



## A STUDY OF SERUM URIC ACID LEVELS IN SUBJECTS OF ESSENTIAL HYPERTENSION WITH SPECIAL REFERENCE TO AGE AND BODY MASS INDEX(BMI) IN JLNMCH, BHAGALPUR

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**ABSTRACT** **OBJECTIVE** To compare serum uric acid levels among hypertensive subjects and controls and to evaluate distribution of serum uric acid levels with increasing age and Body Mass Index (BMI) in hypertensives. **METHODS** The study was conducted in both rural and urban catchment area of JLNMCH, BHAGALPUR and the population included were hypertensive patients according to the Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8), Stage of I and II hypertension were taken as cases. A group of age and sex matched normal controls were taken from the same catchment area and the study period was 1st December 2021 – 30TH December 2022 with 50 patients and 50 controls, selected by simple random selection and study was a Prospective , observational , cross- sectional hospital based single centre study. **RESULTS** There was significant association between age and hyperuricemia. The risk of hyperuricemia was 2.17 times more among the subjects with age $\geq$ 49 years as compared with the subjects with age $<$ 49 years and the risk was significant. The mean SBP of the hyperuricemic group was significantly higher than that of normouricemic group. The mean DBP of the hyperuricemic group was significantly higher than that of normouricemic group. **CONCLUSION** There was significant association between blood pressure and hyperuricemia among the cases and increasing trend of serum uric acid was observed with increasing systolic and diastolic blood pressure. Significant association between category of Body Mass Index and hyperuricemia. The mean Body Mass Index of the hyperuricemic group was significantly higher than that of normouricemic group. Significant association persists between age and hyperuricemia, risk was 2.17 times more among subjects with age  $>$ 49 yrs.

### KEYWORDS :

#### INTRODUCTION

Hypertension is a major health burden and a leading cause of mortality worldwide as well as in India. The prevalence of hypertension ranges from 20-40% in urban adults and 12-17% among rural adults. There is a continuous, consistent, and independent relationship between elevated blood pressure (BP) and risk of cardiovascular events. Subjects with hypertension are known to have a twofold higher risk of developing coronary artery disease, four times higher risk of congestive heart failure and seven times higher risk of cerebrovascular diseases and stroke compared to the normotensive subjects .

Hypertension is a physiological variable associated with age, sex and body mass index (BMI). There is a strong positive and continuous correlation between blood pressure and the risk of stroke, myocardial infarction, heart failure, renal disease, and mortality.

Essential hypertension' is high blood pressure for which there is no clearly defined etiology. From a practical perspective, it is best defined as that level of blood pressure at which treatment to lower blood pressure results in significant clinical benefit—a level which will vary from patient to patient depending on their absolute cardiovascular risk. Uric acid (2,6,8-trihydroxy purine) is the end product of catabolism of purine nucleosides (adenosine and guanosine) in humans. About 10% of Indian population has hyperuricemia once in their lifetime. In human blood plasma, the reference range of Serum Uric Acid (SUA) is typically 3.4-7.2 mg/dL (200-430  $\mu$ mol/L) for men and 2.4-6.1 mg/dL for women (140-360  $\mu$ mol/L).

Uric acid has been hypothesized to activate the renin-angiotensin system, which can lead to injury to pre-renal blood vessels. Hyperuricemia has been postulated to endothelial dysfunction, impaired oxidative metabolism possibly through the generation of reactive oxygen species, stimulation of granulocyte adherence, increased platelet aggregation-all are implicated in the pathogenesis of hypertension .

Uric Acid stimulates vascular smooth muscle cell proliferation mediated by stimulation of mitogen-activated protein kinase,

cyclooxygenase 2, platelet derived growth factor. So elevated uric acid predicts severity of heart failure. Hypertension and hyperuricemia have a 3 to 5 fold increase risk of experiencing coronary artery disease or cerebrovascular disease . Elevated serum uric acid is linked with dyslipidemia, hypertension, insulin resistance, menopause, aging and sedentary lifestyle in several studies.

Serum uric acid level (SUA) is associated with an increased risk for developing hypertension. Higher baseline serum uric acid levels also has higher systolic blood pressure and diastolic blood pressure, greater body mass index, higher triglycerides and total cholesterol.

#### METHODOLOGY

**1). STUDY SITE**– Both rural and urban catchment area of JLNMCH, BHAGALPUR

**2). STUDY POPULATION**-Hypertensive patients according to the Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8), Stage of I and II hypertension were taken as cases.

A group of age and sex matched normal controls were taken from the same catchment area.

They were taken from medical or paramedical staff, relatives of patients with status unrelated to hypertension.

**3). STUDY PERIOD**- 1ST DECEMBER 2021 – 30TH DECEMBER 2022

**4). SAMPLE SIZE** – 50 Patients and 50 Controls

**5). SAMPLE DESIGN** - Simple random selection.

**6). STUDY DESIGN**- Prospective observational cross-sectional hospital based study.

**7). INCLUSION CRITERIA:**

Patients (aged >12 yrs) in whom hypertension is diagnosed on at least 3 separate Occasions according to the Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) Stage of I and II. A group of age and sex matched normal controls were taken from the same catchment area

### 8). EXCLUSION CRITERIA:

The following patients were excluded from the study:

1. All patients with secondary hypertension.
2. Patients with accelerated / Malignant Hypertension Systolic Blood Pressure > 180 mmHg  
Diastolic Blood Pressure >110 mmHg
3. Recent (within last 6months) Myocardial Infarction.
4. Recent (within last 6months) Cerebrovascular event.
5. Recent (within last 6months) angiography with stent placement
6. Serious infection in the month before recruitment
7. Loss of more than 5% body weight during last 6 months
8. Cardiac arrhythmias
9. Active malignant diseases
10. History of Pregnancy induced hypertension within last 12 months.
11. Chronic renal failure ( Calculated Glomerular Filtration Rate <90 ml/min)
12. Chronic liver disease
13. Chronic psychiatric illness
14. Diabetes mellitus
15. Familial hypercholesterolemia, Dyslipidemia
16. Patients on drugs known to cause hyperuricemia, e.g. thiazide diuretics
17. Smokers having >10 cigarettes/day, Alcoholics >2 pegs/day.
18. Patient on drugs that can increase the level of uric acid in blood Like Ascorbic acid, Aspirin, Caffeine, Cisplatin, Diazoxide, Thiazide Diuretics, Epinephrine, Ethambutol, Levodopa, Methylodopa, Nicotinic acid, Phenothiazines, Theophylline.
19. Patient on Drugs that can decrease the level of uric acid in blood like Allopurinol, Azathioprine, Clofibrate, Corticosteroids, Febuxostat, Guaifenesin, Mannitol, Probenecid, Warfarin

### STUDY TECHNIQUE:

All study members were given detailed explanation of the study in their understandable language before obtaining their informed consent for involvement in study and for venipuncture. After that a detailed history including personal data, present complaints and complication, treatment history, past history, family history and personal history was taken followed by thorough physical examination.

Blood pressure was specifically recorded using standard Mercury sphygmomanometer. Before the measurement the individual seat quietly in a chair with feet on the floor for 5 min. Two measurements were recorded and the mean value was taken. The center of the standard cuff (the width of the bladder cuff is about 40% of the arm circumference and the length of the cuff bladder encircles about 80% of the arm circumference) was ensured to be at heart level. The cuff was deflated at the rate of 2 mmHg/sec. Systolic blood pressure was considered as the first of at least two regular "tapping" Korotkoff sounds, and diastolic blood pressure was taken as the point at which the last regular Korotkoff sound is heard.

All patients was selected on the basis of their blood pressure status.

Hypertension was categorized according to blood pressure readings by Joint National Committee 8 definitions.

According to this criteria cut off value for Systolic blood pressure (SBP) was considered as 140mm Hg for stamping Hypertension, whereas for Diastolic blood pressure (DBP) the cut off value for hypertension was 90mm Hg.

Based on JNC 8, patients with sustained hypertension were further divided into stage 1 hypertension (systolic BP 140-159 or diastolic BP 90-99 mmHg), stage 2 hypertension (systolic BP ≥160 or diastolic BP ≥100 mmHg).

Classification	Systolic BP (mmHg)	Diastolic BP (mmHg)
Normal	<120	And <80
Prehypertension	120-139	Or 80-89
Stage 1 hypertension	140-159	Or 90-99
Stage 2 hypertension	≥160	Or ≥100

BP, blood pressure.

Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) [17].

A 12 hour fasting venous blood collected and Serum uric acid estimated using auto analyzer (ERBA-XL-600, Mannheim) of Central Laboratory of JLNMC.

Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m<sup>2</sup>).

$$BMI = \frac{\text{mass(kg)}}{(\text{height(m)})^2}$$

According to BMI five groups were found like Normal (healthy weight) from 18.5 to 25, Overweight from 25 to 30, Obese Class I (Moderately obese) from 30 to 35, Obese Class II (Severely obese) from 35 to 40 and Obese Class III (Very severely obese) over 40.

Based on blood pressure level subjects were divided into two groups-case and controls. Cases includes Stage 1 and Stage 2 hypertensives, Controls includes Prehypertensives and normal people. Serum uric acid assessed in both the groups. Subjects also divided according to BMI in 5 groups ie normal, overweight, obese class 1, obese class II (severely obese), obese class III (Very severely obese).

Serum uric acid levels compared among hypertensive subjects and controls and mean serum uric acid levels observed in various age groups with hypertension. As in men SUA typically is 3.4-7.2 mg/dL (200-430 μmol/L) and 2.4-6.1 mg/dL for women (140-360 μmol/L) for our study purpose SUA >6.5 mg/dL has been taken as a cut off for hyperuricaemia as in previous studies like Shah et al.(2002)[72], Neki et al.(2015)[52] and Woo et al.(1994)[69].

Apart from serum uric acid assessment , all patients and controls undergone following laboratory investigations

- Complete hemogram.
- Fasting blood sugar.
- Liver function test.
- Blood Urea , creatinine.
- Routine and microscopic examination of urine.
- Chest x ray, Ultrasonography of abdomen.
- Electrocardiography.
- Serum electrolytes.
- Total cholesterol, HDL-Cholesterol, LDL-Cholesterol, Triglyceride.

### STUDY TOOLS

Laboratory methods available at hospital (specific methods mentioned earlier).

### ANALYSIS OF DATA

The case records are to be studied analyzed and compared using suitable statistical methods. The latest Epi Info (TM) 3.5.3 which is a trademark of the Centers for Disease Control and Prevention (CDC) has been used for this purpose

## RESULTS

The study was performed for a period of 12 months in JLNMCCH with 50 hypertensive patients as cases and 50 age and sex matched controls having blood pressure normal or prehypertensive range according to Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) Serum uric acid measured in 12 hour fasting venous blood of both case and controls along with Body-Mass Index (BMI).

In our study we have 50 cases fulfilling JNC 8 criteria of Stage I and Stage II hypertension and 50 controls having BP <140/90 mm of Hg. For better understanding controls are further subdivided into Normal with SBP <120 and DBP <90 mm of Hg and Prehypertension with SBP 120-139 mm Hg and DBP 80- 89 mm of Hg.

The risk of hyperuricemia was 2.17 times more among the subjects with age ≥49 years as compared with the subjects with age <49 years [OR=2.17(1.01, 4.87); p= 0.05] and the risk was significant t-test showed that the mean age of the hyperuricaemics was significantly higher than that of normouricaemics (t98=1.98; p=0.05).

The risk of hyperuricemia was 1.31 times more among males as compared with females [OR=1.31(0.59, 2.91); p=0.49] but the risk was not significant.

Pearson Correlation Co-efficient between SBP and SUA was significant (r= 0.45; p=0.001). Thus increasing trend of SUA was observed with increasing SBP.

Pearson Correlation Co-efficient between DBP and SUA was significant (r= 0.44; p=0.001). Thus increasing trend of SUA was observed with increasing DBP.

t-test showed that the mean SBP of the hyperuricaemic group was significantly higher than that of normouricaemic (t98=4.29; p=0.00001). t-test showed that the mean DBP of the hyperuricaemic group was significantly higher than that of normouricaemic group (t98=4.52; p=0.00001).

t-test showed that the mean BMI of the hyperuricaemic group was significantly higher than that of normouricaemic group (t98=7.09; p=0.00001). The mean level of uric acid of the patients with HTN and obesity was significantly higher than that of patients with HTN and without obesity (t42=2.86, p= 0.0052).

## DISCUSSION

This observational study was done in a tertiary care hospital of Bhagalpur, Bihar. 50 hypertensive patients (>12 yrs) fulfilling the inclusion criteria were randomly selected over a period of 18 months along 50 normotensive controls. Serum uric acid (SUA) and Body Mass Index (BMI) were measured in each case and controls. SUA was compared in case and control groups along with age and BMI.

In our study it is evident that significant association persists between age and hyperuricaemia, risk was 2.17 times more among subjects with age >49 yrs but no significant association of age and gender with blood pressure were found.

We found Proportion of hyperuricemia was significantly higher in cases (62.0%) than controls (26.0%). The risk of hyperuricemia was 4.64 times more among cases as compared with controls [OR=4.64(1.98, 10.88); p= 0.0002] and the risk was significant. Chi-square test showed that there was significant association between blood pressure and hyperuricemia among the cases (p=0.04). Chi-square test also showed that there was association between blood pressure and hyperuricemia among the controls but it was not very significant (p=0.33). Pearson Correlation Co-efficient between SBP, DBP and SUA was significant (r= 0.45; p=0.001) (r= 0.44; p=0.001) respectively. Thus increasing trend of SUA was observed with increasing SBP and DBP.

We found significant association between HTN and hyperuricemia (p=0.0001). t-test showed that the mean SBP and DBP of the hyperuricaemic group was significantly higher than that of normouricaemic (t98=4.29; p=0.00001) (t98=4.52; p=0.00001) respectively.

Study revealed there was significant association between category of

BMI and hyperuricemia (p=0.00001). t-test showed that the mean BMI of the hyperuricaemic group was significantly higher than that of normouricaemic group (t98=7.09; p=0.00001).

Significant association was found between obesity and blood pressure (p=0.04). Among Class I Obese 72.7% were hypertensive and all class 2 obese were hypertensive. t-test showed that the mean level of uric acid of the patients with HTN was significantly higher than that of patients without hypertension (t98=4.41, p=0.0001).

We found that the mean level of uric acid of the patients with HTN and age ≥49 years was significantly higher than that of patients without hypertension and age ≥49 (t98=3.02, p= 0.0032).

Study also showed that the mean level of uric acid of the patients with HTN and age <49 years was significantly higher than that of patients without hypertension and age <49 (t98=6.16, p= 0.0001). Study showed that the mean level of uric acid of the patients with HTN and obesity was significantly higher than that of patients without hypertension and obesity (t98=7.30, p=0.0001).

The mean level of uric acid of the patients with HTN and without obesity was significantly higher than that of patients with HTN and without obesity (t98=3.20, p=0.0019).

Also there was no significant difference in mean level of uric acid of the patients with HTN and age ≥49 years and than that of patients with HTN and age <49 years (t42=0.86, p=0.39).

Also the the mean level of uric acid of the patients with HTN and obesity was significantly higher than that of patients with HTN and without obesity (t42=2.86, p=0.0052).

## CONCLUSION

There was significant association between blood pressure and hyperuricemia among the cases.

Proportion of hyperuricemia was significantly higher in cases (62.0%) than controls (26.0%). The risk of hyperuricemia was 4.64 times more among cases as compared with controls.

Increasing trend of serum uric acid was observed with increasing systolic and diastolic blood pressure.

Significant association was found between obesity and blood pressure. Significant association between category of Body Mass Index and hyperuricemia. The mean Body Mass Index of the hyperuricaemic group was significantly higher than that of normouricaemic group.

Significant risk of hyperuricemia was 7.00 times more for Obesity. Significant association persists between age and hyperuricaemia, risk was 2.17 times more among subjects with age >49 yrs.

## REFERENCES

- Enas EA, Singh V, Gupta R, Patel R, et al. Recommendations of the Second Indo-US Health Summit for the prevention and control of cardiovascular disease among Asian Indians. *Indian heart journal*. 2009; 61:265-74.
- Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: Part 1: General considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Lancet*. 2011; 377:505-15.
- Modagan P, Meera K, Suntharavadivelu S. Uric Acid as a Mediator of Endothelial Dysfunction in Hypertension. *International Journal of Research in Pharmaceutical and Biomedical Sciences*. 2013; 4:106-12.
- Krishnan E, Kwok K, Schumacher R, Kuller L. Hyperuricemia and incidence of hypertension among men without metabolic syndrome, *American Heart Association Hypertension*. 2007; 49:298-303.
- Erdogan D, Gullu H, Caliskan M, Yildirim E, Bilgi M, et al. Relationship of serum uric acid to measures of endothelial function and atherosclerosis in healthy Adults. *INT J CLIN PRACT*. 2005; 59(11):1276-82.
- Vyas A, Nikunj R, Patel B, Vyas K. A Study of Correlation between Essential Hypertension and Hyperuricemia. *International Journal of Recent Trends in Science And Technology*. 2013; 7(2): 76-79.
- Soans G, Murgod R. Evaluation of role of hyperuricaemia as an active component of metabolic syndrome. *International journal of analytical, pharmaceutical and biomedical sciences*. 2012; 1(3):58-65.
- Baker JF, Krishnan E, Chen L, Schumacher HR. Serum uric acid and cardiovascular disease: recent developments, and where do they leave us? *Am J Med*. 2005; 118: 816-826.
- Johnson RJ, Feig DI, Herrera-Acosta J, Kang DH. Resurrection of uric acid as a causal risk factor in essential hypertension. *Hypertension*. 2005; 45: 18-20.
- Brand FN, McGee DL, Kannel WB, Stokes J 3rd, Castelli WP. Hyperuricemia as a risk factor of coronary heart disease: the Framingham Study. *Am J Epidemiol*. 1985; 121:11-18.