ORIGINAL RESEARCH PAPER

Medicine

Volume : 6 | Issue : 11 | November 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

EVALUATION OF SERUM URIC ACID IN ESSENTIAL HYPERTENSION

KEYWORDS: hypertension, serum uric acid

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ABSTRACT

Back ground & objectives: The association of raised serum uric acid(SUA) levels with various cardiovascular risk factors has often led to the debate of whether raised serum uric acid levels could be an independent risk factor in essential hypertension. Hence we carried out a study to examine the possibility of hyperuricemia causing hypertension, to see if there is a relationship between the serum uric acid levels and severity & duration of hypertension Methodology: The study was carried out in osmania general hospital, a total of 400 patients were studied of which 200 were cases and 200 controls. The patients were included if they satisfied the JNC VII criteria for hypertension. They were excluded if they were having any other condition known to cause raised serum uric acid levels & secondary hypertension. Results: The study showed that serum uric acid levels were raised in patients with hypertension in comparison to normotensives. The Mean SUA levels between cases and controls were 6.43 ± 1.55 and 5.07± 1.41 respectively with t-value =9.178 , p - value <0.0001. SUA levels in the stages of hypertension showed a mean serum uric acid level in stage 1 hypertension of 6.42 ± 1.56 and stage 2 hypertension 6.43± 1.54 the t- value of -0.045 and p- value = 0.96 which was insignificant . SUA level in patients with hypertension < 5 years was 6.36 ± 1.57 those with ≥ 5 years was 6.50 ± 1.53. t-value of -0.63 p-value = 0.52 which was also insignificant. Conclusion: Present study showed that SUA can be used as an early biochemical marker to determine the presence of hypertension but not the severity and duration.

INTRODUCTION

The concept that uric acid may be involved in hypertension is not a new one. In fact, in the paper published in 1879 that originally described essential hypertension, Frederick Akbar Mohamed noted that many of his subjects came from gouty families. He hypothesized that uric acid might be integral to the development of essential hypertension[1]. Ten years later, this hypothesis reemerged when Haig [2] proposed low-purine diets as a means to prevent hypertension and vascular disease. In 1909, the French academician Henri Huchard noted that renal arteriolosclerosis (the histologic lesion of hypertension) was observed in three groups: Those with gout, those with lead poisoning, and those who have a diet enriched with fatty meat. All of these groups are associated with hyperuricemia[3].

The association between elevated serum uric acid and hypertension was observed and reported repeatedly in the 1950s to 1980s but received relatively little sustained attention because of the lack of a mechanistic explanation[4-6]. Twenty-five to 40% of adult patients with untreated hypertension have hyperuricemia (>6.5 mg/dl), and this number increases dramatically when serum uric acid in the high-normal range is included[7,8]. In certain special cases of hypertension, such as cyclosporine-associated hypertension and pre-eclampsia, the correlation between elevated serum uric acid and hypertension is >70%[9]. Despite these observations, the lack of a causal mechanism led to mild elevations of serum uric acid being largely ignored in medical practice. Uric acid was removed from routine laboratory panels, such as the serum metabolism and chemistries-20 (SMAC-20), in the early 1980s and is not considered a risk factor for hypertension by either the American Heart Association[10] or the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure[11].

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 wheth 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[12].

This study was done to determine whether raised serum uric acid levels were an independent risk factor for developing hypertension.

AIMS AND OBJECTIVES

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

MATERIALS AND METHODS

METHODS

In the following Hospital based study for the evaluation of serum uric acid levels in essential hypertension 400 patients who attended in-patient at the department of Medicine were evaluated for Serum Uric Acid levels of which 200 were cases and 200 were controls.

Adult male and female patients > 18 years of age diagnosed as hypertensive according to JNC VII classification for hypertension were included as cases; patients were excluded if they had any of the following -

- Diabetes Mellitus,
- Ischaemic Heart Disease,
- All cases of secondary hypertension,
- Clinical Findings of gout or extra- articular manifestations of hyperuricemia

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- Obesity (body weight exceeding 25% of body weight
- H/o alcohol abuse
- H/o drugs known to cause hyperuricemia, e.g. thiazide diuretics
- H/o Renal disease
- H/o pre-eclampsic toxemia
- Controls were patients without hypertension or any other condition known to cause hyperuricemia and were matched for age and sex with that of the cases.

The clinical examination consisted of a medical history, a physical examination, blood pressure measurement, anthropometric measurements, measurement of fasting serum uric acid levels and other parameters like Blood haemogram, Renal function tests (blood urea, serum creatinine), Electrocardiogram, Chest X-ray, Lipid profile (Total cholesterol, triglycerides, HDL- cholesterol, LDL-cholesterol), urine for protein and sugar.

Hypertension was defined according to the JNC VII classification of hypertension as those with SBP of < 120 mm hg and DBP of < 80 mm hg as normal, those with SBP of 120-139 mm hg or DBP of 80 - 89 mm hg were labeled pre-hypertensive were not taken up for the study, those with SBP 140 - 159 mm hg or DBP of 90 - 99 mm hg were labeled as having Stage 1 hypertension, and those with SBP ≥ 160 or DBP ≥ 100 mm hg were labeled as Stage 2 hypertension.
Reference Values for SUA levels: 3.4 - 7.0 mg/dl in males and 2.4 - 6.0 mg/dl in females.

The statistical analysis was performed using the SPSS 10.0 software package. The data was analyzed using the t-test (Independent sample t-test).

RESULTS

In the study a total of 400 patients were studied of which 200 patients were cases that were categorized into Stage 1 or Stage 2 hypertension (base on JNC VII classification) and 200 were controls who were patients without hypertension or any other condition known to cause raised serum uric acid levels.

The total number of male cases was 118 and the total no of female cases 82.The age group ranged from 20 years to 90 years.(Table 1)

Table 1. Age distribution for cases and controls

AGE	CASES	CONTROLS
20 - 29	**5**	**5**
30 - 39	**17**	**17**
40 - 49	**53**	**53**
50 - 59	**42**	**42**
60 - 69	**58**	**58**
70 - 79	**21**	**21**
80 - 89	**4**	**4**
Total	**200**	**200**

The Serum Uric Acid levels in male cases ranged from 3.7 mg/dl to 10.1mg/dl and female cases ranged from 2.7 mg/dl to 8.9 mg/dl. The Serum Uric Acid levels in male controls ranged from 3.4 –9.8 mg/dl and female controls ranged from 2.8 – 8.5mg/dl.

The total number of cases were 200 (both male and female), the data analysis of the cases showed the mean SUA level to be 6.43 with a standard deviation of 1.55 (6.43 ± 1.55).

The total number of controls of controls were 200 (both male and female), the data analyzed showed a mean SUA level of 5.07 with a standard deviation of 1.41 (5.07 ± 1.41), as shown in table no 2.

Table 2. SUA Levels between Cases and Controls

Category	Number	Mean ± SD
Cases	200	6.43 ± 1.55
Controls	200	5.07 ± 1.41
t = 9.178 , p = <0.0001		

LThe t-value was found to be 9.178 and the p value <0.0001 which was significant This showed that there was a significant rise in serum uric acid levels in patients with hypertension when compared to normotensive.

The severity of hypertension was divided into stage 1 and stage 2 based on the JNC VII classification of hypertension. In the study done at our hospital the total number of patients assessed to have stage 1 hypertension was 116 patients (both male and female patients), the total number of patients having stage 2 hypertension was 84(both male and female patients).

The mean serum uric acid levels in stage 2 hypertensive patient were 6.43with a standard deviation of 1.54.

The t-value was -0.045 and a p-value of 0.96 which was insignificant. The data analysed showed that there was not a significant rise in hypertension in patients who were having stage 2 hypertension i.e. those with a SBP ≥ 160 and a DBP ≥ 100 than those with stage 1 hypertension (SBP 140- 159 and DBP 90 - 99) table 3.

Table 3. SUA based on stage of Hypertension (JNC VII)

Stage of hypertension	Number	Mean ± SD
Stage 1	116	6.42 ± 1.56
Stage 2	84	6.43 ± 1.54
t = -0.045 , p = 0.96		

The analyzed data showed a t-value of -0.63 and a p-value = 0.52 which showed that there was not a significant increase in SUA levels in patients with hypertension ≥ 5 years than those with a duration of < 5 years (Table 4).

Table 4. SUA Levels Based on duration of Hypertension

DURATION	NUMBER	MEAN
< 5 years	108	6.36 ±1.57
≥ 5 years	92	6.50 ± 1.53
t- value = -0.63 , p =0 .52		

DISCUSSION

Elevated SUA levels have been associated with an increased risk for cardiovascular disease[13]. Because elevated serum uric acid is correlated with several risk factors including renal dysfunction, hypertension, insulin resistance, hyperhomocystenemia and hyperlipidemia, it is debated whether SUA is an independent cardiovascular risk factor.

In the present study the incidence of hyperuricemia in controls was 14.5% and the incidence of hyperuricemia in cases was

Volume : 6 | Issue : 11 | November 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

44%.
Various other studies by Kinsey et al[14]., Koble et al[15]., and C. J. Bulpitt et al[16]., have also shown that increased serum uric acid levels were seen in patients with hypertension.

Ramsay (1979) in his study of 73 men with untreated hypertension had 18 with raised serum uric acid levels (25%)[17]. 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[18].
It certainly is possible that uric acid may be an earlier and more sensitive maker of decreased renal blood flow than serum creatinine. Canon et al considered that an impairment of renal function will raise the SUA levels more commonly than an increased SUA will cause renal damage[19].

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.

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 of hyperuricemia between cases and controls correlated significantly but not with the severity of hypertension. This correlated according to Cannon et al[19] severity of hypertension had no relation to SUA level. But the Kinsey[14] Breckenridge [12] and Tykarski et al[18] studies showed correlation between severity of hyperuricemia and severity of hypertension.

In our study the incidence of Hyperuricemia in cases with stage 1 hypertension was 56 % and those with stage 2 hypertension was 44 % 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. 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[20], 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,[21] are increased in subjects with essential hypertension[22].

In our study we found that there is definite relation in SUA levels between hypertensive patients and normotensive patients but there is no direct proportional relation between the levels of SUA and 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

Our study showed that hyperuricemia is seen in hypertensives but the severity of hypertension is not related to the SUA levels and also duration of hypertension had no significant impact on the SUA levels.

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