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Evaluation of Serum Uric Acid in Essential Hypertension At PMCH, Patna

[1]Dr. Kumar Shivam, Junior Resident, Department of Medicine, Patna Medical College and Hospital, Patna

[2]Dr. Vijay Achari, Professor, Department of Medicine, Patna Medical College and Hospital, Patna

[3]Dr. Rakesh Kumar, Assistant Professor, Department of Medicine, Patna Medical College and Hospital, Patna

[4]Dr. Kaushal Kishore, Professor and Head, Department of Medicine, Patna Medical College and Hospital, Patna

Corresponding Author: Dr. Kumar Shivam, Junior Resident, Department of Medicine, Patna Medical College and Hospital, Patna.

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Abstract

Introduction: Hypertension is one of the leading causes of the global burden of the disease. Adults from all over the world suffer from hypertension, which is one of the leading causes of death and illness. Hypertension doubles the risk of cardiovascular diseases, including coronary heart disease, heart failure, ischemic and haemorrhagic stroke, renal failure and peripheral artery disease. About 90% of cases of hypertension are due to essential hypertension.

Aims: To study the relation between severity and duration of hypertension to the serum uric acid levels.

Materials and methods: During the study period from April 2021 to November 2022 a total of 100 patients were studied of which 50 patients were cases that were categorized into Stage 1 or Stage 2 hypertension (base on JNC VII classification) and 50 were controls who were patients without hypertension or any other condition known to cause raised serum uric acid levels.

Result: The t-value was 8.213 and a p-value of .000 which was significant. The data analysed showed that there was a significant rise in hypertension in patients who were having stage 2 hypertension i.e. those with a SBP $\geq$ 160 and a DBP $\geq$ 100 than those with stage 1 hypertension (SBP 140- 159 and DBP 90 - 99) table – 6.

Conclusion: With the results based on the study carried out we concluded that there can be a direct relation between hyperuricemia and hypertension. Also the study showed that the SUA levels were significantly increased in patients with Stage 2 hypertension in comparison with those with stage 1 hypertension, showing that the severity of hypertension also related to the SUA levels. The study also showed that the duration of hypertension had a significant impact on the SUA levels, those with a

longer duration of hypertension had significantly raised SUA levels when compared with those of a lesser duration.

Keywords: Serum Uric Acid, Hypertension, Hyperuricemia and Disorders.

Introduction

Hypertension is one of the leading causes of the global burden of the disease. Adults from all over the world suffer from hypertension, which is one of the leading causes of death and illness. Hypertension doubles the risk of cardiovascular diseases, including coronary heart disease, heart failure, ischemic and hemorrhagic stroke, renal failure and peripheral artery disease. About 90% of cases of hypertension are due to essential hypertension.

In India, hypertension is a growing health issue. Most people discover they have hypertension after they have already damaged their target organs, such as through a deadly stroke, myocardial infarction, or permanent renal failure. Unfortunately, 78 million people are reported to have hypertension, even in affluent nations like the United States.

Uric acid, which serves no biochemical function other than being an end product of purine metabolism, was first discovered in 1776. A Swedish chemist Scheele isolated it from a urinary tract stone. In 1797, a British chemist Wallaston detected uric acid in a tophus which was removed from his own ear. About 50 years later Alfred Baring Garrod, a British physician showed by chemical isolation that uric acid was abnormally high in gouty patients. In subsequent studies Garrod formulated a rational relationship between hyperuricemia and symptomatology of gouty patients.

Association between hypertension and hyperuricemia was recognized when a family with a unique and unfortunate pedigree attended Hammersmith hospital in 1957. The father and six of the seven siblings had hyperuricemia, while the mother and all the siblings had hypertension1 [1]. This raised the question whether a raised serum uric acid was common in patients with hypertension.

Numerous studies have suggested a significant relationship between elevated serum uric acid levels and a higher risk of coronary heart disease. This relationship is frequently observed in people with essential hypertension, including untreated hypertension, and diabetes mellitus type 2, both of which are independently linked to coronary artery disease.

If elevated blood uric acid levels enhance the risk of hypertension and type 2 diabetes independently of known risk variables such age, obesity, alcohol use, and physical activity [2], it has yet to be determined.

This raised the question whether a raised serum uric acid was common in patients with hypertension. Raised serum uric acid has been reported to be associated with an increased risk of coronary heart disease and is commonly encountered with essential hypertension, even untreated hypertension, and type 2 diabetes, which are in turn associated with coronary heart disease. It is not known whether raised serum uric acid increases the risk of hypertension and type 2 diabetes independently of known risk factors such as age, obesity, alcohol consumption, and physical activity [2].

Hypertension is the emerging public health problem of adult population across the globe, affecting one in every four individuals. The etiological factors associated with hypertension are difficult to predict because hypertension results from a complex interaction of genes and environmental factors. This study was determine whether raised serum uric acid levels as an independent risk factor for developing hypertension.

Materials And Methods

Study Population:

Cases: A total of 50 Patients visiting OPD or being admitted in general medicine ward having essential hypertension in PMCH, Patna were included as cases.

Controls: A total 50 apparently healthy normotensive subjects with age and sex matched were considered as the control group.

Type Of Study: This is a case-control study.

Study Place: The study was done in Department of Medicine at PMCH, Patna.

Study Period: This study was conducted from April 2021 to November 2022.

Inclusion Criteria

1. Adult male and female patients > 18 years of age diagnosed as hypertensives according to JNC VIII classification for hypertension were included as cases.

Exclusion Criteria

1. Diabetes Mellitus - Type 1 and Type 2 or metabolic syndrome
2. Patients with Chronic kidney disease.
3. Hypertensive Patients with known Cerebro vascular disease.
4. Hypertensive Patients with coronary Artery disease - Myocardial Ischemia or Infarction.
5. Patients with long term drug intake like steroids, Anti-Tuberculous Treatment (ATT), diuretics, antimetabolite or chemotherapy drugs.
6. Patients with Lympho or Myelo-proliferative disorders.
7. Patients who had chronic liver disease and metabolic disorders.
8. All causes of secondary Hypertension.
9. Patients in whom BMI >30.

Result And Discussion

Elevated SUA levels have been associated with an increased risk for cardiovascular disease. The potential mechanisms by which SUA may directly affect cardiovascular risk include enhanced platelet aggregation and inflammatory activation of the endothelium[3].

In few studies, the association of SUA with cardiovascular disease was uncertain after multivariate adjustment as in the Framingham Heart Study (1985) and the ARIC study (1996), but in others the association remained certain and significant.

Because elevated serum uric acid is correlated with several risk factors including renal dysfunction, hypertension, insulin resistance, hyper-homocystenemia and hyperlipidemia, it is debated whether SUA is an independent cardiovascular risk factor.

In the present study the incidence of hyperuricemia in controls was 17% and the incidence of hyperuricemia in cases was 37 %.

Various other studies have also shown that increased SUA levels were seen in hypertensive patients. Kinsey (1961) in his study with 100 hypertensive patients reported a 46 % incidence of hyperuricemia in hypertensives43. Kolbe (1965) in his study of 46 hypertensive patients found 26 to be having increased SUA levels (56 %) [4].

A. Breckenridge (1966) showed 274 of 470 patients on antihypertensive treatment (58%) had raised SUA levels and 90 of the 333 patients (27%) attending the clinic for the time had hyperuricemia1. In a study by C. J. Bulpitt (1975), 48 % male hypertensives and 40 % female hypertensives had their SUA level in the hyperuricemic range[5].

Messerli et al (1980) had an incidence of 72 % raised SUA in their study population of 39 established hypertensives. Messerli and Frohlich et al hypothesized that the frequent presence of hyperuricemia in hypertensive patients reflects underlying renal dysfunction or reduced renal perfusion[6].

It certainly is possible that uric acid may be an earlier and more sensitive maker of decreased renal blood flow than serum creatinine. It has been recently suggested that since uric acid may play a role in the formation of free radicals and oxidative stress, the increased risk of hypertension in subjects with raised serum uric acid levels might be associated with this increased generation of free radicals.

Several observations support this concept of free radical mediated inhibition of endothelium dependent vasodilation. An antioxidant deficiency in diet which produces hyperuricemia, contributes to the etiology of hypertension, and the antioxidant drugs also show a blood pressure lowering effect in both diabetic and hypertensive patients[7].

In a study by Tykarski (1991), he showed SUA concentration and the prevalence of hyperuricemia were significantly higher in hypertensive patients. They further demonstrated that tubular secretion of uric acid was significantly lower in hypertensive patients in comparison with normotensive subjects. There was no difference in pre and post- secretory reabsorption of uric acid. They concluded that high prevalence of hyperuricemia in essential hypertension was caused by impaired renal excretion of uric acid[8].

Three possible conclusions can be drawn from the association of hypertension with raised SUA levels -. Hypertension may arise as a result of hyperuricemia, hypertension can cause hyperuricemia and the duration and severity of hypertension is related directly to the SUA levels.

In gouty patients without advanced tophi, however renal failure and hypertension are rare. In a group of 80 patient's attending the Hammer Smith hospital gout clinic only 2 were hypertensive. In a study of gouty patients of Northern India by Kumar et al they found that only one out of 30 patients had hypertension[9].

Hence it is unlikely that hypertension arises as a result of raised SUA levels, but the possibility that uric acid which plays a role in the formation of free radicals and oxidative stress, the increased risk of hypertension in subjects with raised serum uric acid levels might be associated with this increased generation of free radicals. Hence the fact that raised SUA levels can lead to Hypertension cannot be entirely ruled out.

As to the possibility that Hypertension can cause hyperuricemia, it is thought that hyperuricemia can result from either overproduction of uric acid or from under excretion of uric acid.

Overproduction of uric acid can be measured by the rate of incorporation of acid precursors such as Glycine labeled N 15, into the uric acid pool. Such a study carried out in 4 hypertensive patients with raised SUA levels did not show any overproduction of uric acid.

In the study of Breckenridge excretion of uric acid and uric acid clearance were lower in all hypertensive patients than in the normal group. When the uric acid clearance was expressed per 100ml of glomerular filtrate, there was no significant difference between normal subjects and hypertensive patients who had normal SUA levels, but the difference between those 2 groups and the hyperuricemic hypertensives was significant and they suggested a renal tubular

abnormality in the handling of uric acid, the nature of the abnormality was not clear.

Later Messerli et al showed that hyperuricemia in hypertensive is due to early renal vascular involvement, namely, Nephrosclerosis. SUA rises because of impaired renal tubular function, which is the main site of regulation of SUA due to nephrosclerosis. Tykarski in his study showed that SUA levels in hypertensives are due to impaired tubular secretion of urate.

In the present study incidence and severity of hyperuricemia between cases and controls correlated significantly with the severity of hypertension. This correlated with both the Kinsey 43and Breckenridge 1studies, but according to Cannon et al[10] severity of hypertension had no relation to SUA level. Our study agrees with the study of Tykarski et al in that there is a positive correlation between SUA and severity of hypertension[11].

In our study the incidence of Hyperuricemia in cases with stage 1 hypertension was 4.2 % and those with stage 2 hypertension was 42.11 %

As to the possibility as to whether SUA levels was related to the severity and duration of hypertension, Breckenridge in his study showed an increasing incidence of hyperuricemia as the diastolic BP increased in his study, but there was no tendency for hyperuricemia to occur, only with patients with more severe hypertension.

Kinskey also found that hyperuricemia was common in patients with more severe grades of hypertension. Comparison showed that SUA increased significantly with duration of hypertension in our study. This was similar to the finding of Tykarski et al who encountered positive correlation between duration of hypertension and SUA in their study.

The PIUMA study demonstrates a strong independent association between SUA and CV risk in initially untreated and asymptomatic adult subjects with essential hypertension, but it is unable to answer the question of whether SUA exerts direct toxic effects. As extensively reviewed by Puig and Ruilope, [12]both uric acid and superoxide radicals are produced for the effect of xanthine oxidase in the late phase of purine metabolism. Superoxide radicals, which may cause tissue and vascular damage,[13] are increased in subjects with essential hypertension[14].

In our study we found that there is definite relation in SUA levels between hypertensive patients and normotensive patients and there is a directly proportional relation in the levels of SUA in relation to the duration and severity of hypertension. Hence the possibility of serum uric acid acting by the production of free radicals and causing oxidative stress leading to hypertension and whether the duration and severity of hypertension lead to renal dysfunction in the form of nephrosclerosis leading to higher levels of serum uric acid has to be considered as various other studies have also show to have a positive relation in the SUA levels and hypertension.

Conclusion

With the results based on the study carried out we concluded that there can be a direct relation between hyperuricemia and hypertension. Also the study showed that the SUA levels were significantly increased in patients with Stage 2 hypertension in comparison with those with stage 1 hypertension, showing that the severity of hypertension also related to the SUA levels. The study also showed that the duration of hypertension had a significant impact on the SUA levels, those with a longer duration of hypertension had significantly raised

SUA levels when compared with those of a lesser duration.

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Legend Table and Figure

Table 1: SUA Levels between Cases and Controls, stage of Hypertension and Duration of hypertension

		Number	Mean ±SD
Category	Cases	50	6.104±1.576
	Controls	50	5.685±1.338
Stage of Hypertension	Stage 1	12	5.0312±.77
	Stage 2	38	6.4421±1.615
Duration of hypertension	<5 years	23	5.163±1.255
	≥ 5 years	27	6.972±1.326

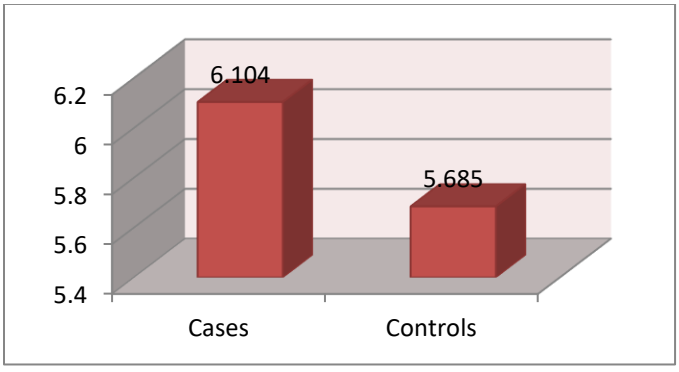

Figure 1: SUA levels cases and controls

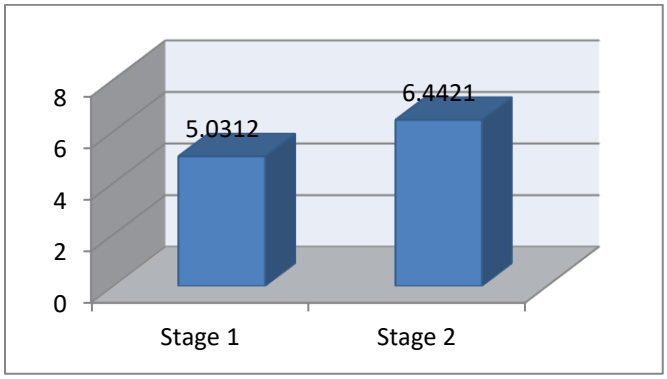

Figure 2: SUA and stage of hypertension

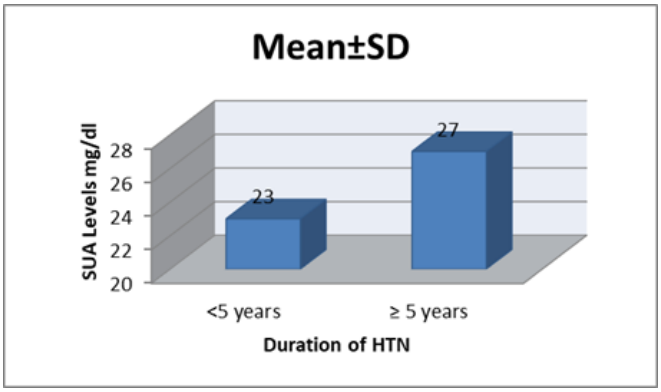

Figure 3: SUA and duration of hypertension

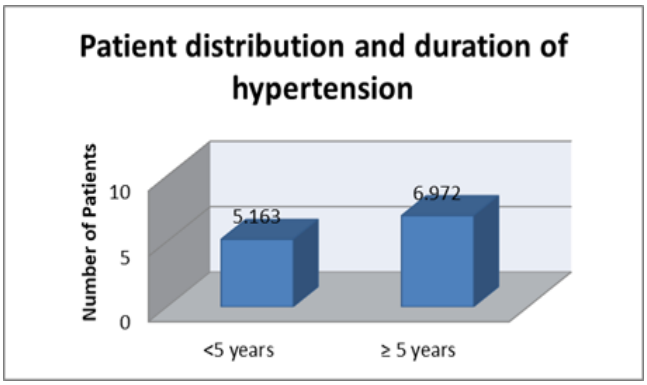

Figure 4: Patient distribution and duration of hypertension