



Study of Serum Uric Acid Levels in patients with Acute ischemic stroke admitted to Tertiary Care Centre Karwar, UK District

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Abstract

Background: Stroke is the second leading cause of death worldwide and was responsible for an estimated 6.5 million deaths and 113 million DALYs in 2013. Stroke. Hyperuricemia has been shown to have a positive association with CV morbidity and mortality. This study helps to find the relationship between serum uric acid and Acute ischemic stroke. **Methodology:** It was a retrospective study conducted at the tertiary hospital Karwar Institute of Medical Sciences. Data of 100 consecutive patients suffering with Acute Ischemic Stroke was collected and 100 controls data was collected matching their age, sex, comorbidities and habits. After obtaining approval from MRD, the patients details were collected from the case sheets. General health characteristics such as age, sex, smoking status, menopausal status, alcohol consumption, and dietary habits (particularly as related to preference) were collected. CT brain report and serum uric acid levels report was collected. The outcome of hospital stay in form of referral, discharge and death was noted. Data collected was analyzed statistically using descriptive statistics and also appropriate parametric or non-parametric tests were applied. **Results:** A total of 100 consecutive cases of Acute Ischemic stroke and 100 controls data was collected. Cases and control were matched for age, sex, habits and comorbidities. There were 62 male patients and 38 female patients each in both groups with male to female ratio of 1.6:1. Mean age of study population was 61.9(\pm 10) years. Out of 100 cases 33 male patients were alcoholic and 43 male patients were smokers. Among cases 69% patients had Hypertension, 38% had Diabetes and 36% patients had dyslipidemia. Mean Uric Acid level among controls was 5.45 mg/dL whereas, mean among Acute Ischemic Stroke patients was 7.17 mg/dl and the difference was statistically significant with $p < 0.0001$. Odds ratio in our study was 6.531 with 95% CI for OR inferring that any person with abnormal uric acid level has 6.531 times more chances (OR= 6.531 with $p < 0.0001$) of suffering from Acute Ischemic Stroke as compared to any person with normal uric acid level. **Conclusion:** Our study suggests that increased risk of Acute Ischemic stroke in patients with Hyperuricemia compared to patients with normal uric acid levels. There are medications available to reduce uric acid levels, which should be made use, to reduce the risk of Acute Ischemic stroke in patients with Hyperuricemia. However further studies in larger population and study using

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urate lowering agents need to be performed to establish the role of urate lowering agents in reducing risk of stroke.

Keywords: Hyperuricemia, Acute Ischemic Stroke, Serum Uric acid.

Introduction: Stroke is the second leading cause of death worldwide and was responsible for an estimated 6.5 million deaths and 113 million DALYs in 2013. Stroke, a major Non Communicable Disease (NCD), is responsible for 3.5% of disability adjusted life year (DALY) in India. In India, studies estimate that incidence of stroke population varies from 116 to 163 per 100,000 population. Recently, ICMR has come out with a report entitled “India: Health of the Nation’s States”, according to which stroke was 4th leading cause of death and 5 Years (DALY) in 2016.[1]

Apart from risk factors like hypertension, diabetes, heart diseases and positive family history, other lifestyle related factors such as unhealthy diet, obesity, lack of physical activity, stress and tobacco use account for its occurrence. Changes in lifestyles, behavioural patterns, demographic profile (aging population), sociocultural and technological advancements are leading to sharp increases in the prevalence of stroke. The disease by and large can be prevented by making simple changes in the way people live their lives or simply by changing our lifestyle.

A stroke is caused by loss of the blood supply to the brain. This cuts off the oxygen and glucose causing irreversible damage to the tissues of brain parenchyma. WHO clinically defines stroke as “the rapid development of clinical signs and symptoms of a focal neurological disturbance lasting more than 24 hours or leading to death with no apparent cause other than vascular origin”. [2]

Hyperuricemia refers to the elevation of uric acid in the plasma. It has no widely accepted single cut-off value, however, values above 6.8mg/dL are generally considered elevated in adults [3]. Hyperuricemia has been shown to have a positive association with CV morbidity and mortality [4,5]. The association between hyperuricemia and Acute ischemic stroke remains controversial despite two recent meta-analytical reviews of prospective studies demonstrating a significant relationship [6,7]. The main reason underlying the endothelial dysfunction is proposed to be oxidative stress secondary to reduced nitric oxide bioavailability following SUA entry into endothelial cells. The uric acid subsequently initiates multiple proinflammatory reactions that result in the release of ROS and potentiate the atherosclerotic process. This will increase risk of ischemic stroke in patients. This study helps to find the relationship between serum uric acid and Acute ischemic stroke. [8,9,10]

Objectives

1. To estimate the serum uric acid levels in patients with Acute ischemic stroke .
2. To find the relationship between the serum uric acid levels and Acute ischemic stroke

Methodology

It was a retrospective study conducted at the tertiary hospital Karwar Institute of Medical Sciences. Data of 100 consecutive patients suffering with Acute Ischemic Stroke was collected and 100 controls data was collected matching their age, sex, comorbidities and habits. Patients with conditions which affect the serum uric acid like CKD and other Kidney problems, Leukemia, Metabolic syndrome, Polycythemia vera Psoriasis, patients on diuretics ,and patients on chemotherapy/ Radiotherapy were excluded from study. After obtaining approval from MRD, the patients details were collected from the case sheets. General health characteristics such as age, sex, smoking status, menopausal status, alcohol consumption, and dietary habits (particularly as related to preference) were collected. CT brain report and

serum uric acid levels report was collected. All the data collected was compiled and tabulated using MS-Excel. Statistical analyses were carried out using SPSS 16.0. Results are expressed as means with SD and t-test is used to compare continuous variables and chi-square test was used to find the association between the discrete variables. Binary logistic regression analysis was used to carry out univariate and multivariate analyses to find the associated risk factors and the p value <0.05 was considered to be significant.

Results

A total of 100 consecutive cases of Acute Ischemic stroke and 100 controls data was collected. Cases and control were matched for age, sex, habits and comorbidities. There were 62 male patients and 38 female patients each in both groups with male to female ratio of 1.6:1. Mean age of study population was 61.9(±10) years.

Out of 100 cases 33 male patients were alcoholic and 43 male patients were smokers. Among cases 69% patients had Hypertension, 38% had Diabetes and 36% patients had dyslipidemia.

Table1: Baseline variables among case group.

Variables	Males	Females	Total
Hypertension	46	23	69%
Diabetes	23	15	38%
Dyslipidemia	16	20	36%
Alcoholic	33	0	33%
Smoker	43	0	43%

Uric acid levels of >7 mg/dl and >6 mg/dl in males and females respectively was taken as hyperuricemia. [11] Mean Uric Acid level among controls was 5.45 mg/dL whereas, mean among Acute Ischemic Stroke patients was 7.17 mg/dl and the difference was statistically significant with p < 0.0001. 61.3% of male patients and 55.3% of females among case group had Hyperuricemia. Among females, 21(55.26%) in case group and 14(36.84%) in control group had hyperuricemia whereas among males, 38(61.29%) in case group and 10(16.13%) in control group had hyperuricemia. 59% of cases and 24% of controls had hyperuricemia.

Table 2: Distribution of Uric acid levels among cases and controls

Group		N	Mean	SD	SE	't' value	p-value
Uric acid levels	Cases	100	5.45	1.65	0.17	6.22	<0.0001
	Controls	100	7.17	2.22	0.22		

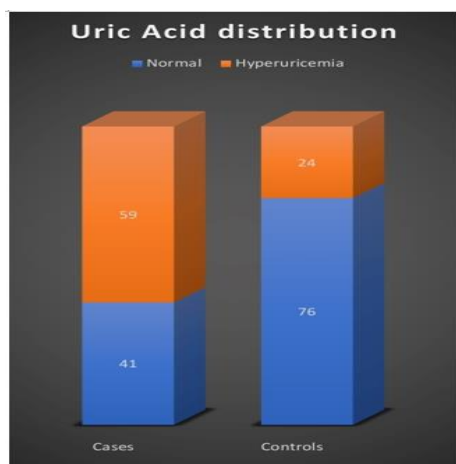


Figure 1: Distribution of Hyperuricemia among case group and control group

Odds ratio in our study was 6.531 with 95% CI for OR inferring that any person with abnormal uric acid level has 6.531 times more chances (OR= 6.531 with $p < 0.0001$) of suffering from Acute Ischemic Stroke as compared to any person with normal uric acid level.

Discussion

Stroke is the second leading cause of death globally and in India. There are several risk factors for development of Stroke. In this study we are studying uric acid as a risk factor in development of Acute Ischemic stroke. This was a retrospective case-control study done at tertiary care hospital at Karwar. Study consisted of 100 consecutive cases of Acute Ischemic stroke and 100 controls admitted from January 2022 to January 2023. Among 100 cases 62% were males and 38% were females with male to female ratio of 1:1.6. Out of 100 cases 33 male patients were alcoholic and 43 male patients were smokers. Among cases 69% patients had Hypertension, 38% had Diabetes and 36% patients had dyslipidemia.

Uric acid levels of >7 mg/dl and >6 mg/dl in males and females respectively was taken as hyperuricemia.[11] Mean Uric Acid level among controls was 5.45 mg/dL whereas, mean among Acute Ischemic Stroke patients was 7.17 mg/dl and the difference was statistically significant with $p < 0.0001$. Among females, 21(55.26%) in case group and 14(36.84%) in control group had hyperuricemia whereas among males, 38(61.29%) in case group and 10(16.13%) in control group had hyperuricemia. So, in terms of gender distribution, uric acid levels were significantly higher in men than in women. 59% of cases and 24% of controls had hyperuricemia. This study shows that the prevalence of hyperuricemia in patients with acute ischemic stroke was significantly higher as compared to the healthy population.

The exact mechanism of development of stroke due to Hyperuricemia is not completely understood. Increased serum uric acid may cause endothelial damage. The main reason underlying the endothelial dysfunction is proposed to be oxidative stress secondary to reduced nitric oxide bioavailability [8] following SUA entry into endothelial cells. The uric acid subsequently initiates multiple proinflammatory reactions that result in the release of ROS and potentiate the atherosclerotic process [9,10]. Odds ratio in our study was 6.531 with 95% CI for OR inferring that any person with abnormal uric acid level has 6.531 times more chances (OR= 6.531 with $p < 0.0001$) of suffering from Acute Ischemic Stroke as compared to any person with normal uric acid level. This implies that Hyperuricemia is one of the important risk factors in development of Acute Ischemic stroke. There are several other studies which have shown Hyperuricemia is risk factor in development of Acute Ischemic stroke. Bansal et al. studied 50 patients with ischemic thrombotic cerebrovascular disease. Hyperuricemia was found in 30% of the cases, and they concluded that elevated serum uric acid level might play a role in the causation of ischemic thrombotic cerebrovascular disease in general, and especially in patients younger than 40 years [12]. Kim et al. conducted a systematic review and meta-analysis of 16 prospective cohort studies, including 238,449 adults, to assess the association between hyperuricemia and risk of stroke incidence and mortality [13]. They found that hyperuricemia may modestly but significantly increase the risk of both stroke incidence and mortality. According to the results of Milionis et al., elevated serum uric acid levels were associated with an increased risk of acute ischemic stroke in the elderly [14].

Furthermore there are studies conducted to see the effects of urate lowering agents in patients with Hyperuricemia and reduction in risk of Stroke. A study conducted in Denmark on a cohort followed over 18 years, aimed to investigate CV outcomes while taking allopurinol in hyperuricemic patients. The study consisted of 65,971 hyperuricemic patients (urate level >6.0 mg/dL) of which 7,127 patients were already being treated with allopurinol. The

researchers concluded that allopurinol use was associated with decreased risk of major CV events which included stroke [15]. A study was conducted by Taheraghdam et al. included 70 patients with both AIS and Hyperuricemia levels who were divided into treatment and placebo groups. They concluded that the administration of allopurinol in these patients might increase their functional status without decreasing the mortality rate and that it may be beneficial to administer allopurinol at the time of acute events [16]. Study conducted by Singh and Yu found a decrease in the risk of ischemic stroke by 9% with allopurinol use and an even greater decrease (12%-21%) with a longer duration of use.[17]

Conclusion

Our study suggests that increased risk of Acute Ischemic stroke in patients with Hyperuricemia compared to patients with normal uric acid levels. There are medications available to reduce uric acid levels, which should be made use, to reduce the risk of Acute Ischemic stroke in patients with Hyperuricemia. However further studies in larger population and study using urate lowering agents need to be performed to establish the role of urate lowering agents in reducing risk of stroke.

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