A Study of Association between Serum Uric Acid Levels with Various Risk Factors in Hemorrhagic Stroke

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Abstract
Background- *The mortality rate of stroke in the acute phase is as high as 20% and it remains higher for several years after the acute event in stroke patients than in the general population. Stroke is also an important cause of morbidity and long term disability: up to 40% of survivors are not expected to recover their independence with self-care and 25% become unable to walk independently.*
Methods- *This study is conducted among 50 patients of acute stroke with CT scan evidence of hemorrhage (ICH and SAH) and CT scan showing no evidence of ischemia. A total of 50 subjects age and sex matched controls (who do not have acute stroke) were also selected*
Results- *The mean value of SUA in dyslipidemia subjects was 6.024 ± 1.310mg/dl whereas in non dyslipidemia subjects was 6.021 ± 1.158mg/dl. No significant association was observed among the presence and absence of dyslipidemia with Serum Uric Acid level in cases*
Conclusion- *Serum uric acid level has significant association with smoking, significant positive correlation with total cholesterol and significant inversely correlated with HDL cholesterol. S. uric acid level increases with age, in males, hypertension, diabetes, dyslipidemia, positive family history and positive previous history of stroke but not statically significant.*
Keywords- *Stroke, Uric acid, Dyslipidemia.*

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I. Introduction

Cerebrovascular diseases include some of the most common and devastating disorders[1]. Stroke is the main cause of disability and mortality among the ageing population, and about 87% of all cases are ischemic stroke while 15% are hemorrhagic stroke[2,3].

The mortality rate of stroke in the acute phase is as high as 20% and it remains higher for several years after the acute event in stroke patients than in the general population. Stroke is also an important cause of morbidity and long term disability: up to 40% of survivors are not expected to recover their independence with self-care and 25% become unable to walk independently[4].

Although stroke can occur to anyone at any time, regardless of age, sex, or race but the incidence of cerebrovascular diseases increases with age, and the number of strokes is projected to increase as the elderly population grows. Stroke is the second cause of disability and dementia in adults aged $\geq$ 65 years worldwide, about 25% of stroke survivors develop dementia[5]. Due to high socio economic burden put on community by stroke. Early identification of individuals at risk could be of help in primary prevention strategies[6].

Numerous risk factors are involved in the development of stroke such as hypertension, cigarette smoking, hyperlipidemia and diabetes. Recent studies indicate that there may be other factors influencing the development or course of disease like serum levels of uric acid.

II. Materials And Methods

Study protocol:
1.   50 patients of hemorrhagic stroke and 50 age and sex matched controls.
2.   Blood samples will be taken from each of the study groups and serum uric acid level will be assessed and compared between case and control group.
3.   Serum uric acid levels will be compared with various risk factors like age, sex, hypertension, diabetes mellitus, smoking, family h/o stroke, and h/o previous stroke in hemorrhagic stroke patients.
STUDY POPULATION :   This study is conducted among 50 patients of acute stroke with CT scan evidence of hemorrhage (ICH and SAH) and CT scan showing no evidence of ischemia. A total of 50 subjects age and sex matched controls (who do not have acute stroke) were also selected

DESIGN OF STUDY: single center (hospital based) observational case control study

INCLUSION CRITERIA :
1.   Patients presented within 48 hours of onset of stroke with CT-scan evidence of hemorrhage (intra cerebral hemorrhage and subarachnoid hemorrhage) and without ischemia admitted in J.L.N. Hospital, Ajmer were selected.
2.   Both sex (male and female) greater than 18 years of age, who has given informed consent to participate in the study.

EXCLUSION CRITERIA
1.   Patients who NCCT-scan show ischemic-infarct or other space occupying lesions other then hemorrhage.
2.   Patients with history of TIA.
3.   Patients with EDH/SDH/ RTA.
4.   Patients who were known cases of gout or show clinical evidences of gout.
5.   Patients who were alcoholics.
6.   Patients taking drugs causing hyperuricemia (Eg. loop diuretics/thiazides/anti cancer drug eg. cisplatin, cyclophosphamide, cyclosporine, ATT eg. pyazinamide and ethambutol, l-dopa, isotretinoin and clofibrate, aspirin, pentamidine, theophylline, ketaconazole)
7.   Patients with previous history of coronary vascular event and known cardiac disease
8.   Patient with Chronic renal failure (CRF).
9.   Patients with known hematological malignancy (leukemia or lymphoma) or myeloproliferative disorder (eg polycythemia).

Statistical analysis:
        Statistical analysis was performed with the help of Quick graph pad scientific software. Qualitative data (Categorical data) was presented as number of subjects (proportions) and to assess any significant association difference by Chi Square($\chi 2$) test .Quantitative data was expressed as mean and SD. Relationship between variables in the patient group was assessed by Pearson's correlation co-efficient. P-value less than 0.05 was considered statistically Significant.
        A total of 50 patients (25 male and 25 female) admitted due to hemorrhagic   stroke and 50 age sex matched control (25 male and 25 female) were included. The association between SUA level and various risk factor of hemorrhagic stroke was observe.

III. Results
Table – 1. Correlation between the Age and Serum Uric Acid

	Mean	Std. Deviation	N	r
Age	60.09	14.87	100	
Serum Uric Acid	5.567	1.326	100	0.437

A Positive correlation Existed between the Age and SUA level (r=0.437) by using karl's pearson's correlation co-efficient but it is not significant (P>0.05).

Table 2. Association of SUA level with Sex

	Serum Uric Acid level		
	≤ 6.8 mg/dl	>6.8 mg/dl	
Male	40	10	50
Female	42	8	50
Total	82	18	100

Chi. Square= 0.271 with 1 degree of freedom   P= 0.60266 (NS)
➤   Mean Serum Uric Acid level in male 5.602 ± 1.361mg/dl.
➤   Mean Serum Uric Acid level in female 5.532 ± 1.302 mg/dl.
➤   Higher level of Serum Uric Acid level in male is not statistically significant.

Table 3. Correlation between SUA and lipid profile

		Tc	Tg	HDL	LDC
Uric Acid	N	100	100	100	100
	r	0.199	0.167	-0.243	0.142
	P value	< 0.05 (S)	>0.05 (NS)	<0.05 (S)	>0.05 (NS)

➤ Inverse correlation between SUA level and HDL- Cholesterol. It is statistically significant [r = -0.243 and p value < 0.05]

➤ A. positive correlation between SUA level and total Cholesterol, serum triglycerides and LDC-Cholesterol but only significant with total cholesterol (P< 0.05).

Table 4. Association of SUA with Hypertension in cases

Hypertension	Serum Uric Acid level (mg/dl)		Total
	≤6.8 mg/dl	>6.8 mg/dl	
Present	27	12	39
Absent	9	2	11
Total	36	14	50

Chi. Square= 0.06743 with 1 degree of freedom;   p=0.411(NS)

➤ The mean value of SUA in Hypertension subjects was 6.085 ± 1.86 mg/dl whereas in non-hypertension subject was 5.800 ± 1.275 mg/dl.

➤ No significant association was observed among the presence and absence of hypertension with Serum Uric Acid level in cases.

Table 5. Association of SUA level with Diabetes mellitus in cases

Diabetes mellitus	Serum Uric Acid level (mg/dl)		Total
	≤6.8 mg/dl	>6.8 mg/dl	
Present	11	8	19
Absent	25	6	31
Total	36	14	50

Chi square= 3.0244 with one degrees of freedom   P= 0.0820 (NS)

➤ The mean value of SUA in diabetes mellitus subjects was 6.163 ± 1.325 mg/dl whereas in non Diabetics subjects was 5.935 ±1.128 mg/dl.

➤ No significant association was observed among presence and absence of diabetes mellitus and Serum Uric Acid level in cases.

Table 6. Association of SUA level with Dyslipidemia in cases

Dyslipidemia	Serum Uric Acid level(mg/dl)		Total
	≤6.8 mg/dl	>6.8 mg/dl	
Present	11	6	17
Absent	25	8	33
Total	36	14	50

Chi. Square =0.6798 with one degree of freedom,   p= 0.4096 (NS)

➤ The mean value of SUA in DYSL ipidemia subjects was 6.024 ± 1.310mg/dl whereas in non DYSL ipidemia subjects was 6.021 ± 1.158mg/dl

➤ No significant association was observed among the presence and absence of DYSL ipidemia with Serum Uric Acid level in cases.

Table 7. Association of Serum Uric Acid level with smoking in cases

History of smoking	Serum Uric Acid level (mg/dl)		Total
	≤6.8 mg/dl	>6.8 mg/dl	
Yes	11	9	20
No	25	5	30
Total	36	14	50

Chi. Square = 4.7784 with one degree of freedom   p=   0.028818 (S)

➤ The mean value of SUA in smokers was 6.365 ± 1.207mg/dl whereas in non smokers was 5.793 ± 1.157mg/dl.

➤ Thus statistically significant association between smoking and serum uric acid level in cases[p<0.05]

IV. Discussion

Stroke can occur to any one at any time, regardless of age, sex or race. It is a major cause of mortality and morbidity in among worldwide. The well recognized risk factors like age, sex, hypertension, diabetes, dyslipidemia, smoking, family history of stroke and previous history of stroke explain only a part of the cases. Hence a search for other risk factors is the need of the hour.

In our study there was a positive correlation between the age of patients and their serum uric acid levels but this correlation was not statistically significant (r=1.4374,p>0.05) . This result in contrast to the study by Conen et al[7] there was a weak but significant positive association between age of patients and their serum uric acid levels. Kotwal et al[8] observed was negative correlation between the age of patients and serum uric acid level (r=-0.19, p=0.18).

In our study, the mean SUA level in diabetics was 6.16±1.3mg/dl and in non diabetics was 5.93±1.12mg / dl .thus does not show any statistically significant association between SUA and diabetes in hemorrhagic stroke patients (p =0.0820).

Mehrpour et al[9] observed no significant association between serum uric acid level and diabetes mellitus, hypertension and smoking. In contrast some previous studies(Chammaro et al[10] and Bonora et al[11]) reported significant association between insulin resistant, systolic and diastolic blood pressure and serum uric acid levels And also Ramesh K et al[12] Elevated SUA is significantly associated with hypertension, diabetes mellitus, smoking, obesity and metabolic syndrome.

In Our study, the mean serum uric acid level in Dyslipidemic patients is 6.024±1.31 mg / dl and in patients without Dysrlipidemia is 6.021 ±1.15mg / dl and does not show any significant association between these variables(p=0.4096)

In our study a significant inverse correlation was found between SUA levels and HDL– cholesterol (r=-0.24 and P< 0.05) and positive correlation between SUA levels and levels of serum triglyceride and LDL – cholesterol but not significant (r = 0.167, P > 0.05 for triglycerides and r= 0.142, P > 0.05 for LDL cholesterol.) and a significant positive correlation between SUA levels and total cholesterol. (r = 0.19, P< 0.05). This was done by using Pearson's correlation. Bonora et al[13] studied 957 young men and demonstrated that there was a significant positive correlation between serum uric acid levels and levels of serum triglyceride, total cholesterol and LDL cholesterol. Another study Conen et al[7] including healthy people in developing countries showed a closely association between serum uric acid level and amount of serum triglyceride[12].

In our study the mean value of SUA level with positive family history stroke of cases was 6.10 ± 1.34 mg/dl whereas with negative family history in cases was 5.99 ± 1.16. Thus no statistically significant association was observed among the presence and absence of family history of stroke and serum uric acid level (P=0.32877).

In our study the mean value of serum uric acid in cases with history of previous stroke was 6.35 ± 1.023mg/dl whereas in cases with no history of previous stroke was 5.88 ± 1.25mg/dl. Thus no statistically significant association was observed among the presence and absence of previous history of stroke and serum uric acid level. (P=0.2160).

In our study, the mean serum uric acid (SUA) level in cases was 6.02±1.19mg/dl whereas it was 5.66+1.38 mg/dl for controls. This shows that the mean serum uric acid level was significantly higher in cases as compared to controls (p=0.0092).thus hemorrhagic stroke patients had a significantly higher SUA levels compared to the controls. Ramesh K et al[12], Observed that stroke patients had a significantly higher SUA levels when compared to the controls (6.74 ± 2.10 mg/dl and 5.66 +1.38 mg/dl, p<0.005). Milionis et al[14], in his study, relationship between uric acid and stroke showed that SUA is an independent risk factor for the occurrence of stroke and observed that the SUA levels were significantly higher in stroke patients compared with controls(5.6 ±1.7 mg/dl vs. 4.8 ± 1.47 mg/dl, p<0.001). Srikrishna R and Suresh DR[15] found that serum uric acid levels were significantly higher in cases as compared to controls (6.56 ±0.73 vs. 4.66 ± 0.47,p<0.05). In the Rotterdam study (Bos et al)[16] High serum uric acid levels were associated with the risk of stroke; age- and sex adjusted hazard ratios for the highest versus the lowest quintile of uric acid were 1.57 (95% C.I. = 1.11 to 2.22)for all strokes, 1.77 (95% C.I. = 1.10 to 2.83) for ischemic strokes, and 1.68 (95% C.I. = 0.68 to 4.15) for hemorrhagic strokes. Thus the uric acid is an independent risk factor for stroke.

V. Conclusion

Serum uric acid level has significant association with smoking, significant positive correlation with total cholesterol and significant inversely correlated with HDL cholesterol. S. uric acid level increases with age, in males, hypertension, diabetes, dyslipidemia, positive family history and positive previous history of stroke but not statically significant. So higher Serum uric acid level can be considered as a contributor to hemorrhagic stroke but more large scale scientific and clinical research is needed before the role of uric acid as a risk factor in hemorrhagic stroke can be established. We also propose large scale prospective study in future to establish serum uric acid as an independent predictor for increased risk of hemorrhagic stroke in normal population.

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