A STUDY ON THE ROLE OF SERUM CALCIUM ALBUMIN AND URIC ACID AS PREDICTOR OF NEUROLOGICAL SEVERITY AND SHORT-TERM OUTCOME IN ACUTE ISCHAEMIC STROKE

Siva Subramanyam S[1], Ramesh Basavaiah[2]

[1]Junior Resident, Department of General Medicine, ESIC Medical College and PGIMSR, Bangalore.
[2]Professor, Department of General Medicine, ESIC Medical College and PGIMSR, Bangalore.

ABSTRACT

BACKGROUND

Stroke is the leading cause of disability worldwide, the second most common cause of dementia and the third leading cause of death. It is unclear whether serum uric acid promotes or protects against the cerebrovascular disease. Hence, a search for other risk factors is the need of the hour.

The aim of the study is to study the role of serum uric acid, serum calcium and serum albumin in acute ischaemic stroke and its effect on stroke outcome.

MATERIALS AND METHODS

A cross-sectional study was carried out in ESIC Medical College and PGIMSR, Rajajinagar, Bengaluru, over a period of 18 months in 100 cases of who met the inclusion criteria were studied. Patients presenting within 72 hours of onset and aged ≥40 years were included in this study. Apart from routine investigations, serum albumin, calcium and uric acid levels were done in all patients.

RESULTS

Out of 100 patients, 63% were males and 37% were females. Ratio was 1.7:1. Majority of stroke population are between 50 to 69 years. Hypertension constitutes the major risk factor in this population as 79% of population is hypertensive. Serum calcium, albumin and uric acid values had a highly significant correlation with neurological severity by NIHSS scores ($p<0.001$) and with the short-term outcome by Barthel index ($p<0.001$).

CONCLUSION

Serum albumin, serum calcium and serum uric acid values can predict initial neurologic severity and short-term outcome in AIS.

KEYWORDS

Calcium, Albumin, Uric Acid, Acute Ischaemic Stroke, NIHSS Score, Barthel Index, Prognosis.

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BACKGROUND

A stroke is defined by the World Health Organization (WHO) as a syndrome of "rapidly developing clinical signs of focal (or global) disturbance of cerebral function with symptoms lasting 24 hours or longer or leading to death with no apparent cause other than of vascular origin."[1] In 1930, increased blood pressure was described as being connected to apoplexia and cerebral haemorrhage by Swartz and Goldinger.[2] It causes significant physical, emotional and cognitive disabilities among survivors, placing stroke within the 10 leading causes of disability irrespective of the development status of countries.[3] Some of the recent studies have elucidated the stroke pattern to considerable extent in our country with a prevalence rate of 471.58/1,00,000 population.[4] Recent study identified that 7% of medical and 45% of neurological admissions were due to stroke with a fatality rate of 9% at hospital discharge and 20% at 28 days.[5] In a recent study conducted in India, Latin-America and China, chronic diseases as a whole (stroke, heart disease, diabetes, chronic respiratory disease and malignancy) accounted for the majority of death among the elderly.[6] Ischaemic strokes account for >80% of total stroke events.[7] Early identification of individuals at risk could be of help in primary prevention strategies.[8] Serum CA levels may reflect the severity of ischaemic injury and maybe a potential therapeutic target for improving stroke outcome.[9] There is a rising interest in the correlation of albumin levels with clinical severity of acute stroke as there underlies an opportunity for a medical intervention.[10] Thrombotic stroke and myocardial infarction are similar in many risk factors and pathophysiology have resulted in considerable attention paid recently.

Aims and Objectives- To study neurologic severity and short-term outcome in patients of Acute Ischaemic Stroke

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Corresponding Author:
Dr. Ramesh Basavaiah,
Professor, Department of General Medicine,
ESIC Medical College and PGIMSR, Bangalore.
E-mail: drrameshsarganur@gmail.com
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(AIS) and its correlation with serum calcium at admission and the correlation of serum albumin on admission with initial neurologic severity and short-term outcome in patients with acute ischaemic stroke. The clinical relevance regarding severity and short-term outcome of acute ischaemic stroke by serum uric acid levels at admission. Neurologic severity assessed by NIHSS score (National Institute of Health Stroke Scale) at admission and short-term outcome by Barthel index at 7 days.

MATERIALS AND METHODS

The proposed study was conducted in the Department of General Medicine, ESIC MC and PGIMSR and MH, Rajajinagar, Bengaluru - 560010, during a period of one year from November 2014 to May 2016.

Source of the Data- The study was conducted on admitted patients with first attack of acute ischaemic stroke to Medicine Ward in the ESIC Medical College and PGIMSR and Model Hospital, Rajajinagar, Bengaluru.

Method of Collection of Data- Patients satisfying inclusion criteria are enrolled within 24 hours of admission after informed consent.
Sample Size- 100 cases satisfying inclusion criteria will be included.
Study Period- November 2014 to May 2016.
Study Design- Longitudinal study.

Inclusion Criteria

1. Patients aged ≥40 years irrespective of gender.
2. Diagnosed as having acute ischaemic cerebrovascular stroke within previous 72 hours by clinical examination and confirmed by either a CT scan or by a MRI scan were included.

Exclusion Criteria

1. Age <40 years.
2. Presenting with haemorrhagic stroke/subarachnoid haemorrhage/cerebral venous sinus thrombosis.
3. Presenting with ischaemic stroke after 72 hours of onset were excluded from study.
4. Patients with previous history of Transient Ischaemic Attack (TIA)/Cerebrovascular Accident (CVA).
5. Patients who are on thiazide diuretics/known cases of gout or show clinical evidences of gout/Chronic Kidney Disease (CKD).
6. Patients who were of known cardiac diseases, which could be sources of emboli or whose echocardiogram shown sources of emboli.
7. Patients with haematological abnormalities (leukaemia, other myeloproliferative disorders).

Study Protocol- Clinical history was taken from either the patient or his/her relatives or attendant. While taking history, importance was given regarding presence or absence of vomiting, headache and convulsions. Past history of HTN, DM, CAD, RHD, TIA, collagen diseases, meningitis, tuberculosis, endocrine disorders and congenital disorders were taken. Personal history regarding dietary habits, smoking, alcohol consumption and tobacco chewing were noted. NIH stroke scale was used in all patients to assess the neurological disability and Barthel index used to assess prognosis at discharge. Detailed neurological examination was done based on proforma. All other systems like cardiovascular system, gastrointestinal system and respiratory system were examined in detail. Serum calcium, serum albumin and serum uric acid is done for all patients at the time of admission. Detailed investigations including blood haemoglobin, TLC, DC, LFT, RFT, urinalysis, FBS, lipid profile, ECG, chest x-ray, 2D-echo and neck vessel Doppler were done. In all cases, plain CT brain was done. MRI brain done whenever required.

RESULTS

The proposed study was conducted in the Department of General Medicine, ESIC MC and PGIMSR and MH, Rajajinagar, Bengaluru - 560010 during a period of one year from November 2014 to May 2016.

Age Group	Male		Female		Total	
	No	%	No	%	No	%
40-49	4	6%	0	0%	4	4%
50-59	25	40%	20	54%	45	45%
60-69	24	38%	14	38%	38	38%
70-79	9	14%	3	8%	12	12%
80 and above	1	2%	0	0%	1	1%
Total	**63**	**100%**	**37**	**100%**	**100**	**100%**

Table 1. Age and Sex Distribution in Study Population

- In our study, out of 100 patients, 63% were males and 37% were females.
- Thus, the ratio of males to females was 1.7:1.
- Maximum patients were in 50-59 years' age group.
- Acute ischaemic stroke is more common between 5th and 6th decade of life.

Overall Distribution	Number of Patients	Percentage of Patients
Female	37	37%
Male	63	63%

Table 2. Sex Distribution

- Our study shows a greater preponderance among men with male-to-female ratio of 1.7:1.
- Males are more likely to have a stroke than women.
- Mean weight and BMI was found to be 70.4 and 25.9, respectively.
- Mean uric acid in the study- 6.3 ± 1.6.
- Mean albumin in the study- 3.6 ± 0.7.
- Mean calcium in the study- 8.5 ± 0.7.
- Mean albumin corrected calcium- 8.8 ± 0.4.

Summary	Number	Min.	Max.	Mean	SD	Variance
SBP	100	128.0	180.0	151.3	9.9	98.3
DBP	100	68.0	110.0	90.2	9.0	80.6
HTN	100	146.0	185.0	164.9	6.3	39.7
Weight	100	54.0	112.0	70.4	9.0	81.6
BMI	100	20.1	35.0	25.9	3.2	10.0
NIHSS	100	4.0	16.0	10.4	3.6	12.9
Barthel index	100	40.0	80.0	57.4	10.3	105.8
S. uric acid	100	3.0	8.8	6.3	1.6	2.5
S. albumin	100	2.8	5.1	3.6	0.7	0.4
S. calcium	100	7.1	10.2	8.5	0.7	0.5
Alb. corr. calcium	100	7.8	10.4	8.8	0.4	0.2
FBS	100	64.0	269.0	112.8	50.0	2498.9
PPBS	100	105.0	408.0	172.7	72.8	5297.3
HbA1c	100	3.1	8.6	5.8	0.9	0.8
Tc	100	112.0	224.0	158.4	22.3	497.7
Tg	100	105.0	284.0	167.4	36.5	1328.9
HDL	100	21.0	67.0	42.6	10.3	106.8
LDL	100	32.0	158.0	82.4	24.0	577.1
VLDL	100	21.0	56.8	33.5	7.3	53.2

Table 3. Summary

Correlation Result	SUA	Albumin	Calcium	Albumin	Corrected Calcium
NIHSS admission	Pearson correlation	0.812	-0.858	-0.830	-0.302
	P-value	0.00	0.000	0.000	0.002
	N	100	100	100	100
Barthel index	Pearson correlation	-0.741	0.710	0.707	0.282
After 1 week	P-value	0.000	0.000	0.000	0.004
	N	100	100	100	100

Table 4. Correlation Analysis Result

Pair	r Value	p Value
NIHSS score on admn. vs. serum uric acid	0.812	<0.001**
NIHSS score on admn. vs. serum albumin	-0.858	<0.001**
NIHSS score on admn. vs. serum calcium	-0.830	<0.001**
NIHSS score on admn. vs. albumin corrected calcium	-0.302	0.002**
NIHSS score on admn. vs. Barthel index score after 1 week	-0.852	<0.001**

Table 5. NIHSS Score

Pair	r value	p value
Barthel index score after 1 week vs. serum uric acid	-0.741	<0.001**
Barthel index score after 1 week vs. serum albumin	0.710	<0.001**
Barthel index score after 1 week vs. serum calcium	0.707	<0.001**
Barthel index score after 1 week vs. albumin corrected CA	0.288	0.004**
Barthel index score after 1 week vs. NIHSS Score on admn.	-0.852	<0.001**

Table 6. Barthel Index Score

DISCUSSION

Stroke is the leading cause of disability worldwide. The second most common cause of dementia and the third leading cause of death.[11]

The mean age of the cases was 61.31 ± 7.15 years with the range of 48 to 80 years. The male-to-female ratio was 1.7:1. Mumbai[12] and Trivandrum[13] registries showed that the mean age of patients with stroke was 66 and 67 years, respectively. In contrast, in the Bangalore study, the mean age was 54.5 years.[14] Our findings are consistent with the data published by Pandiyan et al[15] who observed a male:female ratio of 1.9:1 an mean age of stroke patients as 61.7 ± 13.4 years. Pearce et al[16] observed higher serum uric acid values in males as compared to females (5.28 ± 0.66 vs. 4.47 ± 0.78 mg/dL). Longo-Mbenza et al[17] found significantly higher SUA level in males (6.6 ± 7 vs. 5.8 ± 6 mg/dL, P <0.01). Similar results were obtained in the study by Milionis et al[18] and in the Rotterdam study.[19] Framingham heart study[20] also showed higher SUA levels in males. Patil TB et al[21] studied 100 cases of acute ischaemic stroke with 100 controls. They found there was a significant positive correlation between SUA and NIH stroke scale score on admission as well as at the time of discharge (P <0.05 for both). Chiquete E1, Ruiz-Sandoval JL et al[22] studied 463 patients (52% men, mean age 68 years) with AIS pertaining to the multicenter registry premier and found SUA ≤4.5 mg/dL was positively associated with short-term outcome and concluded that low SUA concentration is modestly associated with a very good short-term outcome. A retrospective study[23] by Kapildev Mondal, Soumabrota

Dutta, Santanu in Kolkata included 100 patients of acute ischaemic stroke observed hyperuricaemia in 40% of acute ischaemic stroke patients. Karagiannis et al[24] found an independent relationship between higher SUA levels on admission and death (OR = 1.37; 95%, C.I. = 1.13-1.67, P = 0.001). Mozos et al[25] also found that the patients who died had a significantly higher SUA values as compared to those who were discharged home (9.5 ± 3 mg/dL vs. 6.9 ± 4 mg/dL, P = 0.003).

Weir et al[26] noted that higher serum urate value was significantly associated with bad outcome (OR = 0.78 per additional 0.1 mmol/L; 95%, C.I. = 0.67-0.91). Srikrishna R and Suresh DR[27] 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). Milionis et al[18] observed that the SUA levels were significantly higher in stroke patients compared with controls (5.6 ± 1.7 mg/dL vs. 4.8 ± 1.4 mg/dL, P <0.001). In the Rotterdam study,[19] high serum uric acid levels were associated with the risk of stroke. In our study of 100 AIS patients, mean uric acid levels in males was 6.31 ± 1.57 mg/dL and 6.28 ± 1.60 mg/dL in females. We found a significant positive correlation between SUA and NIHSS at admission and with Barthel index at 7 days (P value <0.001 for both). Out of 100 cases, 56 cases admitted with NIHSS >10. Mean SUA in this group was 7.51 ± 0.44 mg/dL with p value of 0.00. A study by Idicula et al[28] included 444 patients with ischaemic stroke. Outcome was prognosticated by NIHSS and mRS. They showed high serum albumin was independently associated with a better outcome (OR=1.12; 95%, CI=1.05-1.20, p=0.001) and lower mortality (OR=0.88; 95%, CI=0.830.93, p<0.0001) concluded that high serum albumin maybe neuroprotective in ischaemic stroke in humans. Sharma et al[29] (Delhi) studied the correlation of serum albumin with initial neurologic severity and short-term outcome in patients with AIS. The neurologic severity was measured at admission using NIHSS score and short-term outcome was measured at 7 days using Barthel index. The mean serum albumin level in the study population was 3.73 ± 0.41 g%. Dziedzic et al[30] studied 759 consecutive patients with AIS. Functional outcome was measured 3 months after stroke using Modified Rankin Scale (mRS). Study showed patients with poor outcome had significantly lower serum albumin level than patients with non-poor outcome. A study by Alvarez-Perez et al[31] showed that lower concentration of albumin was associated with worse prognosis and mortality in cardioembolic stroke. In our study, the mean serum albumin level in the study population was 3.6 ± 0.7 g%. The mean NIHSS score was 10.4 and the mean Barthel index score was 57.4 (range 0-100). The serum albumin values had a highly significant correlation with the neurological severity by NIHSS scores (p value <0.001) and with the short-term outcome of the patients as measured by Barthel index (p value <0.001).

Study	No. of Patients	Mean Albumin	p value
Sharma et al[29]	120	3.73	Significant
Idicula et al[28]	444	3.76	<0.05
Dziedzic et al[30]	759	3.55	<0.01
Kasundra et al[10]	50	3.81	<0.001
Present study	100	3.60	<0.001

Table 7. Comparison of Albumin Level with Previous Studies

There are a few clinical studies, which looked at the prognostic significance of serum calcium levels in acute stroke patients. D'Erasmo E et al[32] studied total calcium, albumin corrected calcium and ionised serum calcium levels in patients affected by Transient Ischaemic Attack (TIA) and ischaemic cerebral infarction in order to evaluate the clinical and prognostic significance of calcaemic status during the acute phase of these events. These results demonstrated that the calcium level is decreased in cerebral ischaemia and that more substantial changes are observed in ischaemic cerebral infarction than in TIA and controls (p<0.0001, p <0.02 and p <0.0001, respectively for total calcium, albumin corrected calcium and ionised serum calcium levels). Buck BH, Liebeskind DS, Saver JL, Bang OY, Starkman S, et al[33] reported that higher total serum CA values detected on admission in acute ischaemic stroke patients were associated with smaller cerebral infarct volumes. Ovbiagele and colleagues[34] found that higher total serum CA values measured in the first 24 hours were associated with lesser severity of the stroke and better functional prognosis at discharge. Gaurav M Kasundra, IshaSood, Bharat Bhushan, et al[35] revealed that lower total serum CA values measured in the first 24 hours of ischaemic stroke are associated with more severe clinical findings. Results showed a statistically significant (P<0.05) correlation of AIS with both calcium level and corrected calcium level. In our study, the mean serum calcium and albumin-corrected calcium levels on admission were 8.5 ± 0.7 mg/dL and 8.8 ± 0.4 mg/dL respectively and the mean initial NIHSS score was 10.4. We found a statistically significant (P=0.00) correlation of acute ischaemic stroke with both calcium level and corrected calcium level (0.004). Both serum calcium level and albumin-corrected calcium level has a significant correlation with neurological severity (NIHSS, p value <0.001 and <0.002 in both) and short-term outcome (Barthel index, p value <0.002 and <0.004, respectively) after acute ischaemic stroke in our study.

CONCLUSION

Neurological severity and outcome after acute ischaemic stroke. Serum calcium level and albumin corrected calcium level has a significant correlation with neurological severity and short-term outcome after acute ischaemic stroke. Independently of the other prognostic factors, higher serum uric acid levels predicted neurological severity and correlated with short-term outcome in acute ischaemic stroke. A low SUA concentration is associated with a very good short-term outcome. Serum albumin can predict initial neurologic severity and short-term outcome in acute ischaemic stroke.

Relatively, high serum albumin level in acute stroke patients decreases the risk of poor outcome.

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