in Microsoft excel spread sheet and analysed statistically using standard statistical software. Significance testing of the difference between means was done by unpaired 2 – tailed student 't' test, and correlations were assessed by Pearson coefficient. Significance was considered, if the 'p' value was below 0.05.

III. Results

The total number of subjects included in this study was 200. Of these 100 were study cases (Hypertensive without target end organ damage) and another 100 were controls (Non – Hypertensive).Both the cases and controls selected were adjusted for age distribution, Sex, BMI, selected cardio vascular risk factors 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 whom had met the criteria for metabolic syndrome were excluded from the study.Many studies previously published had indicated that hyperuricemia is also associated with metabolic syndrome, as other conditions like coronary artery disease, stroke, pre-eclampsia, malignant hypertension and chronic kidney disease.Thus, subjects selected for the study after excluding metabolic syndrome were: Cases – 70; Controls – 90.

Table 1 :**Distribution of Socio-demographic and clinical profile in cases and controls**

S. No.		**Cases**	**Controls**
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 – 106 cm.	80 – 106 cm.
7.	Blood Pressure		
	Mean SBP (mm Hg)	155.85	113.00
	Mean DBP (mm Hg)	101.92	74.12
8.	Uric Acid (mg / dl)	3.0 – 8.2	3.0 – 7.2
9.	Mean Uric Acid	5.71±1.07	3.87±0.84

In the present study , the age of the subjects in both groups ranges from 20 – 50 yrs. 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 38 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 ±2.5 and 24.99±2.88 respectively. There is no significant difference among cases and controls with regard to BMI.

Selected Cardiovascular risk factors:

In the present study smoking as cardiovascular risk factor present in 26 cases and 30 controls. Family history as cardiovascular risk factor present in 40 cases and 49 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.

Serum Uric acid & Hyper Uricemia:

In the present study , 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.Statistically significant higher values of serum uric acid were observed in study population compared to control group (p=0.02).

Hyper uricemia was found in 30% (n=21) of the cases compared to only 4.4% (n=4) in controls and this difference was statistically significant (p=0.02).

Table 2: **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

In the present study, the mean of serum uric acid higher in males (6.12)compared to females (5.5) and the difference was statistically significant (p=0.03).

No significant association was found between BMI and Uric acid levels.

No significant association was found between waist abnormality and hyper uricemia.

No significant association was found between smoking and Uric acid levels.

Uric acid and metabolic syndrome:

In the present study, out of 100 cases 30 subjects were found to have metabolic syndrome. Similarly, out of 100 controls 10 subjects were found to have the syndrome. The mean & standard deviation of uric acid in cases with metabolic syndrome is 6.13 ± 0.91 and in controls it is 3.68 ± 0.94.The statistical test shows a significant difference between the two groups with regard to metabolic syndrome (p value = 0.03).

Table 3 : **Uric acid levels in different stages of hypertension**

Stage	**Males**	**Females**	**Total**
Controlled hypertension	5.18 (3.80)	3.80 (1.32)	4.78 (2.32)
Stage 1	4.32 (1.47)	4.60 (1.26)	4.32 (1.38)
Stage 2	6.75 (1.57)	5.83 (1.30)	6.37 (1.55)
Isolated systolic hypertension	4.12 (1.24)	5.10 (0.62)	4.14 (1.14)

In present study the mean serum uric acid levels were found to be 4.78 (2.32) mg/dl, 4.42(1.38) mg/dl, 6.57(1.55) mg/dl and 4.44(1.44) mg/dl in controlled hypertension, stage 1 hypertension, stage 2 hypertension and isolated systolic hypertension respectively.

IV. Discussion

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

In our study the mean serum uric acid in cases was 5.71 ± 1.06 which was close to the results of Tamilmani et al[6] , Perlstein et al[7] , Strasak et al[8] and Kashem et al[9].

The mean of serum uric acid in males is 6.12 ± 0.5 and 5.5 ± 0.7 in females comparable to Kashem et al[9]&Tamilmani et al[6].

In our study mean serum uric acid in stage 1 hypertension was 4.32 ±1.38 mg/dl and those with stage 2 was 6.37 ± 1.55 mg/dl and those isolated systolic hypertension was 4.14 ± 1.14 which was statistically significant and compared to Kashem et al[9].

Mean age of the patients in the present study was close to those of Perlstein et al. where the authors observed the mean age was 53.3 years. Forman et al.[10] observed age range of the patients was 53 to 68 years.

In the present study ,mean systolic blood pressure is 155 ± 12.73 & mean diastolic blood pressure is 101 ± 17.35 which was comparable to Feig et al[11] and Strasak et al[8].

Elevated serum uric acid is associated with essential hypertension is 1.5 fold which is comparable to Kashem et al[9]&Tamilmani et al[6].

Uric acid in relation to BMI in cases: In the present shows the uric acid level between two groups (BMI < 25 and > 25) does not differ. But Nakanishi et al.[12] showed that hyperuricemia is more correlated with low BMI subjects than high BMI subjects in hypertension.

V. Conclusions

Serum uric acid is strongly associated with BP in new and recent onset primary hypertension. An elevated or high–normal serum uric acid value >5.5mg/dl (mean uric acid-5.7 in this study) in an adult being evaluated for hypertension strongly supports the presence of primary hypertension. The remarkable association of uric acid with BP in adults is consistent with recent animal model data and the hypothesis that uric acid might have a pathogenic role in the development of hypertension. Males have a higher degree of hyperuricemia than females in hypertensive patients. Hyperuricemia is associated with metabolic syndrome, as evidenced by other studies.

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