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A study on association between serum albumin and clinical outcome in acute ischemic stroke

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Abstract
Aim: To find out the association between serum albumin and clinical outcome in acute ischemic stroke.
Material and Method: The present prospective cross-sectional study was conducted in the department of Medicine at Chattrapati Shivaji Subharti Hospital from April 2018 to December 2019 among 100 patients, aged 45 years and above with symptoms and signs suggestive of stroke. Hypoalbuminemia is defined as serum albumin level less than 3.5 gram per deciliter. Severity of stroke at admission was assessed using the NIHSS scale. All baseline investigations including FBS and serum albumin was measured. CT scan of the brain was done for all patients. Serum albumin level was analysed within 36 hours of admission. Pearson correlation analysis was used to correlate serum albumin, NIHSS score & MRS score.
Results: 56% of study subjects had MCA infarct, 20% had multi-infarct, 6% had posterior circulation stroke, and 18% had Lacunar stroke. MRS score was significantly associated with the NIHSS Score. Among 41% study subjects, serum albumin level was low (<3.5g/dl). NIHSS score showed statistically significant results when associated with serum albumin. Significant positive correlation was found between Serum Albumin & NIHSS score (0.61), while a negative correlation was seen between Serum Albumin & MRS score (-0.67), and NIHSS score & MRS score (-0.82).
Conclusion: Serum Albumin levels have significant association with the severity as well as short term functional outcome of Ischemic stroke. Improving serum albumin levels may improve the functional outcome of acute ischemic stroke.

Keywords: albumin, stroke, NIHSS

Introduction

Stroke is a global health problem. It is the second most common cause of death and fourth leading cause of disability worldwide [1]. Stroke or cerebrovascular accident is a life threatening neurological disorder. There are three pathological types: ischemic stroke (about 80% in white populations), primary intracerebral haemorrhage (about 15%), and subarachnoid haemorrhage (about 5%) [2]. In developed countries, stroke is the first leading cause for disability, second leading cause of dementia and third leading cause of death. Stroke caused an estimated 5·7 million deaths in 2005 and 87% of these deaths were in low-income and middle income countries. The burden of chronic, non-communicable diseases, including stroke, has remained stable, at about 85% of the total disease burden, in high-income countries over the past 10 years. Without intervention, the number of global deaths is projected to rise to 6·5 million in 2015 and to 7·8 million in 2030 [3].

Westernization of lifestyle and the resulting demographic transition might increase the burden of stroke in developing countries as well. Stroke is also a predisposing factor for epilepsy, falls and depression in developed countries [4] and is a leading cause of functional impairments, with 20% of survivors requiring institutional care after 3 months and 15% - 30% being permanently disabled [5].

Stroke is a medical emergency, and the clinician must work quickly to answer several questions. Was the onset sudden? Can the symptoms be attributed to a focal brain lesion? Is the cause likely to be vascular? The diagnosis of stroke (versus not stroke) is made reasonably accurately on clinical grounds alone by specialists, but in general medical and emergency-department settings up to 20% of patients with suspected stroke turn out to have another diagnosis.

The most common cause of ischemic stroke in India is large vessel atherosclerosis. Common risk factors include hypertension, diabetes, smoking, alcohol and dyslipidemia. These risk factors are not properly controlled due to poor public awareness and inadequate infrastructure. Recent studies in western countries have shown a prognostic role of serum albumin in acute ischemic stroke, a higher level of which correlate with a better prognosis. Albumin infusion therapy in acute ischemic stroke is being studied [6, 7]. There is a rising interest in the correlation of serum albumin with the severity of acute ischemic stroke as there is an opportunity for intervention.

In a developing country like India it is of relevance as a cost effective marker to foresee the prognosis and manage patients accordingly thereby improving the survival benefit of the patients. Albumin as an independent predictor in ischemic stroke has not been studied significantly in Indian population. Only a few Indian studies have been done in this setting. This study is planned to determine the prevalence of hypoalbuminemia in acute ischemic stroke and to study the association between serum albumin and clinical outcome in acute ischemic stroke.

Material and Method

The present prospective cross-sectional study was conducted in the department of Medicine at Chattrapati Shivaji Subharti Hospital from April 2018 to December

2019. The study group consisted of 100 patients, aged 45 years and above with symptoms and signs suggestive of stroke. Patients were enrolled in the study after obtaining written informed consent and approval from the Institutional Ethical Committee. All the patients who will be admitted with symptoms and signs suggestive of stroke, patients of both sex admitted within 72 hours of acute ischaemic stroke confirmed by clinical examination and CT brain and having age>45 years were included in the study. Subjects having age <45 years, recurrent stroke, hemorrhagic stroke, any present infectious manifestation, pregnancy, ischemic stroke presenting after 72 hrs, chronic kidney disease and chronic liver disease were excluded from the study.

Hypoalbuminemia is defined as serum albumin level less than 3.5 gram per deciliter. Stroke is defined as a clinical syndrome of sudden onset of focal or global cerebral deficit with symptoms lasting more than 24 hours with no apparent cause other than vascular origin. Severity of stroke at admission was assessed using the NIHSS scale. All baseline investigations including FBS and serum albumin was measured. CT scan of the brain was done for all patients. Serum albumin level was analysed within 36 hours of admission. A complete blood count was performed for all patients using an automated complete blood count analyzer and the following parameters were studied- haemoglobin, total WBC count, differential count, RBC count, MCV, MCH, MCHC, hematocrit and platelet count. Blood sugar profile, KFT profile, lipid profile and LFT profile was assessed too.

One significant aspect in the evaluation of acute ischemic stroke patients is imaging. Noncontrast computed tomography (CT) remains the primary imaging modality for the initial evaluation of patients with suspected stroke. Three main stages are used to describe the CT manifestations of stroke: acute (less than 24 hours), subacute (24 hours to 5 days) and chronic (weeks). Acute stroke represents cytotoxic edema, and the changes can be subtle but are significant. They are also termed "early ischemic changes "and were formerly termed "hyper-acute". It is intracellular edema and causes loss of the normal gray matter/white matter interface (differentiation) and effacement of the cortical sulci. A thrombus in the proximal middle cerebral artery (MCA) is sometimes seen in the acute phase and appears as hyperattenuation. A subacute stroke represents vasogenic edema, with greater mass effect, hypoattenuation and well-defined margins. Mass effect and risk of herniation is greatest at this stage. Chronic strokes have loss of brain tissue and are hypoattenuating. A noncontrast head CT may identify the early signs of stroke, but most importantly will exclude intracerebral hemorrhage and lesions that might mimic acute ischemic stroke such as tumor or intracerebral hemorrhage [8, 9].

MRI presents practical difficulties for hyperacute stroke patients but can be a valuable contributor to patient work-up, particularly beyond 3 h post-symptom onset. Typical MRI stroke protocols can take 10–15 min to perform but rapid protocols are described allowing patient evaluation in 6 min with a mean delay of only 18 min in workflow when compared with CT scanning at very experienced acute stroke centres. The goals in MRI and CT scanning are identical. Although there is no significant difference in patient outcome, when utilizing unenhanced CT and MR within the first 3 h post-symptom onset, use of MRI may reduce the rate of symptomatic intracerebral haemorrhage [8, 10].

Statistical Analysis

Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using chi square test and the level of significance was set at $p<0.05$. Pearson correlation analysis was used to correlate serum albumin, NIHSS score & MRS score.

Results

The mean age of study subjects was 61.92 ± 13.24 years. Hypertension was seen as a risk factor among 59% study subjects, whereas Diabetes mellitus, Atrial fibrillation, Ischemic heart disease, Transient ischemic attack, Smoking status, and Alcohol Consumption was seen as a risk factor among 30%, 7%, 12%, 8%, 31%, and 18% subjects respectively. 56% of study subjects had MCA infarct, 20% had multi-infarct, 6% had posterior circulation stroke, and 18% had Lacunar stroke (table 1).

Table 1: Risk factors for ischemic stroke and frequency of lesions in brain among the study subjects

Risk factors	N	%
Hypertension	59	59
Diabetes mellitus	30	30
Atrial fibrillation	7	7
Ischemic heart disease	12	12
Transient ischemic attack	8	8
Smoking status	31	31
Alcohol Consumption	18	18
Lesion		
MCA Infarct	56	56
Multi-Infarct	20	20
Posterior Circulation Stroke	6	6
Lacunar Stroke	18	18

Table 2 shows the association of MRS Score with severity of stroke (NIHSS SCORE). When the MRS Score was associated with the NIHSS Score, it showed statistically significant results.

Table 2: Association of MRS Score with severity of stroke (NIHSS SCORE)

NIHSS	MRS Score				Total
	Mild	Moderate	Severe	Death	
Mild (<4)	2	0	0	0	2
Moderate (4-15)	39	22	9	0	70
Severe (16-21)	0	6	8	9	23
Very Sever (>21)	0	0	0	5	5
Chi Square	23.01				
p value	<0.01*				

*: Statistically significant

Table 3 depicted that among 59% study subjects, serum albumin was normal (3.5-5g/dl) whereas among 41% study subjects, serum albumin level was low (<3.5g/dl). NIHSS

score showed statistically significant results when associated with serum albumin.

Table 3: Association of MRS Score with severity of stroke (NIHSS SCORE)

NIHSS	Serum Albumin		Total
	Normal	Low	
Mild (<4)	2	0	2
Moderate (4-15)	55	15	70
Severe (16-21)	2	21	23
Very Severe (>21)	0	5	5
Chi Square	38.78		
p value	<0.01*		

*: statistically significant

Table 4 depicts the association of MRS Score with Serum albumin. It illustrated significant results when MRS Score was associated with serum albumin.

Table 4: Association of MRS Score with severity of stroke (NIHSS SCORE)

Serum Albumin	MRS Score				Total
	Mild	Moderate	Severe	Death	
Normal	40	17	2	0	59
Low	1	11	15	14	41
Chi Square	41.19				
p value	<0.01*				

*: statistically significant

Table 5 showed a positive correlation (0.61) between Serum Albumin & NIHSS score. While a negative correlation was seen between Serum Albumin & MRS score (-0.67), and NIHSS score & MRS score (-0.82). The results were statistically significant.

Table 5: Correlation between serum albumin, NIHSS score & MRS score

Variables	r value	p value
Serum Albumin & NIHSS score	0.61	<0.01*
Serum Albumin & MRS score	-0.67	<0.01*
NIHSS score & MRS score	-0.82	<0.01*

*: statistically significant

Discussion

Albumin has well established important functions in health. It is well known that serum albumin plays a major role in the clinical outcome of vascular diseases. The neuroprotective effect of albumin is due to its various properties like anti-inflammatory and anti-oxidant effects, inhibition of thrombosis in microcirculation [11, 12]. Albumin captures the oxygen free radicals and slows the production of reactive hydroxyl radical species. Albumin has a peculiar property of binding to copper ions by doing so it inhibits the process of copper ion dependent lipid per oxidation at cell membrane. It has also been postulated that albumin exerts neuroprotection by binding to lysophosphatidylcholine. Free lysophosphatidylcholine increases leukocyte adhesion molecules which lead to inflammatory mediated damage on vascular endothelium. It also causes apoptosis when it is present in high concentration [13].

Based on the above said properties it was postulated that albumin infusion post ischemic stroke may be beneficial in long term outcome.Animal studies have shown neuroprotective effect of albumin in ischemic stroke. But this has not been well studied in humans. Though there are quite a few studies from the western world, there are very few Indian studies in this regard. Previous studies have concluded that in ischemic stroke, serum albumin is an independent predictor of outcome.

The present study showed that there were 73% males and 27% females. In the present study, male patients had more severe stroke compared to female patients. The results were in accordance with the study done by Manickam S *et al* [14] and Nair R *et al* [15]. The findings of the study were in contrast with the study by Abubakar *et al* [16].

The current study depicted that 19%, 23%, 54%, and 4% subjects were under the age group of 45-50 years, > 50-59 years, 60-79 years, and ≥ 80 years respectively. The mean age of study subjects was 61.92 ± 13.24 years. These results are in accordance with the study done by Nair R *et al* [15].

The risk factors for ischemic stroke were Hypertension (59%), Diabetes mellitus (30%), Atrial fibrillation (7%), Ischemic heart disease (12%), Transient ischemic attack (8%), Smoking status (31%) and Alcohol Consumption (18%) subjects. Most common risk factors noticed in this study were systemic hypertension and diabetes mellitus. These results were almost similar with the study done by Nair R *et al* [15].

The study indicated that 56% study subjects had MCA infarct, 20% had multi-infarct, 6% had posterior circulation stroke, and 18% had Lacunar stroke. The results were in accordance with the study done by Manickam S *et al* [14] where 30%, 9%, 5%,and 6% study subjects had MCA infarct, had multi-infarct, posterior circulation stroke, and Lacunar stroke.

Mild (<4) NIHSS score was seen in 2% study subjects. Moderate (4-15) NIHSS score was seen in most of the study subjects (70%). Severe (16-21) NIHSS score was seen in 23% study subjects. While a very severe (>21) NIHSS score was seen in 5% study subjects. These findings are similar with the study done by Nair R *et al* [15].

The present study depicted that among 59% study subjects, serum albumin was normal (3.5-5g/dl) whereas among 41% study subjects, serum albumin level was low (<3.5g/dl). These findings were similar with the findings of Manickam S *et al* [14] and Nair R *et al* [15]. The study by Gariballa *et al* [17] has observed of the various markers of nutritional status used in this study, only serum albumin showed a significant and independent association with stroke outcome. Aptaker *et al* [18] found that serum albumin concentrations at admission were significantly related to the rate of medical complications and functional outcome in stroke.

Our study included 100 patients with ischemic stroke. This sample size was small compared to most of the multicentric studies conducted in the western world. But the study results were comparable to that of previous studies. Our study, as in the above mentioned studies, has come out with a significant association between serum albumin levels and the severity of acute ischemic stroke.

There was a significant correlation between serum albumin level and the NIHSS score, also between serum albumin and MRS score, and NIHSS and MRS score. These findings were not in accordance with the studies done by Manickam S *et al* [14] and Nair R *et al* [15].

The limitations of the present study are mentioned below

1. The sample size is small.
2. It has been done in a single center.

3. The postoperative cases, trauma cases, surgical cases have not been included.
4. Only the in hospital mortality has been calculated.
5. Single group of the population has been studied.

Conclusion

Stroke being a major health concern in developing countries it is high time we get a suitable predictor for its outcome. Male patients had more severe stroke compared to female patients. Diabetes and systemic hypertension were the most common risk factors associated. Further larger studies are required to come to ascertain the facts and its implications for therapy. Serum Albumin levels have significant association with the severity as well as short term functional outcome of ischemic stroke. Improving serum albumin levels may improve the functional outcome of acute ischemic stroke.

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