Original Research Article

Serum albumin level as prognostic indicator of acute ischemic stroke in tertiary care hospital admitted patients

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ABSTRACT

Background: Serum Albumin level is an important multifunctional protein in the blood for maintaining the normal permeability across vessel wall by osmotic gradient, in inhibiting platelet aggregation and in reducing blood viscosity. Serum albumin level as a novel parameter for predicting outcome and assessment of severity of coronary artery disease is established. Keeping in mind the scarcity of studies regarding albumin level in ischemic Cerebrovascular Accident (CVA), present study was undertaken to correlate serum albumin level with clinical outcome in acute ischemic stroke (AIS) patients.
Methods: One hundred patients of diagnosed AIS were included in the study. Thorough clinical examination and risk factor profile assessment was done. Severity of stroke was assessed using National Institute of Health Stroke Scale (NIHSS) Score and then followed up to 1 week and 3 months post-admission with serum albumin level and assessment was done using modified Rankin Scale (mRS) score. Institutional ethics committee cleared the study.
Results: In 100 patients with AIS, 58% were male and 42% were female. Mean age was 65±8.160. Motor weakness (85%) was the commonest presenting symptom. Around 75% of patients revealed infarction in middle cerebral artery (MCA) territory. Hypertension (HTN) (74%) was the most frequently associated comorbid condition. Patients with low serum albumin level at admission time were directly proportional to severity of stroke at presentation and poor clinical outcome. 1 week and 3 months follow up mean albumin level (g/dl) was 3.8±0.25 and 3.7±0.23 in patients with poor functional outcome respectively. Significant co-relation between mean serum albumin level and clinical outcome was observed.
Conclusions: Serum albumin level is inversely correlated with severity of stroke at presentation and functional outcome in patients on follow up.

Keywords: Acute ischemic stroke, NIHSS score, mRS score, Serum albumin

INTRODUCTION

Stroke is a global health burden and is the second leading cause of mortality and disability after ischemic heart disease worldwide.[1] The cost of treatment and post stroke care is substantially high. World Health Organisation (WHO) defines stroke as "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.[2] The most common cause of AIS in India is large vessel atherosclerosis. Early identification of individuals at risk could be of help in primary prevention strategies.[3]

However due to poor public awareness and inadequate infrastructure this is not properly addressed.

Thrombolytic therapy, as the generally proven effective treatment for AIS is limited by its narrow therapeutic time window i.e. <4.5 hrs after onset compounded by lack of good hospital set up, competent practitioners and hemorrhagic complications, has remained underutilised.[4]

Several factors such as stroke severity, stroke type, older age, sex, vascular risk factors, impairment of consciousness as predictors of mortality and morbidity following acute stroke are established.[5]

- Due to scarcity of studies regarding prognostication in AIS in India, there is a rising interest in the correlation of serum albumin level with clinical severity of acute stroke, which creates an opportunity for early medical intervention.
- Stroke patients who have associated protein energy malnutrition(PEM) tend to have poor outcome.[6]
- Albumin is an important multifunctional protein in the blood for maintaining the normal permeability across vessel wall by osmotic gradient, inhibiting platelet aggregation and in reducing blood viscosity.[7] Serum albumin is inversely associated with myocardial infarction (MI), atrial fibrillation, cardiovascular diseases and death. However neuromodulation of albumin has not been studied in India.
- Experimental animal studies have shown human albumin in moderate to high doses to be a promising neuroprotectant in focal and global cerebral ischaemia and traumatic brain injury.[8] Therapeutic interventions in mouse models of AIS have shown better prognosis with albumin infusion.[8,9]
- Though interventional trial of Albumin In Acute Stroke (ALIAS) conducted in ischemic stroke patients didn't yield promising reports, the role of serum albumin on stroke outcome in India is not well documented, therefore this study was undertaken.[10,11]

METHODS

The study was an observational cross sectional study conducted at PG Department of Medicine, SCB Medical College and Hospital, Cuttack over a period of one year. 100 cases were included in this study with first ever acute ischemic stroke.

Inclusion criteria

All patients of more than 18 years of age diagnosed with first attack of stroke with a new focal neurological deficit, admitted within 36 hours of symptom onset with clinical and radiological evidence of AIS were included in the study.

Exclusion criteria

Patients who presented after 36 hours of onset of symptoms, haemorrhagic stroke or with liver diseases, cardiac failure, chronic renal failure, nephrotic syndrome,

diabetic nephropathy, Protein losing enteropathies, infectious diseases or chronic inflammatory conditions of any etiology were excluded from the study.

The study is based on prospective observation of data in AIS patients admitted in a tertiary care hospital. It was approved by the Ethics committee of the institution. The patients were included in the study after getting informed consent either from patient or their attendants. Complete history was taken followed by a thorough clinical examination. Stroke severity at presentation was calculated by NIHSS score. Relevant investigations like complete blood count, random blood sugar, renal function test, liver function test, serum albumin and protein, serum electrolytes, lipid profile, ECG and urine routine plus microscopic examination was done. Blood sample for assessment of albumin level was collected at admission within 36 hrs of stroke onset. Functional outcome was measured 1 week post admission and at 3 months during follow up using modified Rankin Scale (mRS).

Table 1: National institute of health stroke scale (NIHSS).

Stroke	Stroke severity
0	No stroke symptoms
1-4	Minor stroke
5-15	Moderate stroke
16-20	Moderate to severe stroke
21-42	Severe stroke

Table 2: Modified rankin scale (mRS).

Score	Symptoms
0	No symptoms
1	No significant disability. Able to carry out all usual activities, despite some symptoms
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities
3	Moderate disability. Requires some help, but able to walk unassisted
4	Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent
6	Dead

Favorable score mRS: 0-3
Unfavorable score mRS: 4-6

Statistical tools

Data collected from the patients was tabulated using Microsoft Excel. The data was entered in the tables as frequency, percentages, mean, standard deviation, graph and pie chart. The data was analysed using Spearman's rank correlation coefficient and student t test. Statistical

analysis for the data collected was done using SPSS (Statistical Package for Social Sciences) 21.0 version. The p value were tested at 5% level of significance.

RESULTS

In this study, about 100 patients with AIS were included. Majority of patients were in the 60-70 years age group with mean age of 65±8.160 years. Among the study population, 58 were males and 42 were females.

About 85 percent patients presented with focal neurological deficit of motor weakness followed by slurring of speech (18%), headache (16%), altered sensorium (9%), convulsion (8%), head reeling (7%), and vomiting (1%) (Figure 1).
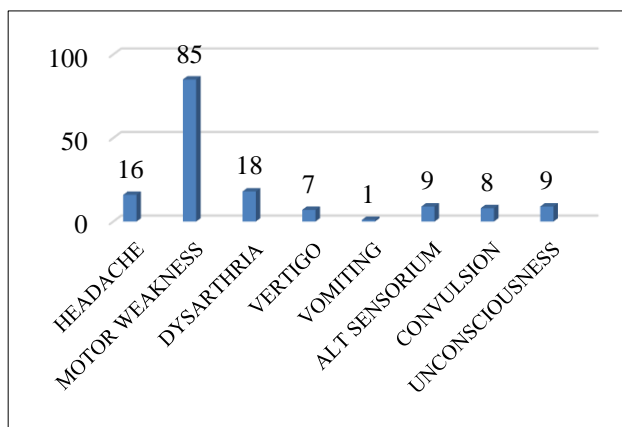

Figure 1: Presenting symptoms in study population.

Brain imaging in 75% of patients revealed infarction in MCA territory followed by lacunar infarcts (10%), multiple infarcts (10%) and posterior circulation infarcts (5%) (Figure 2).
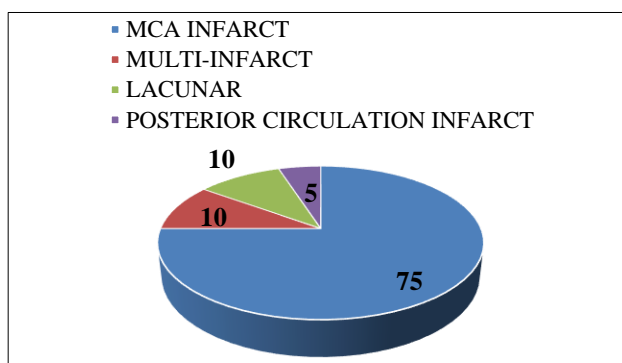

Figure 2: Frequency of lesion in CT scan.

Hypertension (m=40%, f=34%) was found to be the most frequently associated comorbid condition followed by diabetes mellitus (m=18%, f=17%) and dyslipidemia (m=9%, f=13%). Only 9% were smokers in this study (Figure 3).
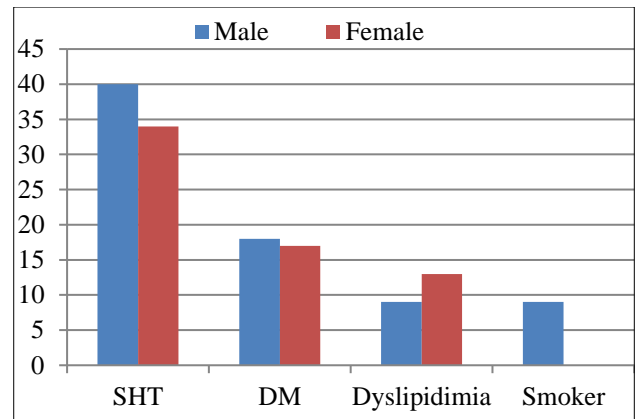

Figure 3: Comorbid conditions among the study population.

Out of the 58 male patients 21 had significant disability, from which 8 deaths occurred at the end of first week. Remaining 37 patients had mild disability. Out of the 42 female patients 16 had significant disability, from which 3 died during the first week. Remaining 26 patients had mild disability (Table 3).

Table 3: Gender and mRS @ 1 week.

Gender	mRS (1 week)		Total
	Less than or equal to 3	More than 3	
Male	37	21	58
Female	26	16	42
Total	63	37	100

Similarly at the 3 months of follow up, among the male patients, number of patients with significant disability increased from 21 to 24 overtime. In the female group, number of patients with mild disability increased from 26 to 31 whereas number of male patients with mild disability decreased from 37 to 34 (Table 4).

Table 4: Gender and mRS @ 3 months.

Gender	mRS (3 months)		Total
	Less than or equal to 3	More than 3	
Male	34	24	58
Female	31	11	42
Total	65	35	100

Table 5: Gender and NIHSS score.

Gender	NIHSS Score		Total
	Less than or equal to 10	More than 10	
Male	31	27	58
Female	23	19	42
Total	54	46	100

Among 100 patients, only six had low serum albumin level i.e <3.5 mg/dl. Majority of patients had albumin levels between 4 to 4.4 with similar gender distribution. At presentation, number of males who had NIHSS more than 10 were 27 and number of females who had NIHSS more than 10 were 19 (Table 5).

Serum albumin level was compared with mRS score at 1 week (Table 6). Out of 6 patients with serum albumin level below 3.5 g/dl, equal number of 3 patients had mRS score less than or equal to 3 and mRS score more than 3 respectively. Out of 41 patients with serum albumin level range of (3.5-3.9) g/dl, 17 had mRS score less than or equal to 3 and 24 had mRS score more than 3. Similarly, out of 53 patients with serum albumin level (4-4.4) g/dl, 43 had mRS score less than or equal to 3 and only 10 had mRS score more than 3.

Table 6: Serum albumin level and mRS at 1week.

Serum albumin level	MRS (1 Week)	
	Less than or equal to 3	More than 3
3-3.4	3	3
3.5-3.9	17	24
4-4.4	43	10
Total	63	37

Serum albumin level was compared with mRS score at 3 months (Table 7). Number of patients with serum albumin level less than 3.5 g/dl and mRS score more than 3 increased from 3 to 6. Out of 41 patients with serum albumin level range of (3.5-3.9) g/dl, 16 had mRS score less than or equal to 3 and 25 had mRS score more than 3. Similarly patients with serum albumin level within (4-4.4) g/dl and mRS score less than or equal to 3 increased from 43 to 49.

Table 7: Serum albumin level and mRS after 3 months.

Serum albumin level	mRS (3Months)	
	≤3	>3
3-3.4	0	6
3.5-3.9	16	25
4-4.4	49	4
Total	65	35

Patients with good outcome had lower NIHSS score and high serum albumin level on admission and those with bad outcome showed high NIHSS score and low serum albumin level. Serum albumin level was compared with mRS score at the end of first week revealing spearman's rank correlation coefficient of r= -0.410 and p value less than 0.001 which is significant. Similarly serum albumin level was compared with mRS score at 3 months of post admission revealing spearman's rank correlation coefficient of r= -0.633 and p value of less than 0.01 revealing significant negative correlation. A lower mRS score indicates a milder disability and better outcome. Hence the higher the serum albumin level, the lower the mRS score and better the outcome.

DISCUSSION

Albumin has well established vital functions in health. Animal studies have revealed neuroprotective effect of albumin in brain ischemia. But this has not been well studied in humans. Though there are quite a few studies from western world, there are very few Indian studies in this aspect. Previous studies concluded that serum albumin is an independent predictor of functional outcome in ischemic stroke.

The study by Gariballa et al, has observed that low serum albumin level is a prognostic indicator of poor functional outcome in stroke. In this study, among the various nutritional markers used, only serum albumin level had significant and independent association with stroke outcome.[12]

Babu et al also observed an association between low admission time serum albumin and poor functional outcome after 3 months of follow up.[13] Also observed that recurrence of stroke is high in patients with low serum albumin level at presentation.

Ramesh et al also identified serum albumin level as an independent predictor of survival in neurosurgical ICU patients.[14]

In the present study, higher male predominance among the AIS patients was observed which may be attributed to a sociocultural bias in India and also males are more exposed to tobacco chewing/ smoking and alcohol. This study was comparable to other Indian studies on stroke patients where greater preponderance was seen among males. Age is one of the non- modifiable risk factors of ischemic stroke.

Diabetes mellitus and HTN were the most common risk factors observed in this study which is supported by other studies like Reeta et al, and Gaurav et al, study.[15,16]

Most of the patients in this study presented with focal neurological deficit of motor weakness in 85% patients, 18% with slurring of speech, 16% headache, 7% head reeling, 9% altered sensorium and 9% with convulsions. Most of the patients those who presented with convulsion had poor outcome and expired which is comparable to other studies like Reeta et al and Gaurav et al study.[15,16] Omkar Prasad Baidya et al in their study reported 84% patients with motor weakness which is consistent with this study.[17]

Mean age of patients with poor outcome at 1 week post-admission was found to be 68 years in this study which is significant according to statistical analysis. Similarly mean age of patients with poor outcome at 3 months

follow up was found to be 68±9 which is again supported by Dziedzic et al study.[18]

Dzeidzic et al, study included 759 patients with AIS where mean age was 68.3±12 and 372 were males. Two hundred sixty-six patients had poor outcome. These patients were significantly older, more often female, and more frequently had ischemic heart disease and atrial fibrillation as comorbid condition. The patients with poor outcome had significantly more severe neurological deficit on admission measured on Scandinavian Stroke Scale. During the 3-month follow-up period, 36% had poor outcome, with 12.9% deaths. Poor outcome patients had mean serum albumin level of 3.4 g/dl Vs 3.6 g/dl in good outcome group. Similarly, Reinhardt et al, study observed that poor outcome patients had mean serum albumin level of <3.4 g/dl Vs >3.5 g/dl in good outcome group. In this study mean serum albumin level was 3.7±0.23 in poor outcome group Vs 4±0.19 in good outcome group.

At first week of follow up in this study, 63 had good outcome with 37 males and 26 females. In them 50 (79.3%) had hypertension, 21 (33.33%) were diabetic, 15 (23.8%) had dyslipidemia and 3.96±0.26 g/dl was the mean serum albumin level. Similarly among poor outcome group of 37 patients, 21 were males, 16 were females, 24 (64.8%) had hypertension, 14 (37.8%) were diabetic, 7 (18.9%) had dyslipidemia and 3.8±0.25 g/dl was the mean serum albumin level which is statistically significant with p value<0.001.

At 3 months of follow up in this study population, among good outcome group of 65 patients, 34 were males and 31 females, 54 (83%) had hypertension, 22 (33.8%) were diabetic, 17 (26%) had dyslipidemia and 4±0.19 g/dl was the mean serum albumin level. Similarly among poor outcome group of 35 patients, 24 were males, 11 females, 20 (57%) had hypertension, 13 (37.1%) were diabetic, 5 (14%) had dyslipidemia and 3.7±0.23 was the mean serum albumin level, which is statistically significant with p value<0.001 and is comparable to Dziedzic et al study. Mortality was 22% in this study which is comparable to other studies such as Abubakar et al study 17.3%, and Idicula et al, study 13%. Mean serum albumin level in this study group was 3.9 g/dl which is comparable with other studies such as Reeta et al, Idicula et al, Dziedzic et al, Gaurav et al, study with mean serum albumin level(in g/dl) 3.73, 3.76, 3.55, 3.81 respectively which is again statistically significant.

In this study, Patients with low NIHSS score, low mRS score and high albumin had good outcome and authors observed statistically significant correlation between severity of ischemic stroke at presentation and serum albumin level. Malnutrition, liver disease, renal disease etc reduce serum albumin level. Catabolic state and neuroendocrine response that follow stroke alter serum albumin level. Malnutrition also down regulate protein synthesis. Nutrition is thought to be the single most important factor regulating albumin synthesis. With exclusion criteria, the serum albumin level in this study is probably a reflection of nutritional status and low serum albumin level and it may be causally related to the increased morbidity and mortality after stroke.

CONCLUSION

Risk of stroke increases with age and most of our patients were above 65 years of age. Systemic hypertension and diabetes mellitus are the most common modifiable risk factors in stroke. NIHSS is relevant for assessing severity of stroke at presentation. There was significant variation of serum albumin with age. Severity of stroke at onset has a definite association with outcome. Serum albumin influences both stroke severity and outcome. Serum albumin being a marker of nutritional status, nutritional support may improve the functional outcome of acute ischemic stroke. As serum albumin level was inversely associated with severity of stroke at onset and thereafter in outcome on follow up, studies involving large number of patients will throw more light in future in this regard.

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