International Journal of Medical and Health Research
ISSN: 2454-9142
Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 3; Issue 11; November 2017; Page No. 102-105

A study on the role of serum calcium, albumin and uric acid as predictors of neurological severity and short term outcome in acute ischemic stroke

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Abstract
Introduction: Stroke is the leading cause of disability worldwide, the second most common cause of dementia and the third leading cause of death. Recent studies in acute ischemic stroke have brought to light newer risk factors like serum levels of calcium, hs CRP, homo cysteine and albumin. Ischemic injury in stroke leads to intracellular calcium accumulation, which activates the enzyme cascade causing cell 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.
Methodology: Patients presenting within 72 hours of onset and aged ≥ 40 years were included in this study. Apart from routine investigations, serum albumin, calcium & uric acid levels were done in all patients.
Results: Serum calcium, albumin & 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 & Serum Uric acid values can predict initial neurologic severity and short-term outcome in AIS.

Keywords: calcium, albumin, uric acid, acute ischemic stroke

Introduction

Some of the recent studies have elucidated the stroke pattern to considerable extent in our country with a prevalence rate of 471.58/100000 population [1]. 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 [2]. 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 [3].

Stroke also entails a high socioeconomic burden due to increased morbidity and mortality. Ischemic strokes account for > 80% of total stroke events [4]. Early identification of individuals at risk could be of help in primary prevention strategies [5].

Calcium (Ca) plays an important role in the pathogenesis of ischemic cell damage. Intracellular Ca accumulation lead to neuronal damage by triggering the cycle of cytotoxic events. High dietary intake of Calcium has been associated with reduced risk of stroke, in addition to hypotensive effect of Calcium, it is also suggested that Calcium reduces platelet aggregation, and lowers plasma cholesterol levels. Clinical studies suggest that serum Ca levels may be associated with severity of clinical symptoms, prognosis and infarct volume. Serum Ca levels may reflect the severity of ischemic injury and may be a potential therapeutic target for improving stroke outcome [6].

Serum albumin is a multifunctional protein offers neuroprotective effects. Experimental animal studies have shown human albumin in moderate to high doses to be a promising neuroprotectant in focal and global cerebral ischemia and traumatic brain injury. Recent studies have shown prognostic role of serum albumin level in cases of Acute Ischemic Stroke (AIS), a higher level of which correlate with a better prognosis. However, these finding have not been validated sufficiently in the Indian population. Therapeutic interventions in murine have shown a better prognosis with albumin infusions alone. Thus 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 [7].

Evidence from epidemiological studies suggests that elevated serum uric acid (SUA) levels may predict an increased risk for cardiovascular events, including stroke. Moreover, therapeutic modalities with a SUA lowering potential have been shown to reduce Cardiovascular disease morbidity and mortality. Elevated serum levels of uric acid were shown to increase the risk of stroke and recurrent infarction in patients suffering from myocardial infarction. The fact that thrombotic stroke and myocardial infarction are similar in many risk factors and pathophysiology, have resulted in considerable attention paid recently to the role of uric acid in patients with stroke [8].

Methodology

The study was conducted on admitted patients with first attack of Acute Ischemic stroke to Medicine ward in the Medical College Hospital.

Patients satisfying inclusion criteria are enrolled within 24 hours of admission after informed consent.100 cases satisfying inclusion criteria were included. Data was collected

using a pretested proforma meeting the objectives of the study. Detailed history, physical examination and necessary investigations were undertaken. The purpose of the study was explained to the patient and informed consent obtained.

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, Serum Uric acid is done for all patients at the time of admission. Detailed investigations including blood hemoglobin, TLC, DC, LFT, RFT, Urinalysis, FBS, Lipid profile, ECG, Chest X-ray, 2D-ECHO, Neck vessel Doppler were done. In all cases, Plain CT Brain was done. MRI brain done whenever required.

Results

Table 1: Study Variables In Relation To Nihss Score of Patients Studied

Study Variables	Nihss		**Total** (N=100)	P Value
	≤10 (N=44)	>10 (N=56)		
Serum Uric Acid				
≤ 7.0 In ♂ ≤ 5.7 In♀	40(90.9%)	5(8.9%)	45(45%)	
> 7 In ♂	4(9.1%)	51(91.1%)	55(55%)	<0.001**
> 5.7 In♀	Serum	Albumin		
< 3.5	0(0%)	56(100%)	56(56%)	<0.001**
≥ 3.5	44(100%)	0(0%)	44(44%)	
Serum Calcium				
< 8.6	4(9.1%)	56(100%)	60(60%)	<0.001**
≥ 8.6	40(90.9%)	0(0%)	40(40%)	
Albumin Corrected Calcium				
< 8.6	10(22.7%)	16(28.6%)	26(26%)	0.508
≥ 8.6	34(77.3%)	40(71.4%)	74(74%)	

Hyperuricemia was present in 55% of patients and of which 51 % of the study population scored NIHSS > 10.

Hypoalbuminemia was documented in 56% of patients, and interestingly in all patients NIHSS score was > 10

Hypocalcemia was documented in 60% of cases, of which in 56% NIHSS score was > 10.

There was significant p value between all study variables and NIHSS score.

Table 2: Study variables in relation to Barthel score of patients studied

Study variables	Barthel index		Total (n=100)	P value
	≤ 60 (n=64)	> 60 (n=36)		
Serum uric acid				
≤ 7.0 in ♂ ≤ 5.7 in ♀	10(15.6%)	35(97.2%)	45(45%)	<0.001**
> 7 in ♂	54(84.4%)	1(2.8%)	55(55%)	
> 5.7 in ♀				
Serum albumin				
< 3.5	55(85.9%)	1(2.8%)	56(56%)	<0.001**
≥ 3.5	9(14.1%)	35(97.2%)	44(44%)	
Serum calcium				
< 8.6	56(87.5%)	4(11.1%)	60(60%)	<0.001**
≥ 8.6	8(12.5%)	32(88.9%)	40(40%)	
Albumin corrected calcium				
<8.6	18(28.1%)	8(22.2%)	26(26%)	0.518
≥8.6	46(71.9%)	28(77.8%)	74(74%)	

Hyperuricemia was present in 55% of patients. Barthel score was < 60 in 84.4 % of the hyperuricemic study population.

Hypoalbuminemia was documented in 56% of patients, and nearly 86% had poor outcome as determined by Barthel index (<60)

Hypocalcemia was documented in 60% of cases, of which in 87.5% Barthel score was < 60.

Table 3: Comparison of Study Variables In Relation To Nihss Score of Patients

Variables	NIHSS		Total	P value
	≤10	>10		
Serum Uric acid	4.75±1.04	7.51±0.45	6.30±1.58	<0.001**
Serum Albumin	4.28±0.47	3.13±0.15	3.64±0.66	<0.001**
Serum Calcium	9.17±0.45	7.99±0.35	8.51±0.71	<0.001**
Albumin Corrected CA	8.94±0.52	8.69±0.32	8.80±0.44	0.003**

P value was found to be significant between NIHSS and all study variables

Table 4: Comparison of study variables in relation to barthel index score

Variables	Barthel index		Total	P value
	≤60	>60		
Serum Uric acid	7.15±1.08	4.78±1.10	6.30±1.58	<0.001**
Serum Albumin	3.33±0.51	4.18±0.52	3.64±0.66	<0.001**
Serum Calcium	8.18±0.58	9.09±0.50	8.51±0.71	<0.001**
Albumin Corrected CA	8.72±0.34	8.94±0.54	8.80±0.44	0.011*

P value was found to be significant between Barthel index and all study variables

Discussion

The role of Serum Uric Acid (SUA) in the development of cardiovascular disease has been debated for over 50 years.

Patil TB, *et al.* [9]. studied 100 cases of acute ischemic 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). SUA levels were significantly higher in the patients who succumbed as compared to those who were discharged from the hospital (P = 0.00). They concluded that SUA can be used as a marker for increased risk of stroke and can also be used for risk stratification after stroke.

Chiquete E1, Ruiz-Sandoval JL, *et al.* [10] 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 [11] by Kapildev Mondal, Soumabrota Dutta, Santanu in Kolkata included 100 patients of acute ischemic stroke. Observed Hyperuricemia in 40 % of acute ischemic stroke patients. Correlated SUA with AIS and concluded hyperuricemia is associated with less chance of good outcome.

Mozos *et al.* [12]. 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).

Srikrishna R and Suresh DR [13] found that serum uric acid levels were significantly higher in cases as compared to controls (6.56 ± 0.73 vs. 4.66 ± o.47, P < 0.05). Milionis *et al*. 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, 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 case, 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.* [14]. included 444 patients with ischemic stroke. Outcome was prognosticated by NIHSS & mRS. They showed high serum albumin was independently associated with a better outcome (OR = 1.1 2, 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 may be neuroprotective in ischemic stroke in humans.

Sharma *et al.* [15]. (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 3.73g%. The mean NIHSS score was 11.1 (range, 1-25) and the mean Barthel index score was 56.48 (range, 0-100). The serum albumin values had a highly significant negative correlation with the NIHSS scores (p value < 0.001) and a significant positive correlation with the short-term outcome of the patients as measured by Barthel index (p value - 0.016).

Dziedzic *et al.* [16]. 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. On logistic regression analysis, serum albumin level remained independent predictor of poor outcome (odds ratio [OR]: 0.43; 95% confidence interval [CI]: 0.26 to 0.70). Study was concluded as relatively high serum albumin level in acute stroke patients decreases the risk of poor outcome.

A study by Alvarez-Perez *et al.* [17]. 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).

Thus, most patients with a better prognosis as determined by their lower NIHSS score or higher Barthel index had a higher serum albumin level, and most with a worse prognosis as per their higher NIHSS score or lower Barthel index had a lower serum albumin level. The p value was < 0.001 (for NIHSS & BI) and thus, there was a highly significant correlation between serum albumin level and a better prognosis at the time of admission with NIHSS. This also correlates with most of the previous studies which included either Barthel index or modified Rankin scale after one week of initial examination.

Conclusion

- Independently of other prognostic factors, higher serum uric acid levels predicted neurological severity and correlated with short term outcome in acute ischemic

stroke. A low SUA concentration is associated with a very good short-term outcome

- Though the role of uric acid in stroke pathophysiology remains uncertain and debated over decades, our findings support the hypothesis that SUA is a marker of the magnitude of the cerebral infarction and proved to be an independent predictor of stroke outcome.

References

1. Das SK, Banerjee TK, Biswas A, Roy T, Raut DK, Mukherjee CS, *et al*. A prospective community-based study of stroke in Kolkata, India. Stroke. 2007; 38(3):906-10.
2. Khare S. Risk factors of transient ischemic attack: An overview. Journal of mid-life health. 2016; 7(1):2.
3. Ferri CP, Acosta D, Guerra M, Huang Y, Llibre-Rodriguez JJ, Salas A, *et al*. Socioeconomic factors and all cause and cause-specific mortality among older people in Latin America, India, and China: a population-based cohort study. PLoS Med. 2012; 9(2):e1001179.
4. Bonita R. Epidemiology of stroke. The Lancet. 1992; 339(8789):342-4.
5. Buckley BM. Healthy ageing: ageing safely. European Heart Journal Supplements. 2001; 3(N):N6-10.
6. Guven H, Çilliler AE, Koker C, Sarikaya SA, Comoglu SS. Association of serum calcium levels with clinical severity of acute ischemic stroke. ACTA Neurologica Belgica. 2011; 111(1):45.
7. Kasundra G, Sood I. Prognostic significance of serum albumin levels in acute ischemic stroke. NJIRM. 2014; 5(2). pISSN: 2230-9969.
8. Iranmanesh F, Sheykholeslami NZ, Gadari F, Ahmady J. Acute ischemic non-embolic stroke and serum level of uric acid. Iranian journal of neurology. 2012; 11(1):1.
9. Patil TB, Pasari AS, Sargar KM, Shegokar VE, Bansod YV, Patil MB. Serum uric acid levels in acute ischemic stroke: A study of 100 patients. Journal of Neurology Research. 2011; 1(5):193-200.
10. Chiquete E, Ruiz-Sandoval JL, Murillo-Bonilla LM, Arauz A, Orozco-Valera DR, Ochoa-Guzman A, *et al*. Serum uric acid and outcome after acute ischemic stroke: PREMIER study. Cerebrovascular Diseases. 2013; 35(2):168-74.
11. Mondal K, Dutta S, Tewari S. a Study of Short-Term Outcome of Ischemic Cerebro Vascular Accident Patients with Special Reference to Serum Uric Acid at Presentation. heart disease. 1995; 141:637-44.
12. Mozos I, Chiulana C, Goruna C, Costeab S. Serum uric acid in stroke. Annals of West University of Timisoara, Series of Chemistry. 2007; 16(2):227-36.
13. Srikrishna R, Suresh DR. Biochemical study of antioxidant profile in acute ischemic stroke. British Journal of Medical Practitioners. 2009; 2(1):35-7.
14. Idicula TT, Waje-Andreassen U, Brogger J, Naess H, Thomassen L. Serum albumin in ischemic stroke patients: The higher the better. Cerebrovascular Diseases. 2009; 28(1):13-7.
15. Giri S, Agarwal MP, Sharma V. Correlation of serum calcium levels with neurologic severity and short-term outcome in acute ischemic stroke. J Assoc Physicians India. 2009; 74:112
16. Dziedzic T, Slowik A, Szczudlik A. Serum albumin level as a predictor of ischemic stroke outcome. Stroke. 2004; 35(6):e156-8.
17. Alvarez-Perez FJ, Castelo-Branco M, Alvarez-Sabin J. Albumin level and stroke. Potential association between lower albumin level and cardioembolic aetiology. International Journal of neuroscience. 2011; 121(1):25-32.