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ORIGINAL ARTICLE

Association between High Serum Uric Acid Level and Good Outcome in patients of Ischemic Stroke

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ABSTRACT

Aim: To determine the relationship of raised levels of uric acid and good prognosis in patients presenting with acute onset ischemic stroke

Study design: A cross-sectional descriptive study.

Place & duration of study: The research was done at Medical Emergency, Departments of Neurology and Medicine Mayo Hospital Lahore from April, 2019 to March 2020.

Methods: Total 230 patients fulfilling selection criteria were enrolled. Serum uric acid levels were measured at the time of admission. The technique used to assemble data was consecutive non-probability convenience sampling. Patients were divided into two groups Group A (115 patients - having uric acid more than or equal to 7 mg/dl) and Group B (115 patients - having uric acid less than 7 mg/dl). After 5 days, Modified Rankin score (mRS) was noted and link between raised uric acid levels and mRS was determined.

Results: Total 230 (115 Group A/ 115 Group B) patients were selected for this study. Among Group A, mean age was 57.2±10.4 years and 58.8±10.1 years among Group B. Among Group A, there were 72(62.6%) males and 43(37.4%) females, while 79(68.7%) males and 36(31.3%) females among Group B . By comparing good outcome between groups, it was found that percentage of good outcome was 42.6% with high uric acid level and 16.5% with normal uric acid level. The difference was significant (p=0.00001) and with odds ratio as 3.751.

Conclusion: There is an association between high serum uric acid level and good outcome in patients presenting with stroke. Patients with high serum uric acid level have significant chances to have good outcome.

Keywords: Serum Uric Acid, Acute Ischemic Stroke, modified Rankin Score

INTRODUCTION

Stroke is as a neurological disorder which effects the central nervous system by a vascular cause like cerebral infarction, intracerebral hemorrhage or subarachnoid hemorrhage[1]. Stroke is regarded to be the foremost cause of death and one of the chief cause of prolonged debilityglobally[2].

In Pakistan, the incidence of stroke is 250/100,000 in comparison with US where it is 200/100,000. Worldwide approximately 13.7 million people suffer from stroke per year[3]. The number of cases of stroke is rising in developing countries. Due to the significantly high mortality rates and huge amount of resources used by system of health, stroke is now being considered as one of the major health concern in these areas[4].

Uric acid is produced by the enzymatic activity of xanthine oxidase and is the final product of purine metabolism,[5]It is a kind of influential endogenous antioxidant agent which may be raised in many oxidative stress conditions like acute stroke[6] in a large amount as compared to other antioxidants. It acts as a scavenger for oxygen, superoxide, and hydroxyl radicals[7]. Raised serum uric acid is defined as serum uric acid concentration more than 7mg/dL. Numerousresearches have revealed that uric acid is an antioxidant and free radical scavenger that shields the brain from oxidative injury, thereby averting poor neurological outcome after stroke[8].

Disability and co-morbidity are common in older populations. The modified Rankin Scale (mRS) is calculated to measure post-stroke recovery[9].

A study conducted by Wu H et al to see the relation between levels of serum uric acid, outcome after one year , and vascular events in patients having stroke which is of ischemic type. It was seen that reduced levels of uric acid in serum were linked to pooreroutcomes and had a greater risk of motality[10].

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Xiaoyan Yu and colleagues proposed that higher level of serum urate was related to improve results in patients presenting with acute stroke who were managed with therapies that involved reperfusion[11].

Tripathi VD et al showed in a research that greater level of uric acid is positively linked with relatively good outcome in patients having ischemic stroke. In subjects with uric acid levels of >7mg%, mRS ≤2 was found in 31% patients and in patients having uric acid levels in serum ≤7mg%, mRS ≤2 was found in 17% of the patients[12].

In patients of acute stroke the extrapolative importance of raised uric acid is still debatable. So we designed a study to determine the relationship of serum uric acid and prognosis of patients having ischemic stroke in our population.

METHODS

The study was conducted at Medical Emergency, Department of Medicine and Neurology, Mayo Hospital, Lahore from April, 2019 till March 2020.Total of 230 patients with ischemic stroke of ages 18-75 years,of both genders were enrolled in the study by Non-Probability Consecutive Sampling. Sample size of 230 patients (115 in each group) was calculated by taking 5% as level of significance with 80% as power of test and expected percentage of good outcome as 31% in patients with uric acid levels of >7mg/dl and 17% in patients with serum uric acid levels of ≤7mg/dl[12].

Patients were divided into two groups Group A (115 patients - having uric acid more than or equal to 7mg/dl) and Group B (115 patients having uric acid less than 7mg/dl). A written consent was taken from patients. Demographic details (name, age and sex) were noted. Serum uric acid levels were measured at admission. However, Patients with cerebral venous thrombosis, intracerebral hemorrhage and subarachnoid hemorrhage were omitted from the study.

After 5 days, mRS was noted and relationship between serum uric acid levels and mRS was determined. Favorable

outcome was defined as modified Rankin score (ranges 0-6) of ≤2 after 5 days of presentation.

All data was collected and analyzed using SPSS v25.0. Quantitative variables like age, serum uric acid levels and modified rankin score were presented as Mean±S.D. Qualitative variable such as gender was calculated aspercentages and frequency . Relative risk was calculated to check association. Data were stratified for age, gender, BMI and duration of stroke. Post-stratification, Odds ratio was calculated.

RESULTS

Out of 230 patients, mean age was 57.2±10.4 years in Group A and 58.8±10.1 years among Group B patients. In Group A there were 72(62.6%) males and 43(37.4%) females, whereas 79(68.7%) males and 36(31.3%) females among Group B (Table I).

According to age distribution among Group A patients, 36(31.3%) were in 40-50 years age group, whereas 31(27%) and 48(41.7%) were in 51-60 years and >60 years age groups respectively.

According to age distribution among Group B patients, 26(22.6%) were in 40-50 years age group, while 36(31.3%) and 53(46.1%) were in 51-60 years and >60 years age groups respectively (Table I).

In Group A 87(75.7%) had BMI near to normal, whereas 24(20.9%) and 4(3.5%) were overweight and obese respectively. In Group B, 78(67.8%) had normal BMI, while 32(27.8%) and 5(4.3%) were overweight and obese respectively (Table I).

In Group A, 70(60.9%) patients had duration of stroke <48 hours, while 45(39.1%) had >48 hours. In Group B, 62(53.9%) had duration of stroke <48 hours, while 53(46.1%) had >48 hours (Table II).

By comparing good outcome between groups, it was found that percentage of good outcome was 42.6% with high uric acid level (Group A) and 16.5% with normal uric acid level (Group B). The difference was significant (p=0.00001) and with odds ratio as 3.751. (Table III)

Table I: Baseline Characteristics

	Group A	Group B	Total
Gender			
Male	72 (62.6%)	79 (68.7%)	151 (65.7%)
Female	43 (37.4%)	36 (31.3%)	79 (34.3%)
Total	115 (100%)	115 (100%)	230 (100%)
Age groups			
40-50 years	36 (31.3%)	26 (22.6%)	62 (27.0%)
51-60 years	31 (27.0%)	36 (31.3%)	67 (29.1%)
>60 years	48 (41.7%)	53 (46.1%)	101 (43.9%)
Total	115 (100%)	115 (100%)	230 (100%)
Body Mass Index (BMI)			
Normal (18-24.9)	87 (75.7%)	78 (67.8%)	165 (71.7%)
Overweight (25-29.9)	24 (20.9%)	32 (27.8%)	56 (24.3%)
Obese (>30)	4 (3.5%)	5 (4.3%)	9 (3.9%)
Total	115 (100%)	115 (100%)	230 (100%)

Table II: Comparison of duration of stroke between two groups

Duration of Stroke	Groups		Total
	A	B	
<48 hours	70(60.9%)	62(53.9%)	132(57.4%)
>48 hours	45(39.1%)	53(46.1%)	98(42.6%)
Total	115(100%)	115(100%)	230(100%)

Table III: Comparison of Good Outcome between two groups

Good Outcome	Groups		Total	P-value	odds ratio
	A	B			
Yes	49	19	68	0.00001	3.751
No	66	96	162		
Total	115	115	230		

DISCUSSION

Cerebrovascular accident has no age limit and can have numerous causes, like cardiovascular embolism, trauma, pregnancy and its complications, oral contraceptive use, hematologic disorders, substance abuse and connective tissue disorders[13]. The relationship between hyperuricemia and cardiovascular disease has been well recognized since ages. However, studies have shown contradictory results on the relationship of hyperuricemia with stroke occurrence and prognosis.

In our study 230 patients having recent onset of ischemic stroke were recruited. Out of 230 patients 65.7% male and 34.3 were female. Most of the patients (43.9%) were between 60 and 75 years. In current study advancing age seems to be an important risk for the development of stroke and high levels of uric acid. Among hyperuricemic patient i.e. Group A, 48(41.7%) were older than 60 years as equated to patients having normal uric acidlevels (Group B) in which 53(46.1%) patients were over sixty years of age. Overall 43.9% patients were older than 60 years. Mean agewas 58.1±12.9 years in stroke patients recruited in our study.

Bansal etal[14]did a study including patients of acute ischemic stroke. Hyperuricemia was present in 30% of these patients with mean level of uric acid 8.94±2.37mg/dl. Interestingly occurrenceof raised amount of serum uric acid was more in subjects aged 60 to 80 years with mean age of 59.40±12.15 years. These findings are in accordance with results of our study.

Furthermore, in our study the presence of hyperuricemia was noted more in men. A Total of 72(62.6%) out of 115 were male and 43(37.4%) females had hyperuricemia as shown in Table I. Men usually are at higher risk of developing hyperuricemia as related to women. This difference of having low uric acid levels in femalespersists tillreaching menopause and after that this variance isvanished. Estrogen plays an important part in developing this uricosuric effect in premenopausal female.

A study done by Chamorro and associates[15]exhibited a noteworthyrelationship between elevated uric acid levels in serum and male genderin stroke (p= 0.0001). Similar findings were present in study done by Millionis et al[16] showing asubstantial relationshipbetween higher serum uric acid levels and male patientshaving acute ischemic stroke (p=0.01). Results of our study have shown the similar relationship of higher uric acid levels in males suffering from acute ischemic stroke.

Modified Rankin's score results showing number 3 or greater than 3 are considered a worse prognosis. Results of our study also showed a major difference between patient with high and low levels of uric acid in terms of significance whether good or bad (p > 0.05).

Weir and colleagues did a study on 3731 patients of acute ischemic stroke and concluded thatraiseduric acid levelsforecast a lesserpossibility of better 90day consequenceregardless of severity and other factors which effects prognosisof stroke. These results are contradictory to the findings in our study.

Chamorro et al[15] studied 881 patients and stated that in patients of acute ischemic stroke there was a 12% upsurge in the odds of betterresult seen clinically for every milligram per deciliter (mg/dl)rise of uric acid level. These results support the importance of oxidative harm in ischemic stroke patients. Our research has shown a significant relation between higher levels of uric acid and good prognosis in patients with acute ischemic stroke patients. By comparing good outcome between two groups, it was found that percentage of good outcome was 42.6% with high uric acid level and 16.5% with normal uric acid level. The difference was statistically significant (p=0.00001) and with odds ratio as 3.751.

Serum urate is an important antioxidant found in plasma and constitute about two third portion of free radicals in body. Serum urate is a free radical which has a significant protective roleon nerves from oxidative damage.

Wu H et al[10] conducted a study to demonstrate the affiliation between serum urate levels and prognosis of patients after one year of acute stroke. They reported that reduced serum uric acid levels were linked to worse outcome and resulted ingreater risk of all-cause death.

Amaro and associates[17]proposed that high serum uric acid is related withrelatively goodprognosis in patients of acute stroke in whom reperfusion therapies were used. They also reinforcedthe role of neuroprotective effect of administration of uric acid in management of acute stroke.

In a study by Kawase S et al[18.], multivariate scrutiny proved that the low levels of serum uric acid in patients of acute stroke wereconsiderablyrelated with bad quality of lifein both genders i.e., males and females.

Tripathi VD et al[12] showed in a study that increased uric acid level is certainly associated with better prognosis in ischemic stroke patients. In patients with serum uric acid levels of >7mg%, mRS ≤2 was found in 31% patients and remarkably in patients having serum uric acid levels of ≤7mg%, mRS ≤2 was found in 17% of the patientswhich is consistent with our study.

In terms of limitations, the current study was conducted at a single center with a small sample size depending upon the study design and prerequisites. The results of our study can only be applied to a very narrow population and have poor generalizability. Further multi-centered trials are warranted to endorse the results of the current study.

CONCLUSION

There is a significant association between raised serum uric acid level and good outcome in patients presenting with ischemic stroke. Therefore, patients of ischemicstroke withhigh serum uric acid level have better prognosis.

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