

Serum Uric Acid Levels in Patients with Acute Stroke

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Abstract

The role of uric acid in patients with stroke or other vascular disease is contentious and there is conflicting data on this subject. In this study, we assessed serum uric acid levels in patients with acute stroke and computed its association with other cerebrovascular risk factors. In this cross sectional study, we assessed patients with acute stroke who were admitted in Government Medical College Jammu from September 2013 to July 2014. Detailed history and physical examination was performed in all patients and their serum uric acid level besides routine investigations was performed. A total of one hundred patients with acute stroke were evaluated, of whom 41% were women and 59% were men. History of hypertension was known in 64% of cases. 8% of patients were smoker, three patients had atrial fibrillation and history of snake bite was present in one patient. Mean age of patients was 65.84 ± 13.37 years. 54% had ischemic stroke and hemorrhagic stroke was seen in 46% of cases. Mean uric acid was 6.14 ± 1.17 . Mean uric acid in men was 6.72 ± 0.67 and women had mean uric acid of 5.74 ± 0.81 . High uric acid level was seen in 45% of cases. There was negative correlation between age of patients and serum uric acid level ($r = -0.19$, $p = 0.18$). There was statistically significant difference in uric acid between men and women ($p = 0.01$). Due to the high prevalence of hyperuricemia in patients with acute stroke, it can be considered as a risk factor for acute stroke.

Key Words

Uric acid, Acute stroke, Hyperuricemia

Introduction

Stroke is one of the leading causes of mortality and morbidity worldwide affecting approximately 20 million people each year and causing 5 million deaths (1). Numerous risk factors are involved in the development of stroke such as hypertension, cigarette smoking, hyperlipidemia and diabetes. Recent studies indicate that there may be other factors influencing the development or course of disease like serum levels of uric acid. Uric acid levels are influenced by age and sex. Women typically have 1 mg/dl less uric acid than men. This lower level in women apparently reflects estrogen related enhancement of renal urate clearance (2). Serum uric acid may be

considered as a marker of acute endothelial dysfunction, since hyperuricemia has been observed to be associated with raised endothelin levels, and there is evidence of uric acid involvement, via purine metabolism, in the process of thrombus formation (3). However, studies regarding role of uric acid in stroke have produced inconsistent results so far (4,5). Higher risk of stroke incidence and mortality was reported in cases of hyperuricemia (6-8). But contrary to this, other studies have advocated uric acid to be neuroprotective due to its antioxidant action (9-11). Some studies have found higher levels of serum uric acid to be associated with

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better outcomes following stroke (12-14). Considering these conflicting data, we undertook this study to evaluate serum uric acid levels in patients with acute stroke.

Material and Methods

This is a cross sectional study conducted in Postgraduate Department of medicine GMC, Jammu from September 2013 to July 2014 on 100 patients admitted with acute stroke. A stroke or cerebrovascular accident (CVA) was defined as abrupt onset of neurological deficit that is attributable to a focal vascular cause. The participating patients were enrolled on the basis of CT Head findings. Total patients taken for study were 100. Exclusion criteria include chronic liver and kidney diseases, malignancy, chronic alcohol use, trauma, drugs like diuretics, use of antioxidants.

There is no universally-accepted definition for hyperuricemia based only on serum UA levels. We defined participants as having hyperuricemia if their serum UA concentration was > 7.0 mg/dL in men or > 6.0 mg/dL in women (4,5). These cut offs were selected because they are commonly used in clinical laboratories and have been proposed in previously published studies.

Informed consent was obtained from each participant of the study and institutional ethical committee clearance was obtained. Detailed history and physical examination was done in all patients. In patients risk factors were taken into account like age, sex, smoking hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, previous CVA. The information about risk factors was obtained from patients, their medical records and history taken from attendants. The severity of the stroke was measured by the NIMS.

CT Head was done in all patients after hospitalization. All routine investigations like complete hemogram, Blood glucose, liver and kidney function test, lipid profile, electrolytes, urine exam ECG were done. Serum uric acid was estimated within 24 Hours of hospitalization by enzymatic uricase method.

Statistical Analysis

was done during SPSS Software for Windows Ver.

16. The data obtained was expressed as mean \pm standard deviation. Correlation was computed by Pearson's correlation coefficient and p value of < 0.01 was taken as statistically significant.

Results

We have studied hundred patients of acute stroke, of whom 41% were women and 59% were men. Mean age of patients was 65.84 ± 13.37 years. 54% had ischemic stroke and haemorrhagic stroke was seen in 46% of cases. None of our haemorrhagic stroke patients received thrombolytic therapy. Serum triglyceride (TG) was 140.15 ± 45.45 , total cholesterol was 170.36 ± 50.45 , low density lipoprotein (LDL) was 110 ± 34.56 and high density lipoprotein (HDL) level was 42.40 ± 10.20 . 12% of patients were having HDL levels less than 40 mg/dl while 20% of patients had TG level more than 150 mg/dl. Mean uric acid was 6.14 ± 1.17 . Mean uric acid in men was 6.72 ± 0.67 and women had mean uric acid of 5.74 ± 0.81 . High uric acid level was seen in 45% of cases with male being 20% and female being 25% (Table 1 & 2). 16% of patient had known history diabetes mellitus. Eight patients were diagnosed diabetic during investigation. Mean blood glucose fasting was 110.38 ± 32.61 and mean postprandial blood glucose was 158 ± 47.46 . History of hypertension was known in 64% of cases. 8% of patients were smoker, three patients had atrial fibrillation and history of snake bite was present in one patient. There was negative correlation between age of patients and serum uric acid level ($r = -0.19$, $p = 0.18$), but it was not statistically significant. There was statistically significant difference in uric acid between men and women ($p = 0.01$) (Fig-1).

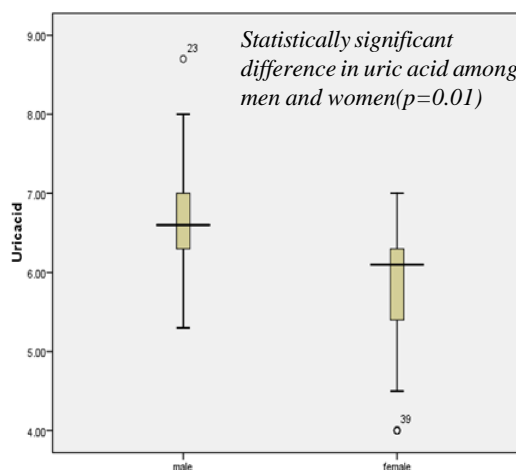
Table 1. Biochemical Parameters of Study Population

Parameter	Mean \pm SD
Uric acid	6.14 ± 1.17
Total cholesterol	170.36 ± 50.45
Triglycerides	140.15 ± 45.45
HDL	42.40 ± 10.20
LDL	110 ± 34.56
BGF	110.38 ± 32.61
BGPP	158 ± 47.46

Table 2. Demographic Profile and Uric Acid levels in Study Population

Gender (n=100)	Men(n=59)	Ratio	
	Women(n=41)	M:F= 1.43:1	
Age	Men	Mean±SD 65.56±14.38	p-value 0.95
	women	66.24±11.92	
Uric acid	Men	6.14±1.17	0.01
	women	5.74±0.81	
Type of stroke	Ischemic (n=54)	Men (n=35) Women (n=19)	0.20
	Haemorrhagic (n=46)	Men (n=24) Women (n=22)	
Risk factors	No.of patients(n)	percentage	total
Hypertension	64	64	64
Diabetes mellitus	16	16	16
Smoking	8	8	8
Atrial fibrillation	3	3	3
Snake bite	1	1	1

Fig 1. Box Plot Showing Uric Acid levels in Men and Women



Discussion

In this study we determined the serum uric acid levels in patients with acute stroke. 45% of our patients were hyperuricemic. Mehrapin M (6) did cross-sectional study on 55 patients of stroke; 47.3% had hyperuricemia and they concluded that due to the high prevalence of hyperuricemia in patients with acute stroke and its

accompanying increase in triglyceride and LDL cholesterol levels, it can be considered as a risk factor for acute stroke.

Bhadra *et al.*(7) conducted a case control study to evaluate the serum uric acid levels in men with stroke and to correlate the levels with stroke severity and found

significantly higher levels of uric acid in men with stroke as compared to control population. Uric acid levels also correlated significantly with stroke severity, increased uric acid levels being associated with greater initial stroke severity (7). According to results of Heo SH (9) increased level of uric acid may be a risk factor for the presence of silent brain infarction (SBI). Serum uric acid levels might be a good serum marker of underlying SBI or future stroke, especially in women (8). The population based study conducted by Lehto *et al.* (14) indicated that hyperuricemia is a strong predictor of stroke events in middle age patients with type 2 diabetes mellitus independently of other cardiovascular risk factors.

Tushar B *et al.* (15) in this study found serum uric acid levels significantly high in the patients who succumbed as compared to those who were discharged from Hospital. On the other hand, study conducted on 881 patients with acute ischemic stroke by Anegl Chamorro *et al.* found 12% increase in the odds of good clinical outcome for each mg/dl increase of Uric Acid (13). Uytienboogaart MK *et al.* (16) found no association between Uric Acid levels and outcome in acute Ischemic Stroke.

In our study, there was no significant association between serum uric acid level and diabetes Mellitus, hypertension and smoking. No significant association was seen between uric acid level and TG, Total Cholesterol, HDL Cholesterol and LDL Cholesterol. Chammaro *et al.* (13) reported the association between serum uric acid level and amount of Triglyceride.

Masoud *et al.* (6) in their study also found that hyperuricemia was associated with increase amounts of triglyceride and LDL. The mechanism for this strong association between serum uric acid levels and triglyceride levels is still poorly understood. Hyperuricemia and hypertriglyceridemia may reflect the patient's life style as a part of metabolic syndrome.

Ours was crosssectional study, so we could not assess the precise association between stroke and hyperuricemia. Long term case control studies are needed to describe the association between them.

Conclusion

Due to the high prevalence of hyperuricemia in patients with acute stroke, it can be considered as a risk factor for acute stroke but more large scale scientific and clinical research is needed before the role of uric acid as a risk stroke factor can be established.

References

1. Dalal P, Bhattacharjee M Varale J, *et al.* UN Millenium Development Goas, can we halt the stroke epidemic in India? *Ann Indian Acad Neurol* 2007; 10:130-6.
- 2) Barr WG. Uric acid. In: Walker HK, Hall WD, Hurst JW, editors. *Clinical Methods. The History, Physical, and Laboratory Examination*, 3rd ed. Boston: Butter worth: 1990 .pp.760-63
- 3) Selby JV, Friedman GD, Quesenberry CPJ. Precursors of essential hypertension: pulmonary function, heart rate, uric acid, serum cholesterol, and other serum chemistries. *Am J Epidemiol* 1990;131:1017-27
- 4) Lohsoonthorn V, Dhanamun B, Williams MA. Prevalence of hyperuricemia and its relationship with metabolic syndrome in Thai adults receiving annual health exams. *Arch Med Res* 2006;37:883-889.
- 5) Nagahama K, Iseki K, Inoue T, *et al.* Hyperuricemia and cardiovascular risk factor clustering in a screened cohort in Okinawa, Japan. *Hypertens Res* 2004;27:227-33.
- 6) Mehrpour M, Khuzen M, Neda Najuni N, *et al.* Serum Uric Acid Level in Acute Stroke Patients. *Medical J Islamic Republic Iran* 2012; 26 (2): 66-72.
- 7) Bhadraj, Makor DS, Seth S, *et al.* Uric Acid in men with acute stroke. *Int J Interdis & Multidisci Studies* 2015; 2(5): 146-52.
- 8) Rajeshwar K, Subash K, Venkates Rao A, *et al.* Association of Serum Uric Acid level with Ischemic Stroke, Stroke Subtypes and Clinical Outcome. *Neurology Asia* 2013; 18(4) : 34
- 9) Heo SH, Lee Sh. High levels of Serum Uric Acid are associated with silent brain infarction. *J Neurol Science* 2010; 297: 6-15.
- 10) Amaco S, Urrax, Gomez-Choco M, *et al.* Uric Acid Levels are relevant in patients with stroke treated with thrombolysis. *Stroke* 2011: 42 (1) : 528-32.
- 11) Squadrito GL, Cueto R, Splenser AE, *et al.* Reaction of uric acid with peroxynitrite and implications for the mechanism of neuroprotection by uric acid. *Arch Biochem Biophys* 2000; 376:333-37.
- 12) Yu ZF, Bruce-Keller AJ, Goodman Y, Mattson MP. Uric acid protects neurons against excitotoxic and metabolic insults in cell culture, and against focal ischemic brain injury in vivo. *J Neurosci Res* 1998; 53:613-25.
- 13) Chamorro A, Obach V, Cervera A, *et al.* Prognostic significance of uric acid serum concentration in patients with acute ischemic stroke. *Stroke* 2002; 33:1048-52.
- 14) Lepto S, Niskanen L, Ronnema T, Lakkso M. Serum Uric Acid is a strong predictor of Stroke in patients with non insulin dependent diabetes mellitus. *Stroke* 1998; 29 (3): 635-9.
- 15) Tushar B, Palil ASP, Kiran MS, *et al.* Serum Uric Acid Levels in Acute Ischemic Stroke : A study of 100 patients. *J Neurol Res* 2011; 1 (5)-193-200
- 16) Uyttenboogaart MJ, Koch M. Lack of association between S. Uric Acid Level and Outcome in acute Ischemic Stroke. *J Neurological Sciences* 2014; 319: 1-2.