

Association of Serum Uric acid with Recent Ischaemic Stroke

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ABSTRACT

Introduction: To evaluate association of serum uric acid with ischemic stroke patients and assess its relationship with cerebrovascular risk factors.

Methods: This was a hospital based cross-sectional observational study conducted at TUTH between May 2016 to May 2017. A total 120 Patients eligible for the study criteria was enrolled for the study. Non-probability convenience sampling was used for the sampling purpose. All patients ages 40 years or above 40 years with confirmed diagnosis of recent ischaemic stroke were included for the analysis.

Results: Mean ages of the enrolled subjects were 60.63 years \pm 11.11 SD and eighty three (69.2%) population were male. Sixty one (50.8%) subjects were smoker and twenty seven (22.5%) were alcoholic. Prevalence of hyperuricemia was 17.5%. Serum uric acid level values were higher in male (69.1%) than female (30.9) population. Higher levels of serum uric acid level were found in both male population who smoked and were alcoholic in contrast serum uric acid levels were higher in both female population who were non smoker and did not consume alcohol in comparison to male. Likewise, both diabetic and dyslipidemic male and female had higher serum uric acid level in comparison to who were non diabetic and did not consume alcohol. The mean score of serum uric acid level in male and female were significantly different ($P=0.029$). Similarly, serum uric acid level was significantly different in smoker and non-smoker group ($p=0.049$), hypertensive and non hypertensive ($p=0.027$) and dyslipidemic and non dyslipidemic group ($p=0.005$)

Conclusions: Our study showed high prevalence of hyperuricemia in ischemic stroke patients and there was a potential link between serum uric acid and cerebrovascular risk factors, indicating possible role of uric acid as the risk factor of ischemic stroke.

Keywords: cerebrovascular risk factor; Uric acid level, recent ischaemic stroke.

INTRODUCTION

World Health Organization defines stroke as “rapidly” developing clinical sign so focal (orglobal) disturbance of cerebral function, with no apparent cause other than of vascular origin”. Stroke is a major health issue in semi-industrialized countries like Nepal. In Nepal, the incidence of stroke is on rise a hospital based study (2006 data) yielded 150 CT-confirmed stroke cases over a period

of one year (104 males and 46 females), with age as young as 7 years, and with 42% having hemorrhagic (intracerebral and subarachnoid) strokes.¹

The main objective of the study is to evaluate the association of serum uric acid in patients with recent ischaemic stroke.

METHODS

This is a single centered hospital based cross-sectional observational study. This is a quantitative type of study. The study site

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is Emergency department of Tribhuvan University Teaching Hospital, Maharajgunj, Kathmandu. Patients of first episode of recent ischemic stroke presenting to emergency department of Tribhuvan University Teaching Hospital, Maharajgunj, Kathmandu were study population.

Non-probability convenience sampling was used for the sampling purpose. All the cases of diagnosed recent first episode ischemic stroke that presented to TUTH emergency from within 48 hours of onset of stroke suggestive symptoms as per the WHO definition of stroke were included in the study after ruling out the exclusion criteria. The study protocol was approved by the institutional review board (IRB) of TUTH. All the patients involved in this study were aware about the study protocol, and their informed consent was sought prior to data collection.

Sample size calculation was done using the below formula.

Sampling formula:

$$\frac{N = Z^2 pq}{D^2}$$

Where,

N=minimal sample size for statistical significant survey

Z= normal deviant at the portion of 95% CI= 1.96

P= prevalence value of ischemic stroke in general population= 8%(42)

Sample size (N)= 113

Total sample size 120 (to optimize the sample size)

Inclusion criteria:

- i. All patients ages 40 years or above 40 years with confirmed diagnosis of acute ischemic stroke
- ii. Ischemic lesion confirmed or hemorrhage

ruled out by CT Scan or MRI brain.

- iii. Patients or a valid surrogate willing to participate in the study with his/her written consent

Exclusion criteria:

- i. Stroke secondary to spontaneous brain hemorrhage, trauma, neoplasm, coagulation disorder, aneurysm or arterio-venous malformation
- ii. Patients diagnosed with recurrent stroke
- iii. Chronic liver disease and chronic kidney disease.
- iv. Malignancy or patients on chemotherapeutic agents
- v. Patients with active infection
- vi. Patients on anti-gout medications

All subjects underwent an intensive interview and appropriate laboratory examinations to identify vascular risk factors.

- i. Hypertension was defined as follows: Subjects with a prior history of hypertension and those who were prescribed any antihypertensive medications or subjects with a systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg at rest.²
- ii. Diabetes was classified to the subjects with diabetes as either alleged diabetes subjects or subjects with fasting glucose ≥ 7.0 mmol/l.³
- iii. Dyslipidemia was determined by aprior diagnosis of dyslipidemia, fasting serum low-density lipoprotein (LDL) cholesterol ≥ 4.1 mmol/L or total cholesterol ≥ 6.3 mmol/L.⁴
- iv. Hyperuricemia was defined by serum uric acid more than 7 mg/dl (416.4 mmol/l) in men and more than 6mg/dl (356.9 mmol/l) in women).⁵

V Smoking and Alcoholism:⁶

- Person who smoked at least 10 cigarettes per day for 6 months/more or the one who has smoked daily for more than 1 year or more regardless of the number of cigarettes smoked per day was considered as smoker.
- Alcohol abuse was defined as drinking more than 5 drinks per day that is 12g alcohol/day.

All data were coded, inserted and was evaluated in SPSS version 20. Continuous data was presented as mean±SD. Frequency table were generated. The level of significance was set at $P < 0.05$ (two-sided).

RESULTS

Table 1. Baseline characteristics.

Variable			
Male : Female	83 : 37		
Smokers : Non smokers	61 : 59		
Alcoholics : Non alcoholics	27 : 93		
	Mean±SD	Maximum	Minimum
Age	60.63±11.11	90	44
SBP	143.25±8.87	240	110
DBP	88.79±8.84	120	70
SUA	447.32±9.46	825	242
BS	262.73±145.63	746	74
TC	191.50±2.6	255	116
LDL-C	151.96±3.9	247	98
HDL-C	48.14±1.76	150	14
TG	116.09±4.2	210	38

SD: standard deviation,

Table 2A. Age distribution in terms of gender in percentage.

Age	Gender		Total
	Male, n (%)	Female, n (%)	
40-49	17(20.48)	6(16.21)	23
50-59	31(37.35)	12(32.43)	43
60-69	17(20.48)	13(35.15)	30
70-79	12(14.45)	3(8.11)	15
80-89	5(6.02)	3(8.11)	8
≥90	1(1.2)	0(0)	1
Total	83(100)	37(30.9)	120

As shown in table 3, out of 120 ischaemic stroke patients, 69.1% (83) patients belonged to male population while 30.9% (37) patients belonged to female population. In male population, 50-59 age group had greater percentage of stroke patients i.e. 31 (37.35%) while in among female population 60-69 age group had greater percentage of stroke patients i.e. 13 (35.15%). Percentage of stroke patients declined from age group 70-79 both in male and female population.

Table 2B. Gender distribution in each age group.

Age Group	Gender		Total
	Male [n(%)]	Female [n(%)]	
40-49	17(73.9)	6 (26.6)	23
50-59	31 (72)	12 (28)	43
60-69	17 (56.6)	13(44.4)	30
70-79	12 (80)	3 (20)	15
80-89	5 (62.5)	3(37.5)	8
≥90	1(100)	0(0)	1
Total	83	37	120

As shown in the above table 2B, percentage of male population is greater in each age group than female like 73.9%, 72%, 56.6% in the age group 40-49, 50-59, 60-69 respectively..

Table 3. Status of hyperuricemia in relation to smoking stratified by age group and gender.

Male ; n = 83					
Age Group	Smoker[n(%)]	Hyperuricemia[n(%)]	Non smoker[n(%)]	Hyperuricemia[n(%)]	Total
40-49	11 (64.7)	3(27.27)	6(35.3)	1(16.6)	17
50-59	20(64.5)	3(15)	11(35.5)	0(0)	31
60-69	12(70.5)	6(50)	5(29.5)	1(20)	17
70-79	6(50)	1(16.66)	6(50)	1(16.6)	12
80-89	3(60)	0(0)	2(40)	1(50)	5
≥ 90	1(100)	0(0)	0(0)	0(0)	1
Total	53(63.8)	13(24.52)	30(34.2)	4(13.3)	83
Female; n = 37					
40-49	0(0)	0(0)	6(100)	1(16.6)	6
50-59	3(25)	0(0)	9(75)	1(11.1)	12
60-69	3(23.1)	0(0)	10(76.9)	1(10)	13
70-79	1(33.4)	1(100)	2(66.6)	0(0)	3
80-89	1(33.4)	0(0)	2(66.6)	0(0)	3
≥ 90	0(0)	0(0)	0(0)	0(0)	0
Total	8(21.6)	1(12.5)	29(78.4)	3(10.3)	37

As shown in the table 4, out of total 61 smoke patients, 22.9 % (14) patients had hyperuricemia. In male population percentage of hyperuricemic patients were seen increasing with increasing age group like 27.7%, 50% in 40-49, 60-69 age groups respectively as compared to non smoker 16.6%, 20% in same age group. In female population hyperuricemia was found more in non smoke age group.

Table 4. Status of hyperuricemia in relation to alcohol stratified by age group gender.

Male ; n = 83					
Age Group	Alcoholic[n(%)]	Hyperuricemia[n(%)]	Not taking alcohol[n(%)]	Hyperuricemia[n(%)]	Total
40-49	6 (35.3)	3(50)	11(64.7)	1(9)	17
50-59	7(22.6)	1(14.28)	24(77.4)	2(8.33)	31
60-69	5(2.5)	3(60)	12(70.5)	4(33.33)	17
70-79	4(33.4)	0(0)	8(66.6)	2(25)	12
80-89	2(30)	0(0)	3(70)	1(33.3)	5
≥ 90	1(100)	0(0)	0(0)	0(0)	1
Total	25(30.1)	72(8)	58(69.9)	10(17.24)	83
Female; n = 37					
40-49	1(16.7)	0(0)	5(83.3)	1(20)	6
50-59	0(0)	0(0)	12(100)	1(8.33)	12
60-69	1(7.7)	0(0)	12(92.3)	1(8.33)	13
70-79	0(0)	0(0)	3(100)	1(33.3)	3
80-89	0(0)	0(0)	3(100)	0(0)	3
≥ 90	0(0)	0(0)	0(0)	0(0)	0
Total	2(5.5)	0(0)	35(94.5)	4(11.4)	37

As shown in the table 5, out of 27 alcoholic patients, 51.8%(14) had hyperuricemia. In male population, percentage of hyperuricemia was seen greater in age group 40-49, 50-59, 60-69 as compared to male not taking alcohol. Likewise, in female population there was no hyperuricemic patient in female alcoholics while there was one patient with hyperuricemia in each age group 40-49, 50-59, 60-69, 70-79 in female patient who didn't take alcohol.

DISCUSSION

Stroke is the one of the main clinical manifestation of CVD and studies investigating the relation between the uric acid and stroke have been inconsistent. Some studies reported a positive independent relationship between uric acid and stroke whereas others demonstrated that uric acid did not relate significantly to stroke occurrence.⁷

The positive association between serum uric acid and cardiovascular diseases such as stroke or ischemic heart disease has been recognized since the 1950s and has been confirmed by numerous epidemiological studies since then.^{8,9}

However, whether uric acid is an independent risk factor for cardiovascular mortality is still disputed as several studies have suggested that hyperuricemia is merely associated with cardiovascular diseases because of confounding factors such as obesity, dyslipidemia, hypertension, use of diuretics and insulin resistance.¹⁰

In the present study, mean ages of the enrolled subjects were 60.63 years with SD ± 11.11 , Minimum 44 years and maximum 90 years. The mean ages group of our study population appeared to be higher than the earlier study,¹¹ where the mean ages were 44.7 years. In similar another study,^{12,13} the mean age of patients was 67 ± 14 years.

According to a large 10 years follow up study by Yanyan Z, Bhavik P, Hyon C the prevalence of hyperuricemia in United state is 20.1%.¹⁴ Another large study in Bangkok population

showed that prevalence of hyperuricemia is 24.4%.¹⁴

In this study, age was not significantly correlated with the serum uric acid level. Also, the prevalence of hyperuricemia was statistically insignificant with the age. In comparison, in previous studies, there was a significant negative correlation between age of patients and their serum uric acid levels.¹² In another study, a weak but significant positive association between age of patients and their serum uric acid levels was reported.¹¹

CONCLUSIONS

This study showed higher serum uric acids levels in male population with ischaemic stroke than in the female. There was significant difference in serum uric acid level among the patients who had cerebrovascular risk factors like hypertension, diabetes and dyslipidemia in both sex in comparison to who didn't have risk factors so there was a potential link between serum uric acid and cerebrovascular risk factors, indicating possible role of uric acid as the risk factor of ischaemic stroke.

CONFLICT OF INTEREST: None.

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