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Serum Uric Acid Level and its Association with Severity in Acute Ischemic Stroke

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Abstract **Original Research Article**

Background: Cerebrovascular diseases (CVDs) are a major public health issue around the world. Elevated serum uric acid levels may predict an increased risk for cerebrovascular events particularly acute ischemic stroke. ***Aim of the study:*** The aim of our study was to assess the association between serum uric acid level and severity of acute ischemic stroke. ***Methods:*** This observational case control study was conducted at the department of Neurology and at the department of Medicine in Dhaka Medical College Hospital from July 2018 to June 2020. This study included 50 acute ischemic stroke patients and 50 age and gender matched healthy controls. Along with the routine investigations, estimation of serum uric acid was done in all participants. The severity of stroke was assessed as per national institutes of health stroke scale (NIHSS). After collection of all the required data, analysis was done by SPSS 23.0. ***Results:*** The mean age and distribution of the age in different age group were matched between case and control groups (p=0.607 and 0.763 respectively). The mean age of the ischemic stroke cases was 62.14±9.77 years. The mean NIHSS score of the patients was 16.34±10.34. Of all, 18% had minor stroke, 32% had moderate stroke, 20% had moderate to severe stroke and 30% had severe stroke. Among stroke patients 58% had elevated uric acid level and among controls 20% had raised uric acid in serum. The number of patients having elevated serum uric acid is statistically significantly higher in case group than control group (p<0.001). Multivariate regression analysis showed hypertension (OR 4.046; 95% CI 1.432–11.432; p=0.008), DM (OR 3.063; 95% CI 1.030-9.105; p=0.044), dyslipidemia (OR 3.031; 95% CI 1.062-8.654; p=0.038) and elevated serum uric acid level (OR 6.019, 95% CI 2.220–16.317; p<0.001) independently associated with acute ischemic stroke (p<0.05). ***Conclusion:*** This study shows elevated serum uric acid level significantly associated with severity of acute ischaemic stroke.

Keywords: Cerebrovascular diseases, Serum uric acid, Acute ischemic stroke, National institutes of health stroke scale (NIHSS).

INTRODUCTION

A stroke is defined by the World Health Organization (WHO) as a clinical syndrome characterized by rapidly developing clinical signs of focal (or global in the case of coma) disruption of cerebral function lasting more than 24 hours or resulting in death with no apparent cause other than a vascular origin [1]. Stroke is the third leading cause of death in the world, behind coronary heart disease and cancer, particularly among the elderly [2]. In Bangladesh, it is also among the main causes of death. According to the WHO, Bangladesh has the world's 84th highest stroke death rate. The reported prevalence of stroke in Bangladesh is 0·3%, although no data on stroke incidence have been recorded [3]. Stroke has been divided into two major types, ischemic and hemorrhagic. Ischemic stroke (IS) is the most common type of stroke, accounting for 80% of all strokes. IS has a poor prognosis and is associated with high mortality rate [4]. Various risk factors are involved for development of ischemic stroke, like hyperlipidemia, diabetes and smoking etc. Recent studies shows that there may be other factors causing the development of stroke like serum uric acid (SUA) level [5]. Uric acid is the breakdown product of purines derived from DNA, RNA, ATP, and cAMP. During this process, the enzyme xanthine oxidase converts hypoxanthine to xanthine and then to uric acid. Both steps induce the release of free radicals. Uric acid may accumulate in the body due to increased production

(cell death, intake of alcohol or purine rich diet) or decreased elimination (impaired renal function, use of diuretics) [6]. Several large studies have provided conflicting results regarding the clinical significance of elevated serum uric acid levels in cerebrovascular diseases. Many studies including the NHANES study concluded that uric acid is an independent risk factor for development of cerebrovascular diseases [7]. In contrast the Framingham heart study concluded that an association between hyperuricemia and cerebrovascular diseases merely reflects the link between serum uric acid and other risk factors, including hypertension, renal disease, elevated lipoprotein levels and the use of diuretics [8]. In patients with acute ischemic stroke, Chamorro *et al*., suggested that there is a 12% increase in the odds of good clinical outcome for each milligram per deciliter increase of serum uric acid [9]. Similarly, a meta-analysis supported that serum uric acid level had a protective effect on neurological outcome after acute ischemic stroke [10]. Therefore, it is unclear whether increased serum uric acid level are protective or acts as an independent risk factor for the development of cerebrovascular disease. If increased serum uric acid level would be identified as an etiological agent in the pathogenesis of vascular diseases, its' therapeutically reduction could contribute to decrease cardiovascular and cerebrovascular morbidity and mortality [11]. So, considering the circumstances the aim of this study was to evaluate the association between serum uric acid level and acute ischemic stroke and its severity in our population.

METHODOLOGY

This observational case control study was conducted at the department of Neurology and at the department of Medicine in Dhaka Medical College Hospital from July 2018 to June 2020. A total 50 cases of acute ischemic stroke patients are grouped as case and 50 age and gender matched healthy controls are grouped as control were enrolled in this study. All participants provided written informed consent. A detailed history and through clinical examination were carried out in each patient. Conventional risk factors for stroke such as hypertension, diabetes mellitus, smoking, and dyslipidemia were noted also. Along with the routine investigations, estimation of serum uric acid was done in all participants. The severity of stroke was assessed as per national institutes of health stroke scale (NIHSS). After collection of all the required data, analysis was done by SPSS 23.0.

RESULT

The mean age and distribution of the age in different age group were matched between case and control groups (p=0.607 and 0.763 respectively). The mean age of the ischemic stroke cases was 62.14±9.77 years. Among the ischemic stroke maximum 40% were in 61-70 years age group, 28% were in 51-60 years age group, 20% were in >70 years age group, and 12% were in 45-50 years age group. Among the ischemic stroke respondents 60% were male and 40% were female. The gender distribution of the patients were matched between case and control groups (p=0.418) (Table-1). Among the ischemic stroke cases 48% had hypertension, 38% had diabetes, 38% had dyslipidemia, 24% were overweight or obese and 36% had history of smoking. Number of patients having hypertension, DM and dyslipidemia were statistically significantly more in case group than control group (P=0.019, 0.022 and 0.038) (Table 2). (Table-3) reveals that among stroke patients 58% had elevated uric acid level and among controls 20% had raised uric acid in serum. The number of patients having elevated serum uric acid is statistically significantly higher in case group than control group (p<0.001). Serum uric acid level was statistically significantly higher in moderate to severe and severe stroke cases in comparison to minor stroke cases (P<0.05). Serum uric acid level was also significantly higher in severe stroke cases in comparison to moderate stroke cases (P<0.05) (Table-4). Study findings in (Table-5) reveals that the number of patients having elevated serum uric acid level was statistically significantly associated with severity of stroke (p=0.002). In minor stroke group 22.22% had elevated uric acid level, in moderate stroke group 37.50% had elevated uric acid level, in moderate to severe stroke group 80% had elevated uric acid level and in severe stroke group 86.67% had elevated uric acid level. Univariate regression analysis of different risk factors for ischemic stroke was done. In univariate regression analysis, ischemic stroke was found to be associated with hypertension, diabetes and elevated serum uric acid level (p<0.05) (Table-6). Multivariate logistic regression analysis of different risk factors for ischemic stroke was done. Ischemic stroke was found to be independently associated with hypertension, diabetes, dyslipidemia and elevated serum uric acid level (p<0.05). Elevated uric acid had OR of 6.019 (95%CI 2.220 – 16.317; p<0.001) (Table-7). Figure-1 shows that the mean NIHSS score of the patients was 16.34±10.34. Among the study cases 18% had minor stroke, 32% had moderate stroke, 20% had moderate to severe stroke and 30% had severe stroke.

Table-1: Age and gender distribution of the studied patients between groups (N=100)

Age (in years)	Case (n=50) No. (%)	Control (n=50) No. (%)	Total (N=100) No. (%)	P-value
45-50	06 (12)	08 (16)	14 (14)	0.763*
51-60	14 (28)	13 (26)	27 (27)	
61-70	20 (40)	16 (32)	36 (36)	

Age (in years)	Case (n=50) No. (%)	Control (n=50) No. (%)	Total (N=100) No. (%)	P-value
>70	10 (20)	13 (26)	23 (23)	
Mean±SD	62.14±9.77	63.20±10.76	62.81±10.51	0.607**
Gender				
Male	30 (60)	32 (64)	62 (62)	0.418
Female	20 (40)	18 (36)	38 (38)	

Table-2: Distribution of participants according to risk factors (N=100)

Risk factors	Case (n=50) No. (%)	Control (n=50) No. (%)	P-value
HTN	24 (48)	13 (26)	0.019
DM	19 (38)	09 (18)	0.022
Dyslipidemia	19 (38)	10 (20)	0.038
Overweight and obesity	12 (24)	08 (16)	0.227
Smoking	18 (36)	15 (30)	0.335

Table-3: Serum uric acid level among cases and controls (N=100)

Serum uric acid category	Case (n=50) No. (%)	Control (n=50) No. (%)	P-value
Elevated (>7 mg/dl for male and >6 mg/dl for female)	29 (58)	10 (20)	<0.001
Normal	21 (42)	40 (80)	

Table-4: Bonferroni test results for multiple comparison (in different severity) for uric acid level (N=50)

Comparison		Mean difference (I-J)	Standard Error	P-value
I	J			
Minor	Moderate	-1.11	0.50	0.184
	Moderate to severe	-2.29	0.55	0.001
	Severe	-3.17	0.50	<0.001
Moderate	Moderate to severe	-1.18	0.48	0.109
	Severe	-2.06	0.43	<0.001
Moderate to severe	Severe	-0.88	0.49	0.463

Table-5: Serum uric acid level among different stroke category group (N=50)

Serum uric acid category	Minor (n=09) No. (%)	Moderate (n=16) No. (%)	Moderate to severe (n=10) No. (%)	Severe (n=15) No. (%)	P-value
Elevated (>7 mg/dl for male and >6 mg/dl for female)	02 (22.22)	06 (37.50)	08 (80)	13 (86.67)	0.002
Normal	07 (77.78)	10 (62.50)	02 (20)	02 (13.33)	

Table-6: Univariate regression analysis of risk factors for ischemic stroke (N=100)

Variables	Odds ratio	95% CI	P-value
Hypertension	2.63	1.13-6.09	0.024
Diabetes	2.79	1.11-7.01	0.024
Elevated uric acid	3.69	1.52-8.97	0.004
Smoking	1.31	0.57-3.03	0.524
Dyslipidemia	2.45	0.99-6.02	0.050
Obesity and overweight	1.66	0.61-4.49	0.320

Table-7: Multivariate logistic regression analysis of risk factors for ischemic stroke (N=100)

Variables	Odds ratio	95% CI	P-value
Hypertension	4.05	1.43-11.43	0.008
Diabetes	3.06	1.03-9.12	0.044
Elevated uric acid	6.02	2.22-16.32	<0.001
Smoking	1.68	0.62-4.63	0.318
Dyslipidemia	3.03	1.06-8.65	0.038
Obesity and overweight	1.93	0.59-6.31	0.275

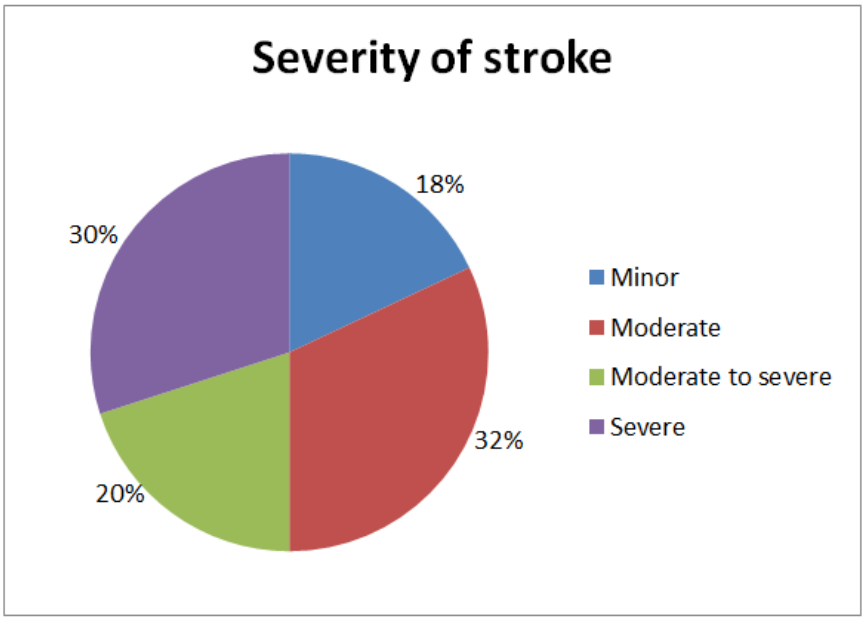

Figure-1: Distribution of severity of stroke among the patients (n=50)

DISCUSSION

This study was aimed to evaluate the association between serum uric acid level and acute ischaemic stroke and its severity. Total 100 respondents (50 case and 50 control) were included into this observational case control study which was conducted in Department of Neurology and Department of Medicine in Dhaka medical college hospital. The average age of the stroke cases was in seventh decade (62.14±9.77 years) and majority (40%) of them were in 61-70 years age group. The mean age and age distribution of the respondents were matched between case and control group (p=0.607 and 0.763). Study conducted by Bhowmik *et al*., Donghua *et al*., and Shams *et al*., found the mean age of their study stroke cases 60.60 years, 60.09 years 59.28±13.98 years respectively and all these findings are concordant to the findings of this study [12, 13, 14]. The gender distribution of the respondents were also matched between case and control groups (p=0.418). Clear male predominance was noticed with 1.5:1 male female ratio. Among the ischemic stroke respondents 60% were male and 40% were female. Study conducted by Habib and co-researchers, Nayak and co-researchers also found maximum (55.40% and 70.19% respectively) of their study stroke cases in male gender group [15, 16]. Diabetes, dyslipidemia and history of hypertension were statistically significantly more common in case group than control group (p=0.022, 0.038 and 0.019 respectively). Hypertension, diabetes mellitus, dyslipidemia, overweight and obesity, and history of smoking was present in 48%, 38%, 38%, 24% and 36% of the study stroke cases respectively. Study conducted by Khandait and co-researchers found almost similar findings in their respective study [17]. Khandait and his colleague found history of smoking and diabetes among their 36.70% and 10% cases respectively and among their study cases 40% had dyslipidemia. The severity of ischemic stroke cases was assessed by national institute of health stroke scale (NIHSS). The mean NIHSS score of the stroke cases were 16.34±10.34 and out of 50 stroke cases 18%, 32%, 20% and 30% were in minor, moderate, moderate to severe and severe stroke group respectively. Study conducted by Ghosh *et al*., found 16%, 51%, 22% and 11% of their stroke cases in minor, moderate, moderate to severe and severe stroke group respectively [18]. Harsh and associates also found maximum (49%) of their study cases in moderate stroke group [5]. In minor stroke group 22.22% had elevated serum uric acid level, in moderate stroke group 37.50% had elevated serum uric acid level, in moderate to severe stroke cases 80% had elevated uric acid and in severe stroke group 86.67% had elevated serum uric acid level. The mean uric acid level was found statistically significantly higher in moderate to severe stroke group in comparison to minor stroke group and severe stroke

group in comparison to minor and moderate stroke group (p<0.001). Study conducted by Harsh and co-researcher also found statistically significant association between serum uric acid and severity of stroke [5]. They found the mean uric acid level 3.69±0.12 mg/dl, 5.82±0.40 mg/dl, 7.14±0.86mg/dl and 8.40±1.2 mg/dl in minor, moderate, moderate to severe and severe stroke group respectively. However another study conducted by Wu and associates did not found any statistically significant association between serum uric acid with severity of norm glycemic stroke cases but they found statistically significant association between serum uric acid level with severity of diabetic stroke cases [19]. Study conducted by Kaur and co-researchers also found statistically significant higher serum uric acid level in severe stroke cases than mild or moderate stroke cases (p=0.0426) [2]. In case group, 58% had elevated serum uric acid level and in control group 20% had elevated serum uric acid level. Number of patients having elevated serum uric acid level was also statistically significantly higher in case group than control group (p<0.001). Both in univariate and multivariate regression analysis elevated uric acid level had statistically significant higher OR of developing ischemic stroke. In multivariate regression analysis the OR was 6.02 (95% CI 2.220 – 16.317; p<0.001). concordant to the finding of this study Kaur and associates also found statistically significant higher mean serum uric acid level in ischemic stroke cases than control respondents (p<0.05). In their study they found the mean serum uric acid level 6.15±1.91 mg/dl in case group and 5.10±1.40 mg/dl in control group [2]. Another study conducted by Mehrpour *et al*., found the mean uric acid level of their study ischemic stroke cases 5.94±1.70 mg/dl and among their study ischemic stroke cases 47.30% had elevated uric acid level [20]. Tariq *et al*., also concluded their meta analysis with the observation that high uric acid levels are associated with increased incidence of stroke [21]. Study conducted by Storhaug and associates also observed elevated serum uric acid level as an independent risk factors of stroke (HRs 1.22 95% CI 1.09-1.35) in their respective study [6]. So, this study revealed elevated serum uric acid level as an independent risk factors of ischemic stroke. This study also revealed significant association between severity of ischemic stroke with serum uric acid level.

Limitation of the study:

This study was a single-center study with a small sample size and a short duration of follow-up, so these findings may not reflect the actual scenario.

CONCLUSION & RECOMMENDATION

After observing and compare with the control, serum uric acid level is significantly higher in case group than control group. The elevated uric acid level also related with higher severity grading of the stroke. Multivariate regression analysis showed hypertension, DM, dyslipidaemia and elevated serum uric acid level independently associated with acute ischemic stroke. At admission serum uric acid level should be checked. Further studies with larger sample size are recommended.

REFERENCES

1. Coupland, A. P., Thapar, A., Qureshi, M. I., Jenkins, H., & Davies, A. H. (2017). The definition of stroke. *Journal of the Royal Society of Medicine*, *110*(1), 9-12.
2. Kaur, I., Khurana, A., Sachdev, J. K., & Mohan, G. (2017). Evaluation of serum uric acid in acute ischaemic stroke. *Int J Adv Med*, *4*(1), 60-65.
3. Islam, M. N., Moniruzzaman, M., Khalil, M. I., Basri, R., Alam, M. K., Loo, K. W., & Gan, S. H. (2013). Burden of stroke in Bangladesh. *International journal of stroke*, *8*(3), 211-213.
4. Yang, Y., Zhang, Y., Li, Y., Ding, L., Sheng, L., Xie, Z., & Wen, C. (2018). U-Shaped relationship between functional outcome and serum uric acid in ischemic stroke. *Cellular Physiology and Biochemistry*, *47*(6), 2369–2379.
5. Harsh, S., & Aparna, P. (2019). The study of serum uric acid levels in ischemic stroke patients. *International Journal of Contemporary Medical Research*, *6*(1), 2–6.
6. Storhaug, H. M., Toft, I., Eriksen, B. O., Zykova, S., Jenssen, T., Norvik, J. V., Solbu, M., Løchen, M. L., White, S., & Chadban, S. (2013). Uric acid is a risk factor for ischemic stroke and all-cause mortality in the general population: A gender specific analysis from The Tromsø Study. *BMC Cardiovascular Disorders*, 13, 115-121.
7. Fang, J., & Alderman, M. H. (2000). Serum uric acid and cardiovascular mortality the Nhanes I epidemiologic follow-up study, 1971-1992. National Health and Nutrition Examination Survey. *JAMA*, *283*(18), 2404-2410.
8. Culleton, B. F., Larson, M. G., Kannel, W. B., & Levy, D. (1999). Serum uric acid and risk for cardiovascular disease and death: the Framingham Heart Study. *Annals of internal medicine*, *131*(1), 7-13.
9. Chamorro, Á., Obach, V., Cervera, Á., Revilla, M., Deulofeu, R., & Aponte, J. H. (2002). Prognostic significance of uric acid serum concentration in patients with acute ischemic stroke. *Stroke*, *33*(4), 1048–1052.
10. Wang, Z., Lin, Y., Liu, Y., Chen, Y., Wang, B., Li, C., Yan, S., Wang, Y., & Zhao, W. (2016). Serum Uric Acid Levels and Outcomes after Acute Ischemic Stroke. *Molecular Neurobiology*, *53*(3), 1753–1759.
11. Behera, B. K., Hui, P. K., & Simethy, R. (2017). Serum uric acid level in acute ischemic stroke in eastern India. *International Journal of Research in Medical Sciences*, *5*(6), 2353-2359.
12. Bhowmik, N. B., Abbas, A., Saifuddin, M., Islam, M. R., Habib, R., Rahman, A., Haque, M. A.,

Hassan, Z., & Wasay, M. (2016). 'Ischemic Strokes: Observations from a Hospital Based Stroke Registry in Bangladesh. *Stroke Research and Treatment*, 16, 1-13.

13. Mi, D., Wang, P., Yang, B., Pu, Y., Yang, Z., & Liu, L. (2018). (2018). Correlation of hyperglycemia with mortality after acute ischemic stroke. *Therapeutic Advances in Neurological disease*, *8*(1), 25–32.
14. Shams, A. B. U., Ali, H., Ara, K. J., Saeed, A., & Shams, S. (2019). Comparison of Personal Profile and Risk Factors between Patients with Ischaemic and Haemorrhagic Stroke. *University Heart Journal*, *15*(2), 42-46.
15. Nayak, A. R., Husain, A. A., Lande, N. H., Kawle, A. P., Kabra, D. P., Taori, G. M., ... & Kashyap, R. S. (2015). Impact of admission time on treatment and outcome of stroke in patients admitted to tertiary care hospital: a pilot study from Central India. *Journal of Clinical and Diagnostic Research: JCDR*, *9*(6), BC01-BC07.
16. Habib, R., Hosen, I., Islam, R., & Bhowmik, N. B. (2018). Risk Factors and Etiologies of Ischemic Stroke in Young Adults: A Hospital-based Study in Bangladesh. *BIRDEM Medical journal*, *8*(2), 138-144.
17. Khandait, V., & Barai, P. (2019). Study of fibrinogen levels in patients of acute stroke. *International Journal of Research in Medical Sciences*, *7*(1), 20.
18. Ghose, S. K., Ahmed, K. G. U., Chowdhury, A. H., Hasan, A. H., Saha, K., Mahmud, R., ... & Habib, M. (2017). Assessment of initial stroke severity by National Institute health stroke scale (NIHSS) score at admission. *Journal of Dhaka Medical College*, *26*(2), 90-93.
19. Wu, S., Pan, Y., Zhang, N., Jun, W. Y., & Wang, C. (2017). Lower serum uric acid level strongly predict short-term poor functional outcome in acute stroke with normoglycaemia: A cohort study in China. *BMC Neurology*, *17*(1), 1-12.
20. Mehrpour, M., Khuzan, M., Najimi, N., Motamed, M. R., & Fereshtehnejad, S. (2012). Serum uric acid level in patients of acute stroke. *Medical journal of Islamic Republic of Iran*, *26*(2), 66–72.
21. Tariq, M. A., Shamim, S. A., Rana, K. F., Saeed, A., & Malik, B. H. (2019). Serum uric acid–risk factor for acute ischemic stroke and poor outcomes. *Cureus*, *11*(10), e6007.