Original Article

Study of Serum Uric Acid Level in Acute Ischemic Stroke

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Abstract

Background: High blood uric acid (SUA) levels are suspected of being a risk factor for cardiovascular disease (CV) mortality and morbidity. Recent research indicates that hypouricemic therapies can effectively prevent CV events.

Objective: To determine the association of acute ischemic stroke with serum uric acid level.

Method: This case control study was conducted in the Department of Medicine, JIMCH, Bajitpur, Kishoreganj from January 2021 to December 2022 for duration of 2 years. Total 120 subjects were included in this study, of them 60 were ischemic stroke patients, enrolled as case and 60 were apparently healthy people, enrolled as control. Ischemic stroke patients who had anyone of the following problems were excluded from this study: active infection, malignancy, renal disease, liver disease, valvular heart disease, atrial fibrillation and history of pain & vasculitis. Written consent was obtained from each study participant prior to data collection. Data were gathered through face-to-face interviews. Information was obtained by reviewing medical history, conducting clinical examinations, and performing subsequent laboratory tests.Statistical analysis was conducted using SPSS 12.0. A p-value <0.05 was deemed statistically significant.

Results: Mean age of the cases was 62.43±9.76 years and the controls was 61.58±9.70. In cases 68.3% were male and 31.7% were female. In controls male and female were also 68.3% and 31.7% respectively. Male and female ratio of stroke patients was 2.16:1. In cases 23.3%, 26.7%, 30.0% and 20.0% patients were housewife, service holder, businessman and farmer respectively. In control group maximum respondents were service holder (33.3%) followed by businessman (23.3%), housewife (30.0%) and farmer (13.3%) (p>0.05). Hypertension, diabetes mellitus and smoking habit was found significantly higher in cases than controls. But no significant difference was found in family history of stroke.Mean SUA level was significantly higher in cases (5.15±1.44 mg/dl) than controls (3.83±1.21 mg/dl). Statistically significant differences were observed between case and control group in term of serum uric acid.

Conclusion: The study results showed that the mean serum uric acid level was within the normal range. Therefore, no association was found between elevated uric acid and the risk of developing ischemic stroke. However, the case group had a significantly higher average serum uric acid concentration compared to the controls.

Keywords: Ischemic stroke and serum uric acid

Introduction

Cerebrovascular disease (CVD) encompasses any abnormality of the brain resulting from a pathological process involving the blood vessels. This includes stroke, carotid stenosis, vascular dementia, and aneurysm, among others.[1,2]

A stroke is a clinical syndrome distinguished by the abrupt initiation of focal or global neurological symptoms or disruption of cerebral functions, persisting for over 24 hours or resulting in mortality, with no clear etiology other than vascular, non-epileptic, and non-traumatic characteristics. This definition encompasses both infarct and hemorrhagic stroke. TIA symptoms are identical to stroke symptoms, with the exception that they persist for a duration of less than twenty-four hours. Primary cerebral ischemia leading to infarction (ischemic stroke) accounts for approximately 85% of all stroke cases, while cerebral hemorrhage accounts for 15% of all cases (hemorrhagic stroke).[2]

Stroke is the second leading cause of death worldwide, with around 5.5 million fatalities annually. This condition not only affects lives but also has a significant impact on health, with up to fifty percent of survivors facing chronic disabilities. Stroke has severe consequences for public health and carries substantial economic and social burdens. With population demographic shifts, particularly in developing countries, stroke is expected to become more prevalent in the coming decades.[3]

There are a lot of factors that increase the risk of stroke. Some of these factors cannot be changed, while others can be modified. The factors that cannot be changed include age, gender, race, heredity, and dislipidemia. The factors that can be modified include high blood pressure, cardiovascular disease, diabetes mellitus, smoking, excessive alcohol consumption, oral contraceptives, and so on.[4,5]

Despite plenty of evidence, there has been a debate over the usefulness of UA as an independent indicator of cardiovascular risk for more than five decades. Some studies have shown that UA administration can protect rats from cerebral ischemia. There have been mixed reports on the outcomes of stroke patients with high UA levels, with some showing improvement and others showing worsening outcomes.[6]

Elevated concentrations of UA have been recognized by several significant epidemiological investigations as a critical indicator of stroke risk in unselected populations. Enhanced serum UA concentrations are additionally correlated with a heightened likelihood of ischemic stroke in patients at high risk, such as those diagnosed with hypertension or type 2 diabetes mellitus.[7] In comparison to patients with normal UA levels, serum UA appears to be a graded indicator of risk for the development of coronary heart disease and ischemic stroke.[8]It has been suggested that increased levels of UA in the serum serve as a separate risk factor for cardiovascular morbidity and mortality. Recent research indicates that the implementation of hypouricaemic treatments may have a beneficial impact on the prevention of cardiovascular events.[9]

Bangladesh has witnessed significant progress in various sectors of health services over the past decade. Numerous public and private healthcare institutions dedicated to stroke management have already been established in Dhaka and other regions of the nation. Stroke incidence and prevalence are on the rise in our nation on a daily basis. This research will contribute to our understanding of the correlation between SUA and ischemic stroke in the populations of Bangladesh.

Method

This case control study was conducted in the Department of Medicine, JIMCH, Bajitpur, Kishoreganj from January 2021 to December 2022 for duration of 2 years. Total 120 subjects were included in this study, of them 60 were ischemic stroke patients, enrolled as case and 60 were apparently healthy people, enrolled as control.

Inclusion criteria (Case):

- Patients with ischemic stroke confirmed by CT scan or MRI of brain according to WHO definition and within 7 days of attack

- Age 18 years and above.

Exclusion criteria (Case):

- Patients undergoing treatment with medications that impact serum uric acid (SUA) levels.

- Patients with active infection

- Patients with malignancy

- Patients with renal or liver disease
- Patients with valvular heart diseases and Atrial Fibrillation
- Patients with history of joint pain and vasculitis

Controls: Age and sex matched healthy individual voluntarily agree to undergo the study.

Written consent was obtained from each study participant prior to data collection. Data were gathered through face-to-face interviews. Information was obtained by reviewing medical history, conducting clinical examinations, and performing subsequent laboratory tests. Approval was obtained from the relevant departments. All participants were briefed about the study's purpose. Data was systematically recorded in a pre-established form. Quantitative data was presented as mean with standard deviation, while qualitative data was presented as frequency distribution with percentage. Risk factors were analyzed using logistic regression. Statistical analysis was conducted using SPSS 12.0. A p-value <0.05 was deemed statistically significant.

Results

Table I: Distribution of the respondents' age by group

	Case n (%)	Control n (%)
Age (years)		
41-50	6 (10.0)	6 (10.0)
51-60	20 (33.3)	20 (33.3)
61-70	22 (36.7)	22 (36.7)
>70	12 (20.0)	12 (20.0)
Mean ± SD	62.43 ± 9.75	61.58 ± 9.70
Gender		
Male	41 (68.3)	41 (68.3)
Female	19 (31.7)	19 (31.7)
Occupation		
Housewife	14 (23.3)	18 (30.0)
Service	16 (26.7)	20 (33.3)
Business	18 (30.0)	14 (23.3)
Farmer	12 (20.0)	8 (13.3)

Mean age of the cases was 62.43±9.76 years and the controls was 61.58±9.70.In cases 68.3% were male and 31.7% were female. In controls male and female were also 68.3% and 31.7% respectively. Male and female ratio of stroke patients was 2.16:1.In cases 23.3%, 26.7%, 30.0% and 20.0% patients were housewife, service holder, businessman and farmer respectively. In control group maximum respondents were service holder(33.3%) followed by businessman (23.3%), housewife (30.0%) and farmer (13.3%) (p>0.05).

Table II: Comorbidities of the study subjects in case and control (N=120)

	Case n (%)	Control n (%)	p-value
Hypertension	34 (56.7)	4 (6.7)	0.001
Diabetes mellitus	20 (33.3)	2 (3.3)	0.001
Smoking	42 (70.0)	24 (40.0)	0.001
Family history of stroke	8 (13.3)	12 (20.0)	0.463

Chi square test was done to measure the level of significance.

Hypertension, diabetes mellitus and smoking habit was found significantly higher in cases than controls. But no significant difference was found in family history of stroke.

Table III: Serum uric acid level in cases and controls (N=120)

	Case n (%)	Control n (%)	p-value
Mean ± SD	5.14 ± 1.43	3.82 ± 1.21	0.001

Unpaired t test was done to measure the level of significance.

Mean SUA level was significantly higher in cases (5.15±1.44 mg/dl) than controls (3.83±1.21 mg/dl). Statistically significant differences were observed between case and control group in term of serum uric acid.

Table IV: Risk factor analysis for ischemic stroke (multiple logistic regression analysis)

	p-value	OR	95.0% CI for OR	
			Lower	Upper
Uric acid	0.043	1.470	0.980	2.206
Smoking	0.001	7.730	2.360	25.323
DM	0.042	5.606	1.060	29.639
HTN	0.001	20:94	4.736	92.587

An elevation of 1 mg/dl in serum uric acid correlates with a 47.0% greater probability of experiencing an ischemic stroke. Obtaining this 47.0% requires substituting Odd for uric acid -1. When comparing smokers and non-smokers, the risk of experiencing an ischemic stroke is 7.73 times the former. In comparison to non-diabetic patients, the risk of ischemic stroke is 5.61 times greater in diabetic patients. The likelihood of ischemic stroke in a hypertensive patient is 20.94 times greater than in a non-hypertensive patient.

Discussion

The purpose of this study was to investigate the correlation between UA and ischemic stroke. An assessment was also made of additional potential modifiable risk factors associated with stroke.

In this study, the average age of patients who experienced an ischemic stroke was 62.43±9.76 years, whereas the control group had an age of 61.58±9.70 years. The majority of the cases (33.3 and 36.7 percent) occurred in the fifth and sixth decades, respectively. The male-to-female ratio of 2.16:1 among stroke patients in this research suggests that the condition is predominately affecting males. The current hospital-based study might not accurately represent the proportion observed in the community, as female stroke patients are not admitted to hospitals due to familial neglect.

A total of 70.0% of the cases (both current and former smokers) and 40.0% of the controls (p<0.05) were smokers. Cigarette smoking is a well-established risk factor for all forms of stroke.[10]

Diabetes mellitus was present in 33.3% of the cases and 3.3% of the controls in this study (p<0.05). Particularly ischemic strokes, diabetes is a significant modifiable risk factor for stroke.[11]

Hypertension was present in 6.7% of controls and 56.7% of cases in this study (p<0.05). Consistent findings were condemned in additional research. According to Carrieri'set al.[12] analysis of risk factors for stroke, 52.11% of patients who experienced the condition had hypertension. Hypertension was identified in 61% of the stroke patients in Pakistan, according to Basharat et al.[13]. Analogous findings were documented in additional domestic and international research.[14] Each of these results aligns with the outcome of the current investigation.

While several epidemiological studies have identified elevated serum uric acid concentrations as a significant risk factor for stroke in unselected populations, it remains unclear whether such levels actively promote or prevent the onset of stroke, or merely serve as a circumstantial/passive indicator of increased risk.[7,15-17] The relationship between SUA and other well-defined stroke risk factors, which would indicate whether SUA is an indirect marker of adverse outcome or an independent risk factor and predictor of mortality and morbidity in patients with vascular disease, is another contentious issue.[18,19] After adjusting for the use of diuretics, the Framingham study found no independent association between hyperuricemia and the risk of stroke or mortality.[20] Nevertheless, an independent association has been established in subjects aged 45 and above, according to data from larger studies (NHANES I), irrespective of confounding variables including sex, menopausal status, diuretic use, stroke presence, or race.[15] Higher levels of serum uric acid predicted a poor prognosis and an increased likelihood of a recurrent stroke event in a retrospective study of 2498 patients admitted with acute stroke, independent of other prognostic factors.[16]

The mean levels of uric acid in the case and control groups were 5.15±1.44 mg/dl and 3.83±1.21 mg/dl, respectively. These values were both within the normal range. However, a statistically significant difference (p<0.05) was observed between the two groups. Consistent with this result, Millionis et al.[9] found that stroke patients had higher serum uric acid concentrations than controls (5.6±1.7mg/dl vs. 4.8±1.4mg/dl, p=0.001). The logistic regression analysis showed that the Odds Ratio (OR) for serum uric acid increased by 1 mg/dl was 1.42 (95% CI 1.21-1.64, p<0.0001).

Higher urate levels have been found to increase the risk of stroke in several studies, including Weir et al.[16] (2003) and Millionis et al.[9]. The current study's findings align with those of previous investigations and suggest that a 1 mg/dl increase in serum uric acid (SUA) levels is associated with a 47.0% increase in the likelihood of experiencing an ischemic stroke. Notably, smokers had 7.73 times higher odds of experiencing an ischemic stroke compared to nonsmokers, diabetic patients had 5.60 times higher odds compared to non-diabetic patients, and hypertensive patients had 20.94 times higher odds compared to non-hypertensive patients.

Conclusion

The mean serum uric acid level was within the normal range, hence this investigation showed no association between elevated uric acid and ischemic stroke risk. We found that the case group had a considerably higher average serum uric acid concentration than the controls. Serum uric acid's role in acute ischemic stroke needs further study.

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