

SIGNIFICANCE OF LOWERING SERUM URIC ACID LEVEL IN HYPERTENSIVE PATIENTS*Barochia D. V¹, Bhattacharyya P. C², Manabendra Nayak³*¹DNB Fellow, Department of Medicine, Down Town Hospital, Guwahati, Assam.²Academic Incharge and Senior Consultant, Department of Medicine, Down Town Hospital, Guwahati, Assam.³Postgraduate Teacher and Senior Consultant, Department of Medicine, Down Town Hospital, Guwahati, Assam.

ABSTRACT

BACKGROUND

Worldwide, hypertension is an important public health challenge because of its high frequency and concomitant risk of coronary heart disease, stroke, kidney disease and other vascular complications. Interestingly, serum uric acid can have relation with hypertension (HTN), stroke, dyslipidaemia, diabetes mellitus and obesity. This led many people to get involved in the study to find out the exact correlation between hyperuricemia and hypertension.

MATERIALS AND METHODS

It was a hospital based, time bound, case control study done in the Department of Medicine, Down Town hospital, Guwahati, Assam. All patients diagnosed with hypertension in the period of November 2014 to October 2015 were studied; 50 patients of hypertension were taken as study cases and 50 normal OPD patients were taken as control for comparison. Serum uric acid level was compared between non-hypertensive and hypertensive group and statistical analysis was done by using Microsoft Word, Excel 2007 software.

RESULTS

A total of 100 persons of age >18 years having hypertension were studied; 50 persons were in hypertensive group and 50 persons were in control group. Serum uric acid level of more than 6.8 mg/dl was considered significant. Hyperuricemia among hypertensive pts. was most prevalent in 41-60 yrs. age group (43.75%). There was no significant difference in prevalence of hyperuricemia among hypertensive male (35.29%) and female (37.50%) pts.

CONCLUSION

The prevalence of hyperuricemia is significantly higher in 40 to 60 years age group and not very significant difference between male and female. With the increase in duration of age (>60 years) hyperuricemia is less responsible for hypertension.

KEYWORDS

Serum Uric acid level, Hyperuricemia, Hypertension.

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BACKGROUND

Serum uric acid is usually known for its harmful effects and not for beneficial effects. Harmful effects are gout and urolithiasis where hyperuricemia is a common feature. It has beneficial effects as an antioxidant and neuroprotective activity (Feig DI et al 2009).¹

As early as 1972, in the Israeli Heart Trial, a study conducted by Kahn HA et al in 1972,² it was demonstrated that the higher level of uric acid was associated with double risk of incidence of HTN within 5 years. They found 20% increase in BP per 1 mg/dl increment in serum uric acid (UAC).

Khan Faisel et al 2008³ in their study showed elevated Serum UAC level to be associated with increased arterial

stiffness, endothelial dysfunction and blunted vasodilatory response.

In vitro studies also have elucidated the possible mechanism of uric acid mediated atherosclerosis. Primary human vascular smooth muscle cells are induced to proliferate by addition of uric acid to the growth medium in a dose dependent manner (Kang DH, et al 2005⁴). Hyperuricemia has been associated with increased morbidity in patients with HTN and is associated with increased mortality in women and elderly population (Kim SY et al 2008⁵).

In recent decades, the diet and lifestyle that predispose individuals to hyperuricemia and gout have become increasingly common. Asymptomatic hyperuricemia is currently not considered as an indication for treatment. Due to the increasing evidence of the association of uric acid with HTN and cardiovascular diseases, it is likely that the indication for treating hyperuricemia will be extended in patients with other risk factors.

As the hyperuricemia is one of the important risk factors for developing HTN, we should give emphasis and checking the Serum UAC level of all the hypertensive patients and treating them accordingly. This will not only reduce the long-

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Corresponding Author:

Dr. Manabendra Nayak,

House No. 2, Raghu Nath Choudhury Path,

Lachit Nagar, Guwahati- 781007, Assam.

E-mail: dr.mnayak@yahoo.co.in

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term complications of hyperuricemia but will also help in better control of HTN and will thereby help in managing its various complications efficiently. Thus, it will offer a better quality of life to hypertensive patients.

There is also increasing evidence that uric acid may have direct effect on adipocytes, hepatocytes, pancreatic islet cells, and renal tubular cells that may play a major role in obesity, fatty liver, islet dysfunction, acute and chronic renal injury, and metabolic syndrome. There is also increasing evidence that uric acid may have neural effects leading to increased response time and impulsivity.

MATERIALS AND METHODS

Study Site

The site of the study is the department of Medicine, Down Town Hospital, Guwahati, Assam.

Study Population

Total of 100 persons were taken up for study (50 normal persons and 50 hypertensive patients).

Study Design

Case control study with random selection of cases.

Justification of Sample Size

Keeping in mind the given duration of the study and concerned patients flow in our hospital, sample size will be 100 subjects, with the aim to complete the study within the stipulated time period.

Time frame to address the study

1 year of time duration starting from November 2014 to October 2015.

Inclusion Criteria

- Patients with essential hypertension (BP >140/90 mmHg only).
- Age more than 18 years.
- Both genders.

Exclusion Criteria

- Age below 18 years.
- Secondary hypertension.
- Diabetes mellitus, Thyroid disorders, Cardiac diseases, Renal diseases and other co-morbidities.
- Those who do not wish to give the consent or non-cooperative patients.

The study participants are persons with hypertension aged 18 years and above and apparently healthy people who served as controls and consented to be part of the study.

Methodology

100 consecutive cases with or without hypertension, above the age of 18 years of any gender coming to medicine OPD of Down Town Hospital Guwahati between November 2014 to October 2015 will be included in the study. Consent will be taken from ethical committees of Down Town Hospital for this study. Consent will be taken from patients also. Random samples of all participants more than 18 years reviewed to retrieve medical and personal data, including baseline demographic characteristics, history of smoking, alcohol

consumption, hypertension, and use of antihypertensive or lipid-lowering medications, and co-morbidity.

A physical examination was done on all subjects including blood pressure (BP) and anthropometry. The BP was measured in the right arm of seated participants after five minutes of rest using a random zero mercury sphygmomanometer keeping at the level of heart. SBP >140 mmHg and DBP >90 mmHg is taken as a marker of presence of HTN, stage 1 HTN - BP = 140-159/90-99 mmHg and stage 2 HTN - BP >160/100 mmHg according to JNC 8 criteria. Second reading was taken after 10 minutes by same as mentioned above. The average of first and second readings was accepted.

This Uric Acid was measured by enzymatic procedure. In this procedure Uric acid is converted by uricase to allantoin and hydrogen peroxide. Hydrogen peroxide reacts with 4-aminoantipyrine (4-AAP) in the presence of N, N-bis (4-sulfobutyl)-3, 5-dimethylaniline, disodium salt (MADB) to produce a chromophore which is read bichromatically at 660/800 nm. The amount of dye formed is proportional to the uric acid concentration in the sample.

Reagents:

Phosphate buffer (pH 7.5) 42 mmol/L

Peroxidase \geq 5.9 kU/L

MADB 0.15 mmol/L

4-Aminophenazone 0.30 mmol/L

EDTA 0.44 mmol/L

Uricase \geq 250 U/L

Also contains preservatives

No special patient preparation is necessary. But special precaution is to centrifuge specimens and remove the serum from the cellular material within 4 hours of collection.

Specimen Type	Serum
Container	3 ml vacutainer
Specimen Required	2 mL of serum, minimum 0.2 mL.
Patient Preparation	Not required
Specimen Processing	
Instructions	Serum: Allow to clot. Centrifuge at 1100-2000 g for a minimum of 10 minutes.
Transport Temperature	Refrigerated
Specimen Collection	

Data collection technique

For primary data - History taking, physical examination and observation of the management of the patients

For secondary data - Review of literature, text books, journals, hospital records and websites

Tools

Direct observations, interview schedule, protocols, tests, examination of medical records, and collection of writing samples.

Statistical Methods

Descriptive statistical analysis is carried out in the present study.

Results of continuous measurements – Age, SBP and DBP will be presented in Mean + SD (min – max) and results of categorical measurements gender, uric acid level findings are presented in frequency and percentages. Data will be presented in pie charts, table formats and bar diagram for the ease of understanding and interpretation. The significance of differences in prevalence will be explored using Pearson's Chi-square test whereas the differences in group means will be assessed using unpaired t-tests. A difference or correlation giving a P-value ≤ 0.05 will be considered statistically significant.

Microsoft Office word 2007 and Microsoft Office Excel 2007 will be used to generate table, Pie diagram, bar diagram etc.

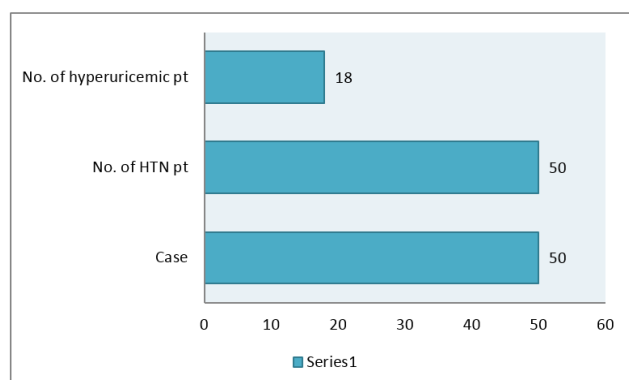
RESULTS

All the cases were subjected to a thorough history taking, clinical examination and laboratory investigations as per the requirement of the case. In this study 50 pts of essential HTN were selected. They were evaluated for hyperuricemia (symptomatic or asymptomatic). Maximum 44% and 20% of hypertensive males and females respectively were in 41-60 yrs. age group, 18% & 8% males and females were in 18-40 yrs. age group and 6% and 4% males and female respectively were present in 61-80 yrs. age group.

Hyperuricemia was present in 78% in 41-60 yrs. age group, 17% in 18-40 yrs. age group and 5% in 61-80 yrs. age group of total hyperuricaemic pts. It suggests that hyperuricemia was more common in 41-60 yrs. age group of hypertensive cases.

Case	No. of HTN Pts.	No. of Hyperuricaemic Pts.
50	50	18

Table 1. Number of Hyperuricaemic Pts. in Cases



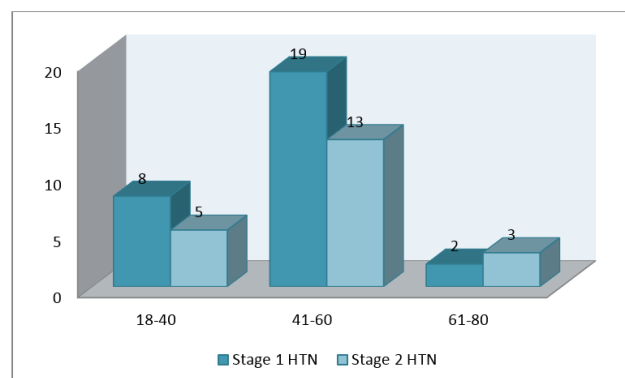
Graph 1. Number of Hyperuricaemic Pts. in Cases

Hyperuricemia was found to be present in 36% of hypertensive pts.

Studies showed highest no. of male (50%) and female (27.78%) were in 41-60 yrs. of age group, male (11.11%) and female (5.56%) in 18-40 yrs., 5.56% male and 0.0% female were present in 61-80 yrs. of age group.

Age (yrs.)	Stage 1 HTN	Stage 2 HTN	Total
18-40	8	5	13
41-60	19	13	32
61-80	2	3	5
Total	29	21	50

Table 2. Distribution of Cases according to Blood Pressure Level in Different Age Groups

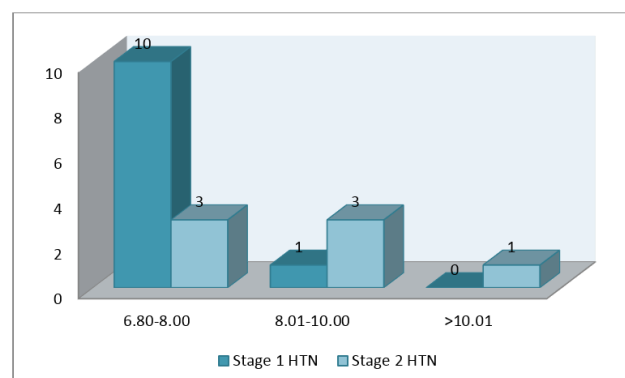


Graph 2. Distribution of Cases According to Blood Pressure Level in Different Age Groups

In our study 29 cases (58%) were having stage 1 HTN (BP= 140-159/90-99 mmHg) and 21 cases (42%) were having stage 2 HTN (BP>160/100 mmHg).

SUA Level	Stage 1 HTN	Stage 2 HTN	Total
6.80-8.00	10	3	13
8.01-10.00	1	3	4
>10.01	0	1	1

Table 3. Distribution of Cases According to the Level of Uric Acid and Stage of HTN

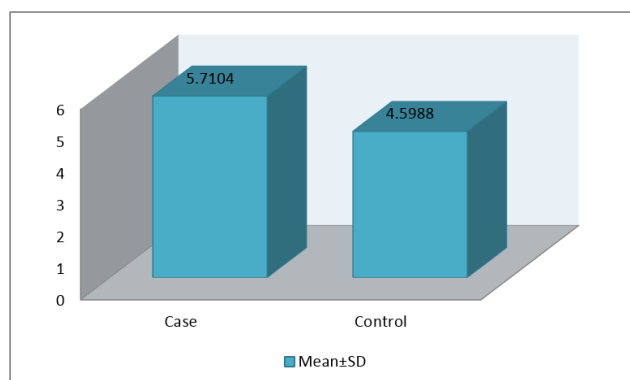


Graph 3. Distribution of Cases According to the Level of Uric Acid and Stage of HTN

We found 72.22% of cases were present in Serum UAC = 6.80-8.00 mg/dl, 22.22% in 8.01-10.00 and 5.56% were having Serum UAC level more than 10.01 mg/dl.

	Case	Control	Unpaired t test
Mean ± SD	5.7104 ± 1.8508	4.5988 ± 0.8984	t = 3.8206 p = 0.0002 Significant

Table 4. Mean Wise Comparison of Case and Control in the Present Study



Graph 4. Mean Wise Comparison of Case and Control in the Present Study

Unpaired t test was used, and p value showed very significant result between case and control group.

	Hyperuricaemic Male	Normal Male	Unpaired t Test
Mean ± SD	8.1083 ± 1.0093	4.5838 ± 0.8638	t = 12.4278 p = 0.0001 Significant

Table 5. Mean Wise Comparison of Male in the Present Study

Our Study showed highly significant difference between mean of normal male and hyperuricaemic male.

	Hyperuricaemic female	Normal female	Unpaired t test
Mean ± SD	7.3967 ± 0.4464	4.5063 ± 0.9129	t = 7.4897 p = 0.0001 Significant

Table 6. Mean Wise Comparison of Female in the Present Study

We found showed very significant difference between mean of normal and hyperuricaemic females.

DISCUSSION

In our study hyperuricemia was present in 36% of hypertensive patients. The observations in our study were nearly similar to other studies. Deleaval P et al 2005⁶ their study found that 25% of untreated hypertensive pts were hyperuricaemic. Iliesiu A et al 2010⁷ reported that hyperuricemia is present in 25-40% of untreated hypertensive individuals. In a study done by Cannon P J et al 1966,⁸ they observed that 25 to 40% of adult patients with untreated HTN had hyperuricemia.

Khan Faisel et al 2008³ study showed elevated Serum UAC level is associated with increased arterial stiffness, endothelial dysfunction and blunted vasodilatory response. Serum uric acid is projected as a marker of development of HTN in studies done by Perlstein et al in 2006⁹ and Krishnan E et al in 2007.¹⁰

The prevalence of hyperuricemia among hypertensive cases in this study among males and female was 24% and 12% respectively. Prevalence of hyperuricemia in normal adult population, as observed in different studies are: male – 35.2%, female – 8.7% by Conen D et al 2004,¹¹ 25.8% in male and 15.0% in female by Lin KC et al in 2000,¹² 21.5% in male and 10.2% in female by Fan XH et al in 2009,¹³ 21.6% in male and 8.6% in female by Liu B, Wang T et al 2011.¹⁴ The results of our study showed that the prevalence of hyperuricemia is more in hypertensive males and females as compared to normal population.

In our study hyperuricemia was most common (28%) in the 41-60 yrs. age group, followed by 6% in 18-40 yrs age group and 2% in 61-80 yrs. age group. The findings of our study are similar to the data reported by other workers.

Hyperuricemia was present in 37.4% of the hypertensive pts as reported by Ahmed N et al in 2009.

In this study 36% of total hypertensive (male & female) pts having hyperuricemia in 18-80 yrs. of age.

A systematic review and meta-analysis conducted to determine if hyperuricemia was associated with hypertension, suggested that females were associated more with hypertension (Grayson P C et al 2011¹⁵). In this study 35.29% of hypertensive male pts and 37.5% of hypertensive female pts had hyperuricemia.

Serum UAC and high BP showed a significant relation in the overall population, when evaluated it according to different age groups (<40, 40-59, ≥60) it was only significant in the non-elderly population under age 60 in both genders. There have been several studies suggesting that the strength of the relationship between serum UA and high BP is more dominant in the younger age groups and decreases during the aging process (Lee et al 2015¹⁶).

The results of this present study and previous other studies showed hyperuricemia induced HTN to be more common in less than 60 years of age group. The weakening relationship between uric acid and hypertension with age is one of the few possible explanations. Uric acid damages small renal vessels, which leads to irreversible salt-sensitive hypertension. This hypertension persists regardless of uric acid levels when hypertension develops in the elderly, other pathophysiological mechanisms such as decreased arterial compliance may play a larger role in hypertension than hyperuricemia (Jin M, Yang F et al 2012¹⁷).

In this study 43.75% of total hypertensive pts having hyperuricemia in 41-60 yrs. age group. We found that 23.08% of total hypertensive pts having hyperuricemia in 18-40 yrs age group. We found that 20% of total hypertensive pts having hyperuricemia in 61-80 yrs age group.

CONCLUSION

- Prevalence of hyperuricemia is significantly higher in hypertensive patients.
- Prevalence of hyperuricemia in hypertensive male and female is not very significant different.
- With the increase in duration of age (>60 yrs.) hyperuricemia is less responsible for hypertension.
- Prevalence of hyperuricemia in hypertensives is more common in less than 60 years of patients.

However, for stronger conclusion we need a larger study.

Epidemiologic and experimental findings support the hypothesis that the increase in serum uric acid level can antedate the development of hypertension and can play a major pathogenic role in the development of cardiovascular disease.

REFERENCES

- [1] Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. *N Engl J Med* 2009;360(17):1811-1821.
- [2] Kahn HA, Medalie JH, Neufeld HN, et al. The incidence of hypertension and associated factors: the Israel ischemic heart study. *Am Heart J* 1972;84(2):171-182.
- [3] Khan F, George J, Wong K, et al. The association between serum urate levels and arterial stiffness/endothelial function in stroke survivors. *Atherosclerosis* 2008;200(2):374-379.
- [4] Kang DH, Park SK, Lee IK, et al. Uric acid induced C-reactive protein expression: implication on cell proliferation and nitric oxide production of human vascular cells. *J Am Soc Nephrol* 2005;16(12):3553-3562.
- [5] Kim SY, De Vera MA, Choi HK. Gout and mortality. *Clin Exp Rheumatol* 2008;26(5 Suppl 51):S115-S119.
- [6] Deleaval P, Burnier M. Hyperuricemia in hypertension: any clinical implication? *Rev Med Suisse* 2005;1(32):2072-2074.
- [7] Iliesiu A, Campeanu A, Dusceac D. Serum uric acid and cardiovascular disease. *Maedica (Buchar)* 2010;5(3):186-192.
- [8] Cannon PJ, Stason WB, Demartini FE, et al. Hyperuricemia in primary and renal hypertension. *N Engl J Med* 1966;275(9):457-464.
- [9] Perlstein TS, Gumieniak O, Williams GH, et al. Uric acid and the development of hypertension: the normative aging study. *Hypertension* 2006;48(6):1031-1036.
- [10] Krishnan E, Kwok CK, Schumacher HR, et al. Hyperuricemia and incidence of hypertension among men without metabolic syndrome. *Hypertension* 2007;49(2):298-303.
- [11] Conen D, Wietlisbach V, Bovet P, et al. Prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country. *BMC Public Health* 2004;4:9.
- [12] Lin KC, Tsai ST, Lin HY, et al. Different progressions of hyperglycemia and diabetes among hyperuricemic men and women in the kinmen study. *J Rheumatol* 2004;31(6):1159-1165.
- [13] Fan XH, Sun K, Wang YB, et al. Prevalence and associated risk factors of hyperuricemia in rural hypertensive patients. *Zhonghua Yi Xue Za Zhi* 2009;89(38):2667-2670.
- [14] Liu B, Wang T, Zhao HN, et al. The prevalence of hyperuricemia in China: a meta-analysis. *BMC Public Health* 2011;11:832.
- [15] Grayson PC, Kim SY, LaValley M, et al. Hyperuricemia and incident hypertension: a systematic review and meta-analysis. *Arthritis Care Res (Hoboken)* 2011;63(1):102-110.
- [16] Lee JJ, Ahn J, Hwang J, et al. Relationship between uric acid and blood pressure in different age groups. *Clin Hypertens* 2015;21:14.
- [17] Jin M, Yang F, Yang I, et al. Uric acid, hyperuricemia and vascular diseases. *Front Biosci (Landmark Ed)* 2012;17:656-669.