



Original Article

Frequency of Hyperuricemia in Patients Presenting with Acute Ischaemic Stroke

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ABSTRACT

Hyperuricemia refers to elevated serum uric acid concentration above the upper limit of normal.

Objective: To determine hyperuricemia in patients presenting with acute ischemic stroke to the Neurology ward of Lady Reading Hospital, Peshawar. **Methods:** A total of 153 patients were observed to the frequency of hyperuricemia in patients presenting with acute ischemic stroke. Study design was cross sectional study which was conducted for the period of 6 months. The total Sample size was calculated by using WHO sample size calculator. It was calculated using the World Health Organization software. **Results:** A total of 153 patients were observed to the frequency of hyperuricemia in patients presenting with acute ischemic stroke. Mean age of study participants was 52.45±1.14 years. Distribution of hyperuricemia was 114(74.5%). Mean serum uric acid level among cases of acute ischemic stroke was 06.15 ± 01.91 mg/dl while the mean serum uric acid level among control group was 05.1 ± 01.4 mg/dl. The results were highly significant p-value < 0.0001. **Conclusions:** Serum uric acid levels can be used to predict stroke risk. Moreover, serum uric acid can be utilized to stratify risk following a stroke. Long-term prospective research is needed to determine the involvement of serum uric acid in ischemic stroke. A trial of serum uric acid reducing medications in stroke patients as well as those at high risk of stroke may also be worthwhile.

INTRODUCTION

Hyperuricemia refers to elevated serum uric acid concentration above the upper limit of normal. It has been recognized as an independent risk factor for stroke since 1950s [1]. It has also been demonstrated by studies to be linked with adverse clinical outcomes among stroke patients e.g., increased stroke severity and early mortality after an acute stroke [2, 3]. This increase in the risk of cerebrovascular disease is because elevated serum uric acid level causes endothelial dysfunction and thus increases oxidative stress. This in turn induces vascular smooth muscle cell proliferation and reduces endothelial nitric oxide bio availability which leads to increased

propensity for atherosclerosis [4]. It is also recognized that amyloid angiopathies raise the risk of dementia and stroke. Autosomal dominant inheritance describes the causal nature of mutations in the CST3 gene. Amyloid will be widely deposited in the brains of sufferers. The symptoms usually appear in the third or fourth decade of life, and death usually occurs before the age of 60 [5]. However, this association is currently a matter of debate because there are other studies which have suggested that this correlation of hyperuricemia with cardiovascular disease is merely because of confounding factors such as obesity, dyslipidemia, hypertension, use of diuretics and insulin

resistance [6]. Border-zone or vascular watershed infarctions happen in the furthest reaches between arterial territories. They are thought to be due to embolic phenomena or severe hypoperfusion, which can happen in conditions like carotid blockage or protracted hypotension, for example [7-10]. Therefore, further studies are needed in order to fully understand the relationship between hyperuricemia and cerebrovascular disease and to resolve this controversy. This study aims to find out the frequency of hyperuricemia in the local population of ischemic stroke patients. This study will therefore form a basis of more advanced comparative studies in the future including case-control studies and prospective cohort study.

METHODS

A Cross-sectional Study was conducted in Neurology ward of Lady Reading Hospital, Peshawar for time period of 6 months after approval of synopsis. Sample size were at least 123 based on formula. It was calculated using the World Health Organization software "Sample Size Determination in Health Studies". The formula for "Estimating a population proportion with specified absolute precision" were used based on the following assumptions: Confidence Interval Strength: 95%. Absolute Precision: 8% and Anticipated proportion of hyperuricemia in patients with acute ischemic stroke: 29% [10]. Non-probability consecutive sampling was done. Sample Selection criteria include 20 to 70 years old patients of either sex with acute ischemic stroke. The Exclusion criteria exclude the patients with ischemic stroke due to a known thrombophilic condition were excluded from the study. Patients with hyperuricemia due to high cell turnover secondary to cancer chemotherapy will also be excluded from the study. The study was conducted after getting approval from hospital ethics and research committee. The patients meeting the inclusion criteria in the neurology ward of Lady Reading Hospital, Peshawar were recruited in the study after taking written informed consent. The purpose of the study and the details of what this study entails were explained to all the recruited patients. The diagnosis of acute ischemic stroke was made by physician on acute ischemic diagnosis criteria. These patients will have their blood drawn to measure serum uric acid levels in the laboratory. They will also be asked about any history of elevated uric acid in the past. An assessment for other risk factors of cerebrovascular disease as confounders/effect modifiers will also be made by asking about known history of hypertension, measuring patient's fasting blood glucose and HbA1c, asking about known history of diabetes, asking about smoking history and measuring fasting lipid profile to look for elevated serum

cholesterol. These patients with acute ischemic stroke were managed according to the routine standard of care received by such stroke patients. Hyperuricemia is defined as a high uric acid level in the blood. Anything beyond 7 mg/dL is regarded as saturated, and symptoms may appear. The typical upper limit is 6.8 mg/dL. This elevated level is caused on by either increased uric acid production, decreased uric acid excretion, or a combination of both processes [11]. Normal value of serum uric acid ranging from 0.35 to 7.2 mg/dL. Mean serum uric acid level of patients with ischemic stroke were compared with healthy control who have no ischemic stroke. The data were analyzed using SPSS version 23.0. Descriptive statistics were used to analyze the data. Frequencies and percentages were calculated for categorical variables such as gender, presence/absence of hyperuricemia, hypertension, diabetes, hypercholesterolemia, and smoking. T test was used between hyperuricemia in patients with acute ischemic stroke and control group. Mean and standard deviation were calculated for the numerical variables for example age and serum uric acid level. Post-stratification chi squared test were applied in which a p-value of 0.05 or less were considered significant. All data were presented in the form of graphs and tables.

RESULTS

This study was conducted at Department Neurology ward of Lady Reading Hospital, Peshawar in which a total of 153 patients were observed to the frequency of hyperuricemia in patients presenting with acute ischemic stroke results were analyzed as: Age distribution among 153 patients was analyzed as 20-30 Years 14(9.2), 31-40 Years 17(11.1), 41-50 Years 32(20.9) 51-60 Years 37(24.2), 60-70 Years 53(34.6) and the Mean age was 52.45±1.142 years with standard deviation. Distribution of gender among patients was analyzed as: Male was (49) 31.7% and Female was (104)68.63% as shown in Table 1.

| Variables | Frequency (%) |
|---------------|---------------|
| Age | |
| 20-30 Years | 14 (9.2%) |
| 31-40 Years | 17 (11.1%) |
| 41-50 Years | 32 (20.9%) |
| 51-60 Years | 37 (24.2%) |
| 60-70 Years | 53 (34.6%) |
| Gender | |
| Male | 49 (31.7%) |
| Female | 104 (68.63%) |

Table 1: Age Wise Distribution of Sample Size (N=153)

The diabetes and smoking status of the study participants were shown in Table 2. Among 153 patients 58.8% were diabetes and 96(62.7%) patients were smokers.

| Variables | Frequency (%) |
|-----------------------|---------------|
| Diabetes | |
| Yes | 90 (58.8%) |
| No | 63 (41.2%) |
| Smoking Status | |
| Smoker | 96 (62.7%) |
| Non-Smoker | 57 (37.3%) |

Table 2: Distribution of Previous History of Known Diabetes and smoking status(N=153)

Distribution of hyperuricemia was 114(74.5%). About 101 (66%) patients show hypertension while 52 patients were no hypertensions history. Most of the patients 70 (45.8%) patients were more than 48 hours of disease duration as shown in Table 3.

| Variables | Frequency (%) |
|-----------------------------|---------------|
| Hyperuricemia Status | |
| Yes | 114 (74.5%) |
| No | 39 (25.5%) |
| Total | 153 (100%) |
| Hypertension | |
| Yes | 101 (66%) |
| No | 52 (34%) |
| Duration of Disease | |
| 12 - 24 Hours | 24 (15.7%) |
| 36-48 Hours | 59 (38.6%) |
| More than 48 Hours | 70 (45.8%) |

Table 3: Distribution of hyperuricemia, hypertension, and duration of disease

Most of the hyperuricemia were noted in the age group 60 (34 participants) followed by age group 51-60 (31 patients) which was statistically significant as shown in Table 4.

| Hyperuricemia | Age wise Distribution | | | | | Total |
|---------------|-----------------------|-------------|-------------|-------------|-------------|-------|
| | 20-30 Years | 31-40 Years | 41-50 Years | 51-60 Years | 60-70 Years | |
| Yes | 14 | 16 | 19 | 31 | 34 | 114 |
| No | 0 | 1 | 13 | 6 | 19 | 39 |
| Total | 14 | 17 | 32 | 37 | 53 | 153 |

Table 4: Hyperuricemia* Age Wise Distribution

Chi square test applied p-value was 0<.020

Mean serum uric acid level of patients with ischemic stroke were compared with healthy control who have no ischemic stroke for better presentation of hyperuricemia in ischemic stroke patients. The mean uric acid level was high among acute ischemic patients as compared with health control. Mean serum uric acid level among cases of acute ischemic stroke was 06.15 ± 01.91 mg/dl while the mean serum uric acid level among control group was 05.1 ± 01.4 mg/dl. The results were highly significant p-value < 0.0001 as shown in Figure 1.

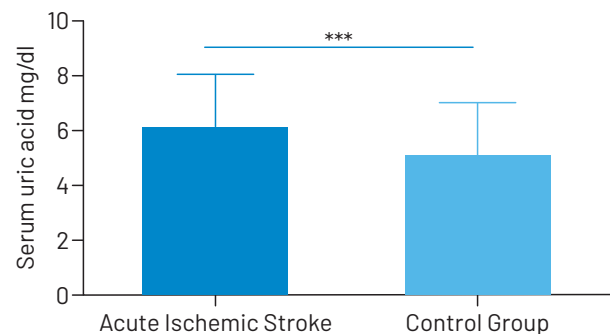


Figure 1: Mean serum uric acid level in acute ischemic stroke and healthy control

DISCUSSION

A stroke or cerebrovascular accident is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause. Stroke is an important cause of morbidity and long-term disability; up to 40% survivors are not expected to recover their independence with self-care and 25% unable to walk independently [1, 12]. Cerebral ischemia initiates a complex cascade of metabolic events, generating nitric oxide and free oxygen radicals [3]. Serum uric acid being one of the major aqueous antioxidants in human beings should have a protective role in stroke patients [13]. Therefore, the role of uric acid as a risk factor for acute ischemic stroke is controversial. Amidst this controversy and lack of Indian data, it was decided to carry out the present study with the aim of studying uric acid levels in patients of acute ischemic stroke. In our study we determined the role of serum uric acid in acute stroke patients and its prognostic significance on stroke outcome. Both the groups (cases and controls) were comparable for baseline characteristics representing the mean age, sex distribution, kidney function parameters and lipid profile. Amongst cases of acute ischemic stroke mean serum uric acid level was 6.15 ± 1.91 mg/dl and 38% (male 30%, female 50%) of them were hyperuricemia. Amongst control group mean serum uric acid level was 5.1 ± 1.4 mg/dl and 22% (male 14%, female 32%) of them had hyperuricemia. The prevalence of hyperuricemia among the patients, attending medical center in Nepal was 28.33% (male 30.06%, female 26.61%) [14]. Another large study in Bangkok population showed that prevalence of hyperuricemia is 24.4% [15, 16]. Hyperuricemia is common in China's economically developed districts. In 2009-2010, the adjusted prevalence of hyperuricemia among Chinese adults was 8.4% [17]. According to these studies prevalence of hyperuricemia is significantly higher in patients with acute stroke than normal population. Age is the most common non-modifiable risk factor for the development of stroke. In our study, 60% of the patients are between 60 to 79 years with 17 males (56%) and 13

females (65%). Mullins *et al.*, in their study of 163 patients above 70 years for association of serum uric acid and stroke found that serum uric acid is associated with an increased risk for acute ischemic/nonembolic stroke in elderly patients independently of concurrent metabolic derangements [18]. In the German dataset, a maximum male preponderance was found for patients aged between 55 and 64 years (proportion of male patients 0.67 (95% CI: 0.66–0.67), whereas patients older than 84 years revealed a strong overbalance of females (0.27 (0.26–0.28)) [19]. These results are analogous to the findings in this study with majority of patients belonging to age group between 60–79 years with male preponderance. In our study amongst cases the mean serum uric acid levels were higher among males than females, but this difference did not attain statistical significance. Smitha *et al.*, observed higher serum uric acid values in males as compared to females (5.28±0.66 versus 4.47±0.78 mg/dl) [20]. Another study found significantly higher serum uric acid level in males (6.6±7 versus 5.8±6 mg/dl, $p < 0.01$) [21]. In present study the severity of stroke was assessed by Glasgow Coma Scale (GCS). Mean serum uric acid in acute stroke patients who had severe GCS score (6.77±2.43 mg/dl) was higher than that those who had mild/moderate GCS score (5.67±1.21mg/dl) and the difference was statistically significant ($p = 0.0426$). Ahn *et al.*, 2013 found that high uric acid levels cause a modest but statistically significant increase in the risk of both stroke incidence and mortality even after adjusting for known risk factors of stroke like age, hypertension, diabetes mellitus, and cholesterol [22]. A low serum uric acid concentration is marginally associated with an excellent short-term result [23].

CONCLUSIONS

Serum uric acid can be used as a marker for increased risk of stroke. Furthermore, serum uric acid can be utilized to stratify risk following a stroke. Long-term prospective research is needed to determine the involvement of serum uric acid in ischemic stroke. Additionally, it may be worthwhile to test serum uric acid-lowering medications on stroke victims and people who are at higher risk of having a stroke.

Conflicts of Interest

The authors declare no conflict of interest.

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