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Serum Albumin as a Predictor of Functional Outcomes Following Acute Ischemic Stroke

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Introduction

Stroke is currently the leading cause of neurological disability in adults [1]. Two-thirds of stroke survivors have residual neurological deficits that impair their function, and approximately 50% are left with disabilities, making them dependent on others for activities of daily living [2].

Following a stroke, the central nervous system undergoes reorganization during the process of functional recovery. However, the degree of recovery is variable and the processes subserving this recovery is incompletely understood. Neurophysiologic changes associated with recovery often begin within one to two weeks following a stroke and may plateau within two and three months, depending on the degree and extent of the neurologic deficit [3]. A large number of factors such as admission functional ability, hemineglect, incontinence, age, and others may influence the functional outcome of stroke patients [4].

In undernourished people, strokelike acute illness may lead to a negative energy balance and greater nutritional demand. Stroke patients may not able to meet these increased demands [5]. The level of serum albumin has been acknowledged to bear marker of nutritional status [6]. It can be a useful measure when acute changes in nutrition need to be assessed. Baseline measurements of serum albumin (<24 hours) may not be affected by the acute stress response after stroke. Hypoalbuminaemia at admission may be associated with premorbid nutritional status attributable to the long half-life of albumin [7].

Albumin is said to be helpful in patient with acute ischemic stroke due to its antioxidant, hemodiltion, and neuroprotective effect. In this study, we correlated the serum Albumin level and functional outcome following the acute ischemic stroke [8]. Hypoalbuminemia at admission may cause negative influences on neuroprotection in acute stroke patients. If this hypothesis is found to be true, treating patients having hypoalbuminemia in acute stroke might enhance their functional outcome.

Method

This prospective observational study was conducted in KMC Hospital Manipal, Karnataka, India. Here, we included patients admitted in Neurology and General Medicine ward between May 2015 and August 2016. The ethical committee clearance obtained from the appropriate authority appointed by the institution.

Inclusion criteria

Patients who presented within seven days following an acute ischemic stroke in the anterior circulation territory, who had a power of MRC grade 3/5 or less in the hemiplegic upper extremity at presentation.

Exclusion criteria:

Patients with hemorrhagic stroke and stroke involving the vertebral-basilar circulation were excluded.

Cases were defined as per WHO definition of stroke. Hypertension was considered according to JNC 8 guidelines or if there was a history of hypertension or on antihypertensive medication, likewise diabetes, history of smoking, harmful alcohol consumption were considered according to the standard guideline. Cardiac disease was considered if there was history or electrocardiogram or echocardiogram suggestive of the same. The possibility of sleep apnea was considered if there was a history from bed partner suggestive of excessive snoring and pauses in breathing during night time and excessive daytime sleepiness. All the patients underwent a CT scan of the brain, followed by MRI if there was an indication for the same.

A total of 118 patients was included in the study. Stroke severity was measured by NIHSS score at the time of

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admission. Detailed neurological examination, routine blood investigation, hematology, renal function test, liver function test including serum albumin, thyroid function test, the cardiac evaluation including ECG and echocardiogram were done. Functional dependency was measured on the seventh day and third month using Barthel index. The Barthel index is a scale that measures disability or dependence in activities of daily living. It uses 10 variables describing ADL and mobility. A higher number is associated with a greater likelihood of being able to live at home with a degree of independence. A score of 0–20 is taken as a total dependency, 21–60 as severe dependency, 61–90 as moderate dependency, 91–99 as slight dependency, 100 as independence. Because of the relatively small number of patients in our study, we have broadly divided the total and severe dependency as one group, and moderate and slight dependency as the other group. There was not even a single patient who attained complete independence even in the third month of onset of stroke.

Data entry and statistical analysis

The data were entered in Microsoft Excel and analyzed in EpiData Analysis 3.0 software. The continuous variables such age, serum albumin levels, NIHSS score, and Barthel score were expressed as a mean and standard deviation. The association between serum albumin and Barthel index (as a categorical variable) on the seventh day and third month after the onset of stroke was assessed using unpaired "*t*" test.

Results

A total of 118 patients were taken for the present study, out of which 17 patients were lost for any form of follow-up. Hence, only a total of 101 patients were included in the study. Out of which six people died before three months, the major reason being the cardiovascular cause.

The mean age of the patients in the series were 60.7 years. The highest numbers of patients were in the 60–79 year age group. There was male preponderance in the study group, i.e., 71 (70.3%) were males and remaining 30 (29.7%) were females. Hypertension was seen in 57 (56.4%) of the study population and 29 (28.7%) of the study population were diabetic. A total of eight patients (7.9%) had a history of atrial fibrillation, on treatment or detected to have atrial fibrillation. Ischemic heart disease was present in 10 (9.9%) of the patients included. Modifiable risk factors such as smoking were present in 33 (32.7%) patients studied. Sleep apnea from The Sleep Disorders Questionnaire, Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome and The Epworth Sleepiness Scale was considered in 30 (29%) patients. History of harmful alcohol consumption was present in about 13 (12.9%) of the patients.

Table 1. Age distribution of study participants

Age of the participants	Frequency (%)
<50 years	20 (19.8)
50–59 years	21 (20.8)
60–79 years	52 (51.5)
≥80 years	8 (7.9)
Total	101 (100)
Mean (SD) age	60.7 (14.4)

Table 2. Risk factors for ischemic stroke.

	Present	Absent
Hyertension	57 (56.4)	44 (43.6)
Diabetes mellitus	29 (28.7)	72 (71.3)
Atrial fibrillation	8 (7.9)	93 (92.1)
Ischemic heart disease	10 (9.9)	91 (90.1)
Transient ischemic attack	6 (5.9)	95 (94.1)
Smoking status	33 (32.7)	68 (67.3)
Harmful alcohol consumption	13 (12.9)	88 (87.1)
Sleep apnea	30 (29.7)	71 (70.3)

Table 3. Categorization of NIHSS score

Categorization of NIHSS	Frequency (%)
Mild (NIHSS < 4)	1 (1.0)
Moderate (4–15)	69 (68.3)
Severe (16–21)	25 (24.8)
Very severe (>21)	6 (5.9)
Total	101 (100)

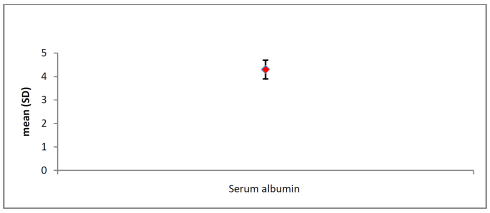

Figure 1. Serum albumin level ug/dl.

Table 4. Serum albumin level

Serum albumin	Blood level ug/dl
<4.0g/dl	19 (18.8)
≥4.0g/dl	82 (81.2)
Total	101 (100.0)
Mean (SD) of serum albumin	4.3 (0.4)

NIHSS at admission (Table 3) mild (NIHSS < 4) was seen in only one patient, moderate (4–15) in 69 (68.3%), severe (16–21) in 25 (24.9%), and very severe disease in 6 (5.9%) patients.

Hypoalbuminemia, i.e., albumin level of <4g/dl was present in 19 (18.8%) of the study population (Table 3; Figure 1). Mean serum albumin level was 4.3 g/dl (SD 0.4).

Error bar diagram: Shows the mean standard deviation of serum albumin of 4.3 (0.4).

Serum albumin level was taken as the continuous variable and compared with function independence using Barthel index on the seventh day and third months from the onset of stroke; we divided Barthel's index into different functional groups depending on the Barthel score, since the number of patients is less, we considered total and severe dependency as one group and slight and moderate dependency as another group. We compared the baseline serum albumin in patient s with total/severe dependency and moderate/mild dependency There was no significant difference in the serum albumin level between these two groups using unpaired "*t*" test (Table 5; Figure 2). At the end of three months follow-up, we compared the baseline albumin value of patients who remained or entered the total/severe dependency with baseline value of moderate/mild dependency, having taken serum albumin level as a continuous variable, baseline serum albumin level was more in moderate/ slight dependency; unpaired "*t*" test showed the difference was statistically significant with ($P = 0.008$) (Table 6; Figure 3).

Unpaired student *t* test: mean SD of serum albumin among in total/severe dependency (mean 4.26 SD 0.41) and moderate/ slight dependency (mean 4.57 with SD 0.36) at seventh day of stroke ($p = 0.098$).

Unpaired student "*t*" test: mean SD of serum albumin in total/severe dependency (mean 4.02 SD 0.52) and in moderate or slight dependency (mean 4.32 with SD 0.37) on third month of stroke ($p = 0.008$).

Discussion

Our study was a prospective observational study in which we measured the baseline serum albumin in patients with acute ischemic stroke in anterior circulation with hemiplegic upper limb power 3/5 or less, and we compared the albumin with functional recovery using the Barthel score, which showed that low albumin levels are associated with poor functional outcome and better outcome was seen in higher serum albumin levels.

Numerous studies have demonstrated that albumin might have a neuroprotective function via multiple mechanisms in different pathophysiological conditions. For many decades hemodilution has been investigated as a potential therapy for ischemic stroke. Albumin causes hemodilution. Transient focal cerebral ischemia induced by middle cerebral artery occlusion in the rat model showed that 5% albumin administration on the onset of ischemia decreased ischemic brain damage as confirmed by reduced hematocrit, infarct volume, and cerebral edema [9]. Another study, administration of concentrated (20 %) HSA 1 % body weight, intravenously to rats at the onset of recirculation induced substantial diminution of infarct volume together with a clear decrease of brain edema. As a result, it is suggested that albumin might modify water homeostasis and eventually reduce edema of the ischemic brain [10].

Other studies in human subjects, Dziedzic *et al.* [13] studied 759 patients with acute ischemic stroke. Here, serum albumin level was measured between 12 and 36 hours after stroke, and functional outcome was meas-

Table 5. Association between serum albumin and Barthel index on the seventh day of stroke

	Barthel index Total/severe dependency	Barthel index Moderate/slight dependency	*F* value*	*P* value
Mean (SD)	4.26 (0.41)	4.57 (0.36)	2.78	0.098

*Unpaired *t* test

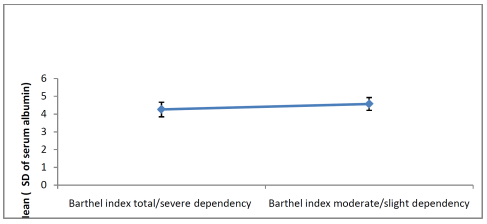

Figure 2. Association between serum albumin and Barthel index on the seventh day of stroke.

Table 6. Association between serum albumin and Barthel index at third month

	Barthel index Total/severe dependency	Barthel index Moderate/slight dependency	*F* value*	*P* value
Serum albumin-Mean (SD)	4.02 (0.52)	4.32 (0.37)	7.38	0.008

*Unpaired *t* test

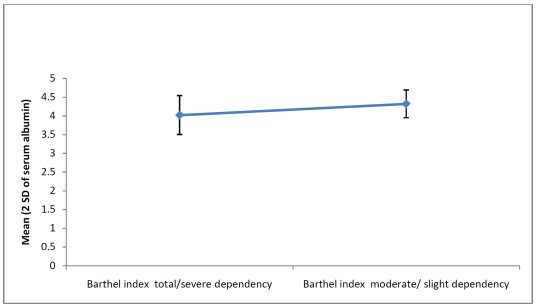

Figure 3. Association between serum albumin and Barthel index after three months.

ured in the third month after stroke using a modified Rankin scale. The results showed that patients with a poor outcome had significantly lower serum albumin level than patients with the nonpoor outcome. On logistic regression analysis, serum albumin level remained an independent predictor of poorer outcome [13]. Abubakar *et al.* [14] studied 75 patients of acute stroke. In this study, admission serum albumin was compared with 30 days mortality, and functional outcome using the modified Rankin scale. This study showed that mean serum albumin of 3.03g/dL with favorable outcome was significantly higher than 2.08g/dL of those with unfavorable outcome. Patients who died had significantly lower serum albumin (1.66 g/dl) than the survivors [14]. Aptaker *et al.* [16], in a study, examined the value of serum albumin level as a predictor of medical complications and functional outcomes in 79 patients aged 65 years or older, who underwent comprehensive inpatient interdisciplinary rehabilitation for the first-time, unilateral, thromboembolic stroke. Serum albumin levels at the time of admission and modified Barthel index scores on admission and discharge were assessed, and the result showed that serum albumin levels appear to be related to the medical complication rate and functional outcome in geriatric stroke patients [15].

Our study also supports the fact that high serum albumin is associated with better functional outcome following acute ischemic stroke. It is also known that protein-energy malnutrition is associated with poor outcome following stroke. Serum albumin serves as the biochemical marker of nutritional status. Hence, administering serum albumin to the patient with acute stroke may help in reducing the infarct volume, edema and thus the morbidity. However, large randomized controlled studies in humans are required.

Conclusion

Serum albumin, which is an indicator of the nutritional status of the body, has been proposed to have neuroprotection function. We tested this hypothesis by comparing the serum albumin level at the time of stroke and functional outcome at the third month. We found that serum albumin is an independent predictor of functional outcome following an acute ischemic stroke. Based on this observation, we conclude that the functional outcome of patients with ischemic stroke having low albumin levels might be enhanced by the administration of albumin during the acute phase.

Acknowledgments

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