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Serum Uric Acid in Hypertension and Cerebrovascular Accident

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ABSTRACT

A case control study was undertaken to evaluate any association of serum uric acid level with hypertension and to study whether serum uric acid level is elevated in cases of cerebrovascular accident or not. A total of 100 subjects were included in this study to assess the possible association of serum uric acid level in diagnosed cases of hypertension and cerebrovascular accident. Among the subjects, 20 cases suffered from essential hypertension, 30 cases were of cerebrovascular accident and 50 subjects served as control group. Serum uric acid level was estimated in all the subjects calorimetrically. The mean serum uric acid levels in control group, hypertension and cerebrovascular accident cases were 3.34 ± 0.46 mg/dl, 4.95 ± 1.38 mg/dl and 5.00 ± 0.83 mg/dl respectively with a significance of P < 0.001. It was found to be increased significantly not only in hypertension cases but also in cerebrovascular accident cases. Conclusion: A significant association between high serum uric acid level and hypertension as well as cerebrovascular accident was observed. Thus by estimating the serum uric acid level in diagnosed cases of hypertension we can screen out the patients that may have the chance of developing cerebrovascular accident in future.

***Keywords**: Hyperuricemia, uricase/PAP method, cerebral hemorrhage, cerebral thrombosis*

INTRODUCTION

Hypertension is a common health problem with sometimes devastating consequences and often remains asymptomatic until late in its course. It is one of the most important risk factors for both coronary artery disease and cerebrovascular accidents; hypertension can lead to cardiac hypertrophy and potentially, heart failure, aortic dissection and renal failure. It is widely acknowledged that hypertension is a complex, multifactorial disease that has both genetic and environmental determinants.

Among the etiological factors for cerebrovascular disease, hypertension is the most important one causing mainly atherosclerotic changes with thrombus formation and haemorrhage in the cerebral vessel. In the pathogenesis of cerebrovascular disease in hypertensive patients high blood pressure is not the sole factor to cause the vascular changes but blood biochemistry and metabolites have a definite role. Heyman et al[1], Feldman et al[2], Katsuki et al[3], Jakobson et al[4] and later John Pearce and Hasan Aziz[5] had shown that serum lipids were consistently higher in cerebrovascular disease than normal population. Meyer et al[6] pointed out that cerebral ischemia and infarction

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might occur in the presence of normal serum lipid levels. So there must be other metabolites that may play in the pathogenesis of cerebrovascular disease. Hyperuricemia was first associated with hypertension and cerebrovascular disease in 1879.[7] Since that time, many have attributed this association to a simple clustering of hyperuricemia with well established cardiovascular risk factors, and an elevated serum uric acid level by itself has generally been regarded as insignificant or incidental. Breckenridge A (1966)[8] had shown that the incidence of cerebrovascular disease in hypertensive patients with high uric acid level was much more than that of normal uric acid level. Hyperuricemia in hypertension without typical gouty arthritis has been described first by Dollery et al[9] and subsequently by Pomerantz[10] and Freis.[11] In 1965, Kolbet et al also studied the relation of hyperuricemia with hypertension.

Breckenridge has established a definite relation of hyperuricemia with hypertension without gouty arthritis and without taking any antihypertensive drugs. He also pointed out that there is no tendency for hyperuricemia to occur only in patient with more severe degree of hypertension.[12] Again the incidence of cerebrovascular disease is high in hypertensive patients with high uric acid level than normal uric acid level. John Pearce and Hasan Aziz also studied the prevalence of hyperuricemia with cerebrovascular disease.

The aim of the study was to evaluate any association of serum uric acid level with hypertension irrespective of degree of hypertension and the use of antihypertensive drugs and to study whether serum uric acid level is elevated in cases of cerebrovascular accident or not.

MATERIALS AND METHODS

The present study was designed as a case control hospital based study in tertiary care medical college and hospital. Three groups of subjects selected for the study are as follows:

(i) **Control group**: In the control group only those subjects were selected who gave no history suggestive of hypertension or any major illness in the recent past and in whom clinical examination did not reveal any abnormality relating to the system. Fifty numbers of male (31) & female (19) age and sex matched healthy controls were included in this study that co-operated voluntarily.

(ii) **Test group**: In test group 20 subjects (male-13 & female-7) suffering from hypertension and another 30 subjects (male-18 & female-12) of cerebrovascular accidents cases were selected.

SELECTION OF CASES

1. The criterias for accepting patients as hypertensive are to be persistent elevation of systolic pressure 140-159 mm Hg and or above it and diastolic pressure 90-99 mm Hg and or above it in adults (JNC VII classification).[13]
2. Patients complaining of weakness or paralysis of sudden or gradual onset with or without loss of consciousness having upper motor neuron type of lesion and suggestive of cerebrovascular accidents regardless of age or severity of neurological deficit were selected for the present study.
3. General physical and complete neurological examinations were carried out with the physician at the time of admission. The type of stroke was diagnosed and confirmed by CT scan of brain.
4. Cases having renal disease, liver disease, myocardial infarction and definite history of gout were carefully excluded from the study. Patients complaining of weakness or paralysis with or without loss of consciousness suggestive of traumatic intracranial vascular accidents were excluded from the study.
5. 5 ml of blood sample was collected from each subject irrespective of the fasting state using a sterilized syringe into clotted vials. The samples were then allowed to stand for some time and then centrifuged for separation of sera. This serum was then used for estimation of serum uric acid.

Analysis of uric acid was done using the kit of Crest Bio systems. Serum uric acid was estimated by Uricase / PAP Method:[14, 15]

Principle: Uricase converts uric acid to allantoin and hydrogen peroxide. The hydrogen peroxide formed further reacts with a phenolic compound and 4 aminoantipyrine by the catalytic action of peroxidase to form a red coloured quinoneimine dye complex. Intensity of the colour formed is directly proportional to the amount of uric acid present in the sample, which is measured at 520 nm.

$$\text{Uric Acid} + H_2O \xrightarrow{\text{uricase}} \text{Allantoin} + H_2O_2$$

$$H_2O_2 + 4\ \text{Aminoantipyrine} + \text{Phenolic Compound} \xrightarrow{\text{Peroxidase}} \text{Red Quinoneimine dye} + H_2O.$$

STATISTICAL ANALYSIS

The values of the measured parameter were grouped and tabulated. The data was expressed as mean ± standard deviation. The student t test was used for evaluation of the significance of differences in means of different groups. The mean serum uric acid level in control group, hypertension and cerebrovascular accident cases were 3.34 ± 0.46 mg/dl, 4.95±1.38 mg/dl and 5.00±0.83 mg/dl respectively with a significance of P< 0.001.

RESULT AND OBSERVATION

Our study population comprised of a total of 100 subjects. Among them 50 healthy controls designated as group A, 20 patients suffered from hypertension (designated as cases, group B) and 30 patients were of cerebrovascular accident (designated as cases, group C). Serum uric acid levels were significantly elevated in patients of both groups, B and C when compared to that of group- A. The results are shown in **Table 1**, **Table 2, Table 3** and **Table 4**.

The serum uric acid levels in 50 healthy control cases were found to be ranged from 2.5 to 4.8 mg% with the mean level being 3.34 ± 0.46 mg%. The serum uric acid was highest (3.90 ± 0.57 mg%) in the 7th decade of life and it is higher in case of male than female. In the hypertensive group the mean value is 4.95 ± 1.38 mg% with the range of 2.9-7.8 mg%. High uric acid level was not correlated with the duration of hypertension but depends on the degree of severity of hypertension. In 30 cases of cerebrovascular accident, the mean value is 5.00 ± 0.83 mg% with the range 3.4-6.2 mg% (P<.001). In the haemorrhagic group the mean value is 5.24 ± 0. 78 mg% with the range 3.8-6.2 mg% (P<.001) and in the ischaemic group the mean value is 4.89 ± 0.87 mg% with the range 3.4-6.0 mg %(P<.001). The incidence of cerebrovascular accident was found to be significantly greater in those hypertensive patients who had a raised serum uric acid level.

Table 1 Showing the distribution of severity of hypertension in relation to age (After JNC VII Report)

Age group (Yrs)	Prehypertension Systolic BP =120-139 mm HgDiastolic BP=80-90 mm Hg	Stage-I hypertension Systolic BP =140-159 mm HgDiastolic BP=90-99 mm Hg	Stage-II hypertension Systolic BP =e"160 mm HgDiastolic BP=e"100 mm Hg
Up to 40	2	1	-
40 - <50	5	1	-
50 - <60	3	2	1
60 - <70	2	-	-
70 - <80	-	2	1
80 e"	-	-	-
Total	12 (60%)	6 (30%)	2 (10%)

Table 1 Shows that out of 20 hypertensive patients 12 (60%) were in prehypertension group, 6 (30%) were in Stage-I hypertension and 2 (10%) were in Stage-II hypertension. Prehypertensive were found in the age group 32 to 69, Stage-I were found in between 28 to 70 years and Stage-II hypertensive patients were found in between 50 to 80 years of age.

Table 2 Number of cases with percentage in major types of cerebrovascular accident (CVA)

Type of CVA	No of cases	Percentage
Hemorrhagic stroke	10	33.33
Ischemic stroke	20	66.67
Total	30	100

Table-2 shows that out of 30 cases of CVA 10(33.33%) cases were Haemorrhagic stroke and 20 (66.67%) cases were Ischaemic stroke.

Table 3 Showing serum uric acid level in different study group

STUDY GROUPS	N0S	MEAN	SD
Hypertension	20	4.95	1.38
CVA	30	5.00	0.83
Control	50	3.34	0.46

Table 4 Statistical analysis and their significance of the result of serum uric acid in study groups

Groups	Degrees of freedom	Serum Uric Acid		
		't'	'p'	Significance
Control Vs Hypertension	68	7.38	<0.001	Very highly significance
Control Vs CVA	78	11.59	<0.001	Very highly significance
Control Vs Haemorrhagic Stroke	58	10.55	<0.001	Very highly significance
Control Vs Ischaemic Stroke	68	9.76	<0.001	Very highly significance

DISCUSSION

This study shows that, serum uric acid levels in both hypertension and cerebrovascular accident cases have a significantly higher value compared to control subjects (P<0.001). High blood pressure is one of the most common chronic health problems in our society. Most of the patients with pre hypertension and Stage-I hypertension group and indeed some with dangerously high levels are asymptomatic and are diagnosed accidentally in the course of a routine physical examination. Symptoms occur in asymptomatic patients when the target organs are affected. It constitutes one of the major causes of disability and death.

Various investigations have been done to evaluate the aetiological aspects of hypertension and cerebrovascular disease but the exact cause is still obscure. Multiple interrelated factors have been shown to play a role in the evolution of hypertension and cerebrovascular disease. Hyperuricemia is one of them, the incidence of cerebrovascular disease in hypertensive patients with high uric acid level is much more than that of normal uric acid level.(Breckenridge, A 1966).[8]

In the field of serum uric acid studies many workers has observed high serum uric acid level in hypertensive groups of patients irrespective of getting antihypertensive drugs. Kinsey D et al[16] studied 400 patients with hypertensive disease and found that more than 40 percent (183 out of 400) of all the cases had high serum uric acid level. The incidence of hyperuricaemia is more in case of men (52%) than in women (43%) and there is no correlation between kidney functions and hyperuricaemia unless the blood urea was over 30mg%. Moreover, the hyperuricaemia is significantly higher with severe hypertension compared to the more benign hypertension.

In the present study, the mean value of serum uric acid in hypertensive cases was 4.95 ± 1.38 mg% with a range 2.9 to 7.8 mg%. Out of 20 cases 9 (45%) showed high uric acid level irrespective of degree of hypertension. The elevation of serum uric acid in cases of hypertension was found to be significant compared to the controls on statistical analysis (P< .001).

In the cerebrovascular accident group out of 30 cases, hyperuricaemia occurs in 19 cases (63.33%) and normal uric acid level in 11 cases (36.67%). In thrombosis group 11 (55%) out of 20 had high uric acid level, in haemorrhagic group 8 (80%) out of 10 had high uric acid level. These results correlate with the observation done by Breckenridge A.[8]

The mean value of serum uric acid in cerebrovascular accident was found to be 5.00± 0.83 mg% with a range of 3.4-6.2 mg%. In thrombosis groups the mean value of serum uric acid was found to be 4.89±0.87 with a range of 3.4-6.0 mg% and in the haemorrhagic group the range was 3.8 to 6.2 mg% with the mean value of 5.24 ± 0.78 mg%. The elevation of serum uric acid level in cerebrovascular accident was found to be significant compared to the controls on statistical analysis (P<.001).

The result of the present study shows that a significant portion of patients with cerebral infarction or cerebral haemorrhage showed high uric acid level. This approximately correlates with Hansen (1965)[17], Meyer et al[18], Pearce J et al[19] and correlates exactly with Breckenridge A.[8] It seems therefore that hyperuricaemia in the absence of gout or any other known predisposing cause is present in a significant portion of patients with sustained hypertension and with cerebral infarction or cerebral haemorrhage.[19]

CONCLUSION

From this study, it is found that hypertension may raise the serum uric acid level by overproduction or under excretion of the same. On the other hand high blood pressure acts as a major risk factor in the occurrence of cerebrovascular accident and uric acid levels were found to be high in this group of cerebrovascular accident. Therefore we came to the conclusion that high uric acid has a definite role in hypertension as well as in cerebrovascular accident and thus by estimating the uric acid level in hypertensive patients, we can screen out the patients that may have the chance of developing cerebrovascular accident in future. But due to some practical difficulties and time limitation, it was not possible

to find out the exact mechanism of uric acid in genesis of hypertension and cerebrovascular accident.

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REFERENCES

1. Heyman A, Nefzger MD, Estes EH. Serum cholesterol level in cerebral infarction. Arch Neurol 1961 Sep;5:264–268.
2. Feldman RG, Albrink MJ. Serum lipid and cerebrovascular disease. Arch Neurol 1964;10:91-100.
3. Katsuki S, Uzawa H, Fujimi S, Shiratsuchi K, Ito Y. Studies on blood lipids in cases with cerebrovascular diseases- a preliminary report. Jpn Heart J 1964 Mar;5:101–107.
4. Jakobson T. Glucose tolerance and serum lipid levels in patients with cerebrovascular disease. Acta Medica Scandinavica 1967 Jan/Dec;182(2):233-243.
5. Pearce J, Hasan Aziz. Uric acid and plasma lipids in cerebrovascular disease part-II. Uric acid and plasma lipids correlations. J Neurol Neurosurg Psychiat 1970;33:88-91.
6. Meyer JS, Waltz AG, Hess JW, Zak B. Cholesterol levels in cerebrovascular disease. A M A Arch Neurol 1959;1:303-311.
7. Mahomed FA. On chronic Bright's disease, and its essential symptoms. The Lancet 1879;1:399-401.
8. Breckenridge A. Hypertension and hyperuricemia The Lancet 1966 Jan;1:15-18.
9. Dollery CT, Duncan H, Schumer B. Hyperuricaemia related to treatment of hypertension. Br Med J 1960;11:832.
10. Pomerantz HZ. Coronary artery disease in the young, an analysis of 162 cases. C M A J 1960;82:842.
11. Freis ED. Double blind control study of antihypertensive agents. Arch Intern Med 1962;110:230.
12. Cannon PJ, Stason WB, Demartini FE, Sommers SC, Laragh JH. Treatment for cardiovascular disease. Ann Int Med 1965;62:667-74.
13. Chobanian AV, Bakris GL, Black HR. The seventh report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure: JNC 7 Report. express version. JAMA 2003;289:2560-2572 Complete version: Hypertension 2003;42:1206-1252.
14. Trinder P. Chromogenic system for measuring hydrogen peroxide: the enzymatic uric acid assay. Ann Clin Biochem 1969;6:24.
15. Fossati P, Prencipe L. Chromogenic system for measuring hydrogen peroxide: the enzymatic uric acid assay. Clin. Chem 1980;26:227.
16. Kinsey D, Walther R, Herbert S, WhiteLow G, Smithwick R. Hyperuricemia in primary and renal hypertension. Boston Massachusetts 1961 Circulation;24:972.
17. Hansen OE. Hyperuricemia in cerebral infarction. Acta Neurologica Scandinevica 1965;41:357.
18. Meyer JS, Kypros GP, Gilroy J. Uric acid and plasma lipids in cerebrovascular disease. W V Med J 1964;60:150.
19. Pearce J, Hason Aziz. Uric acid and plasma lipids in cerebrovascular disease, Part-I Prevalence of Hyperuricemia. Br Med J 1969;4:78-80.