Hyperuricemia as a Risk Factor for Hypertension: A Case-control Study in a Tertiary Care Hospital in Eastern India

*Nivedita Sinha[1], Bikas Saurabh[2], Sandeep Kumar Singh[3]

[1] *Associate Professor,*
Department of Community Medicine,PMCH, Patna.
[2] *Head of Department of Internal Medicine,*
Paras-HMRI Hospital, Patna.
[3] *JR, Paras-HMRI Hospital,Patna.*

***Abstract**: A case control study done in Eastern India to find relation, if any, between hypertension and hyperuricemia. OR and Pearson Correlation highly significant. Mean Systolic BP among cases was 151.7mmHg (sd +/-6.69)and among controls was 112.7 (sd +/-7.54).Mean Diastolic BP among cases and controls were 97.00mm Hg (sd +/-3.44) and 76.48mm Hg(SD +/-8.58). Among cases,58.8% had stage 1hypertension. Among controls,65.5% were prehypertensive.*

Keywords: hyperuricemia ,hypertension, risk factor, Eastern India.

Introduction

Many literatures quote hyperuricemia as a risk factor for hypertension and several other cardiovascular complications. Uric acid has been hypothesized to activate the Renin-Angiotensin System which leads to injury to pre-renal blood vessels. It is postulated to cause endothelial dysfunction, impaired oxidative metabolism, possibly through generation of reactive oxygen species, stimulation of granulocyte adherence, increased platelet aggregation-all implicated in pathogenesis of hypertension. [1]
Food habits and lifestyles, important variables in causation of both hypertension and hyperuricemia, vary from region to region. Although studies relating hypertension and hyperuricemia are mostly from foreign countries, few have also been done in Northern India. However there is scarcity of literature from Eastern parts of India, so this study was thought pertinent to be undertaken. Also, studies as this, could go a long way in helping establish hyperuricemia as a cause for hypertension rather than a risk factor.

Aims & Objectives:

1. To determine the serum uric acid (SUA) levels in cases of hypertension (HT) and in matched controls.
2. To evaluate relationship, if any, between hypertension and increased levels of SUA.

Material and Methods:

This was an observational case-control study conducted in a tertiary-care hospital in Patna, on people attending the Primary Health Clinic for routine health checkups, preliminary health checkup for jobs, visas and so on. The study population consisted of -

i .People diagnosed as being hypertensives as per JNC 7/8 criteria [2,3]
ii. A group of sex- and age- matched normal controls. These were taken from relatives of patients, with status unrelated to hypertension.
This study was conducted for a period of 18 months from June 2017 to December 2018.
Sample size was calculated using Open Epi, Ver-3 open source calculator – SS Proper, with Confidence Level = 95% and Confidence limit – 5%. Thus 148 patients were selected by random sampling, and 148 controls were considered.
Inclusion Criteria for patients were: those aged > 12 years in whom hypertension was present on at least three separate occasions according to the 7th and 8th reports of the Joint National Committee (JNC) on prevention Detection, Evaluation and Treatment of high blood pressure (JNC 7/8).
A group of age- and sex- matched normal controls were taken.
While selection of cases, Exclusion Criteria applied were-
All patients with secondary causes of hypertension (HT) including obesity.
Patients with accelerated HT (Systemic Blood Pressure > 180mmHg and/or Diastolic BP > 110mm).
Recent (within last 6months) myocardial infarction
Recent(within last 6months) cardiovascular event
Recent (within last 6 months) angiography with stent replacement
Any serious infection in the month before recruitment.
Involuntary loss of > 5% body weight within last 6 months.
Cardiac arrhythmias.
Active malignant disease
History of Pregnancy- Induced HT.
Chronic Renal Failure (Calculated GFR < 90ml/min.)
Chronic Liver Disease.
Chronic Psychiatric illness.
Diabetes Mellitus
Familial Hypercholesterolemia, dyslipidemia
Patients on drugs known to cause hyperuricemia e.g thiazide diuretics, Ascorbic Acid Asprin etc
Smokers having > 10 cigarettes per day.
Alcoholics consuming >2 units /day (1 unit = 30ml ethyl alcohol).
Patient on drugs that decrease the level of uric acid in blood eg. Azathioprine, Clofibrate, Corticosteroids, Febuxostat, Mannitol, Guanafenesin, Probenecid, Warfarin .

For the purpose of data collection & measuring serum Uric acid levels and for other laboratory tests, informed consent was taken from patients.
A detailed personal history, history of present- and past- complaints and family history were taken, followed by a thorough physical examination.
BP was recorded using standard Mercury sphygmomanometer. Before the measurement, the patient was made to remain seated quietly in a chair with both feet on the floor, for 5 minutes. Mean value of two measurements was taken.
JNC criteria was used for classifying the hypertension using JNC-7, which were-

	SBP		DBP
Normal	<120	&	<80
Pre HT	120-139	or	80-90
Stage I HT	140-159	or	90-99
Stage 2 HT	>160	or	>100

Serum Uric acid (SUA) levels were estimated using auto analyzer available at the hospital, after collection of sample in 12-hour fasting patients.

BMI was calculated using formula

$$BM = \frac{\text{mass (kg)}}{(\text{ht in m})^2}$$

and classified as normal (BMI=18.5 – 25), overweight = 25-30 , Obese Class I (BMI=30-35), obese class II (BMI=35 – 40) obese Class III (BMI=Over 40).

Based on blood pressure levels, subjects were divided into 2 groups – cases and controls. Stage I & stage 2 hypertensive subjects formed the cases, while non-hypertensive and pre-hypertensive subjects formed controls. Serum uric acids were assessed in both the groups. The mean serum uric acid levels were noted in various age groups, having hypertension. Since SUA level typically is between 3.4 – 7.2mg/dl (200-430micromol/l) in males and 2.4–6.1 mg/dl (140-360micromol/l) in females, for our study purpose, SUA > 6.5mg/dl was taken as a cut off for hyperuricemia, as done in previous studies like by Shah et al 2002 [4] , Neki et al (2015) [5] & Woo et at (1994) [6]
Apart from serum uric acid assessment, all patients and controls underwent following laboratory investigations:-
Complete haemogram
Fasting Blood Sugar
Liver Function Tests
Blood Urea, Creatinine
Routine and microscopic examination of urine
Chest X – Ray, USG of abdomen
Electrocardiogram (ECG)
Serum Electrolytes
Lipid profile
Thyroid Stimulating Hormone estimation.

Results

With changing trends in the prevalence of non-communicable diseases, in developing countries like India, insights into the risk factors are of utmost importance. Our study, undertaken to study the role of hyperuricemia in causing hypertension, was an observational case–control study conducted on 148 cases and 148 controls

Table 1. Distribution of Blood Pressure in Case and Control Groups

Blood Pressure	Case (%)	Control (%)	Total (%)
Normal	-	51 (34.5)	51 (17.2)
Pre-hypertension	-	97 (65.5)	97 (32.8)
Stage1 hypertension	87 (58.8)	-	87 (29.4)

Stage2 hypertension	61 (41.2)	-	61 (20.6)
	148 (100)	148 (100)	296 (100)

Table 2. Showing Distribution of Gender Among Cases and Controls.

Gender	Cases		Controls		Total	
	n	**%**	**n**	**%**	**n**	**%**
Male	78	52.7	81	54.7	159	53.7
Female	70	47.3	67	45.3	137	46.3
Total	148	100	148	100	296	100

Chi sq.=0.122 , p=0.72

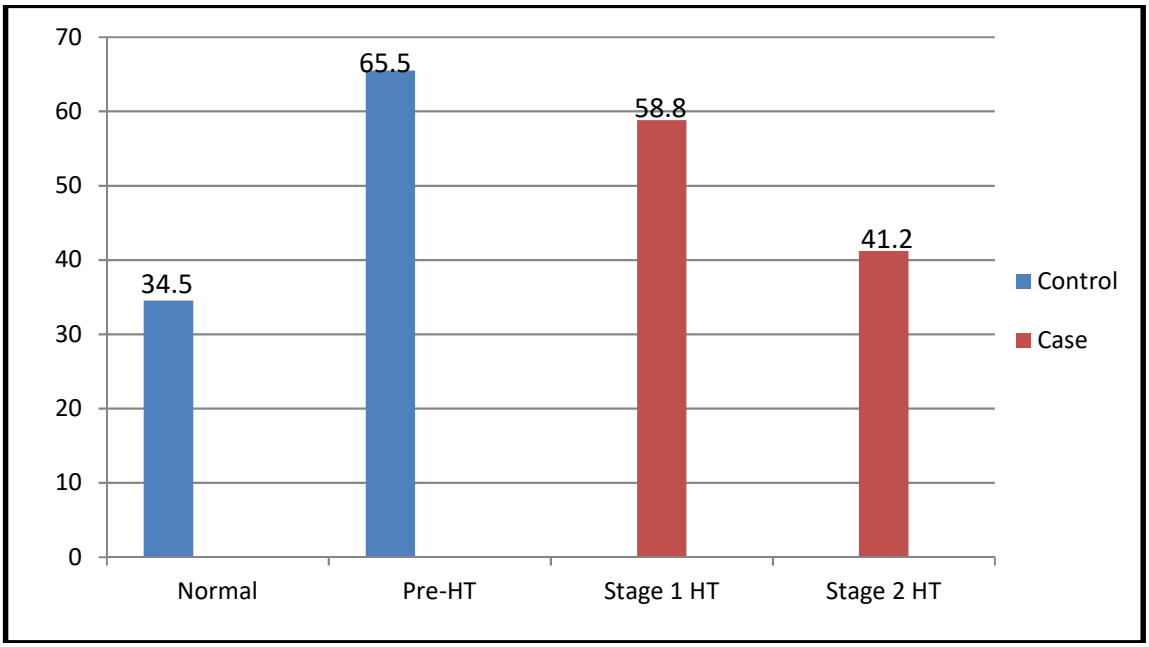

Figure:1 Distribution of blood pressure in case and control groups.

Table 3. Mean of Systolic and Diastolic Blood Pressure in Cases and Control

Blood Pressure	**Case**	**Control**
SBP	151.71±6.69	112.7±7.54

(Mean±s.d.)		
DBP (Mean±s.d.)	97.00±3.44	76.48±8.58

Table 4. Showing Distribution of Hyperuricemia Among Cases and Controls.

	Hyperurecemia +ve	Hyperurecemia -ve
Cases	120	28
Controls	11	137

OR=53.57

Table 5: Correlation Between Systolic and Diastolic Blood Pressure with SUA in Cases

Correlation	**Pearson Correlation Coefficient (r)**
SBP with SUA	0.770
DBP with SUA	0.672

Pearson correlation Coefficient between SBP and SUA was significant (r=0.77, p<0.001).

Table 6. Association of Gender with Blood Pressure in Cases

CASE	**Stage-1(HTN) %**	**Stage-2(HTN) %**	**Total %**
Female	42 48.28	28 45.9	70 47.3
Male	45 51.72	33 54.1	78 52.7
	87 100	61 100	148 100

Chi-square =0.081, p=0.776, Not significant

.

The males constituted 52.7% of hypertensives and 54.7% of controls. Out of 148 cases of hypertension chosen, 87(58.8%) belonged to stage I hypertension and 61 (41.2%) were stage II hypertensives. Out of 148 controls, 51 (34.5%) were normal and 97 (65.5%) were pre-hypertensives.
The mean Systolic BP among cases was 151.7mmHg (sd +/-6.69) and among controls was 112.7 (sd +/- 7.54), while the mean Diastolic BP among cases and controls were 97.00mm Hg (sd +/-3.44) and 76.48mm Hg(SD +/-8.58) respectively. Its t-values were 47.06 (with $P<0.001$) and 26.95 ($p < 0.001$). Out of cases, 87(58.8%) had Stage I hypertension and 61(41.2%) had stage II hypertension. Among controls, 51(34.5%) had normal BP and 97(65.5%) were pre-hypertensives.

Out of the 70 females cases, 42 were stage I hypertensives while 28 were stage II hypertensives. Among males, out of 78 cases, 45 had stage I Hypertension, 33 were stage II hypertensives. The associations between gender and blood pressure was found by Chi Square test. Its P value was 0.776. Chi-square test showed no significant association between gender and blood pressure of cases.
The number of hyperuricemics among cases was 120, while among cases,it was only 11.
The Pearson Correlation Co-efficient of systolic blood pressure with SUA was 0.770 & diastolic blood pressure with SUA is 0.672.

Discussion

The proportion of females was less in both the cases and controls. The gender distribution among cases and among controls was found to be not significant. This is in tune with previous studies like Kinsey [7] Zhang [8] and Whelton [9]. This proved that cases and controls were matched for their gender.
Among 148 controls in our study, 34.5%were normotensives and 65.5% were pre-hypertensives (overall 32.7%), while overall prevalence of pre-hypertension was 32.77%. We compared this finding with some other studies in order to get a picture of the prevalence of pre-hypertension, since these could be at risk of HT.In a study regarding the prevalence of pre-hypertension , conducted in urban South India , it was found to be 55%[10]. In a study by Yadav et al of Lucknow in North India, pre-hypertension prevalence was found to be 32.3% [11]. In another study conducted at Varanasi, Uttar Pradesh, pre-hypertension prevalence was 41.7% [12].Thus in our study, the percentage of pre-hypertensives was more, compared to other studies. The possible contributing factor could be the common genes of hypertension among cases and controls, since the controls were age and sex-matched members from same family. It may due to differences in lifestyles.
Among cases, 58.8% had stage I hypertension and 41.2% had stage II hypertension.
In a study regarding prevalence of stage I hypertension, it was estimated that among hypertensives “a total of 70% of these would be Stage hypertension”[13] while in another study by Viazzi et al. [14], it was77% of cases.
Table 5 showed that applying t-test on SBP and DBP among cases and controls, p value was less than 0.001, proving that the systolic and diastolic blood pressure among cases was significantly higher than among controls.
The odds of having hypertension was 53.57 times higher in hyperuricemics compared to that in non-hyperurecemics. In a study [15] by Sujeet Raina et al conducted in sub-Himalayan region, OR was 6 in male hyperuricemic hypertensives versus hyperuricemic normotensives, while the corresponding figure in females was 4.46.

To test the linear relationship of hypertension and hyperuricemia, Pearson correlation was applied. The association was significant and showing very high strength of association, proving that hyperuricemia is an independent risk factor for hypertension.

Conclusion

The study provides conclusive evidences of hyperuricemia as a risk factor for hypertension. The OR was significantly higher than in other similar studies, one factor for which could be demographic differences related to region. Interventions to keep serum uric acid levels within normal limits would thus go a long way in decreasing incidence of hypertension. With recent increasing trends in incidences, morbidity and mortality due to non –communicable diseases, hypertension being one of them, controlling hyperuricemia could go a long way in bringing them down. Given the limited economic resources in a developing country like ours, and also given the fact that several non-communicable diseases have common risk factors, the findings may have long-term results in overall control of NCDs.

Bibliography

1. 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.
2. Chobanian AV, Bakris GL, Black HR, et al. “ Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure” National Heart, Lung and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension: 2003 December, 42(6) 1206-52.
3. Paul A James, Suzanne Oparil, Barry L Carter. “2014 Evidence-Based Guidelines for the Management of High Blood Pressure in Adults”,JAMA., 2014;311(5):507-520.
4. Shah A, Keenan R.T. “Gout, Hyperuricemia, and the Risk of Cardiovascular Disease: Cause and Effect?”, Curr Rheumatol Rep. ,12**,** 118–124 (2010).
5. Neki NS. “A Study of Serum Uric Acid Level in Essential Hypertension”, JIMSA., January-March 201528:121-128
6. Woo J, Swaminathan RK, Cockram C, Lau H. “Association Between Serum uric acid and Some Cardiovascular Risk Factors in a Chinese Population”, Postgrad Med J.,1994;70:486-491.
7. Kinsey D, Walther R, Wise HS, Whitelaw G,Smithwick R. “Incidence of hyperuricemia in 400 hypertensive patients” Circulation, 1961;24:972.
8. Zhang W,Sun K,Yang Y,Zhang H,Frank B. “Plasma Uric Acid and Hypertension in a Chinese Community:Prospective Study and Meta-Analysis”,Clinical Chemistry.,2009;55(11):2026-2034.
9. Whelton A. “Hyperurecemia and Hypertension,A Confluence of Concepts.,2012;60:1112-1113.
10. Parthaje PM, Unnikrishnan B, Thankappan KR,Thapar R, et al. “Prevalance and Correlates of Prehypertension Among Adults in Urban South India”, Asia Pac J Public Health ., 2016 January;28(1 Suppl):93S-101S.
11. Yadav S et al., “Prevalance and Risk Factors of Pre-hypertension and Hypertension In An Affluent North Indian Population”, Indian J Med Res.,2008 December.
12. Shikha Singh, Ravi Shankar, Gyan Prakash Singh, “Prevalance of Associated Risk factors of Hypertension:A Cross-sectional Study in Urban Varanasi”, International Journal of Hypertension, vol.2017.
13. GuptaR. “Trends In Hypertension Epidemiology In India”,J Hum Hypertens.,2004Feb;18(2):73-8.
14. Viazzi F,Parodi D,Leoncini G,Parodi A. “Serum Uric Acid and Target Organ Damagein Primary Hypertension”., Hypertension.2005;45:991-996.
15. Raina S, Agarwal VK, Kapoor D, Sharma KN, Yadav RS. “Hypertension as determinant of hyperurecemia:A case control study from sub Himalayan region in north India”, Journal of the Association of Physicians of India, vol 66.