A Study of Serum Albumin Levels in Acute Ischemic Stroke and its Correlation with Clinical Outcome

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ABSTRACT

Introduction:: Stroke is a global health problem. Studies have shown that serum albumin level is an independent predictor of ischemic stroke outcome. In the present study we compared the serum albumin and the volume of infarct with the clinical outcome.

Material and methods: Fifty patients of age more than 18 years with clinical and radiological evidence of acute ischemic stroke were included in the study. The severity of stroke at admission was assessed by National Institute of Health stroke scale (NIHSS). Serum albumin levels were measured at admission within 36 hours after stroke onset. Functional outcome was measured 1 week post admission and after 3 months during follow up using modified Rankin scale (mRs). A score of mRs >3 or death was taken as poor outcome. Statistical analysis and interpretation of the data was done. *P* value of <0.05 was taken as statistically significant.

Results: The mean age group of the study population was 53 years, male patients had more severe stroke compared to female patients. Most common risk factors were diabetes mellitus and systemic hypertension. Patients with a good outcome had lower NIHSS score, low mRS score, high albumin and low volume of infarct. Those with worst outcome had higher NIHSS, high mRS and high volume of infarct.

Conclusion: Relatively high serum albumin level in acute stroke patients decreases the risk of poor outcome. It is not only serum albumin but volume of infarct also does play a role in the final outcome of the patient.

Keywords: Acute Ischemic Stroke, Serum Albumin, Volume of Infarct, Functional Outcome

INTRODUCTION

Stroke is a global health problem. Around 20 million people suffer from stroke every year and about 5 million people among them do not survive.[1,2] It is the second most common cause of death and fourth leading cause of disability worldwide.[3] Stroke is also a predisposing factor for epilepsy, falls and depression in developed countries.[4] It is a leading cause of functional impairments, with 20% of survivors requiring institutional care after 3 months and 15% - 30% being permanently disabled.[5]

It is a well known fact that if stroke patients have associated protein energy malnutrition they tend to have poor outcome.[6] Studies have shown that serum albumin level is an independent predictor of ischemic stroke outcome.[7,8] Experimental studies have shown that human albumin infusion after stroke onset significantly improves the neurological function and reduces the infarct volume.[9] Although low serum albumin is associated with poor neurological outcome, albumin

therapy in acute stroke patients is not beneficial as shown by the ALIAS (Albumin in Acute Ischemic Stroke) part 1 and 2 trials which evaluated the efficacy and safety of human albumin therapy in acute ischemic stroke.[10,11] The volume of infarct and its co-relation with the serum albumin was not studied in any of the previous studies. In the present study we compared the serum albumin and also the volume of infarct with the clinical outcome.

MATERIAL AND METHODS

The study was a Hospital based prospective study which included a total of fifty patients of age more than 18 years with clinical and radiological evidence of acute ischemic stroke admitted to the department of General Medicine and Neurology in a tertiary care centre in South India. Patients with Cerebral haemorrhage of any aetiology, Liver disease; Cardiac failure, Nephrotic syndrome, Diabetic nephropathy, Protein losing enteropathies and Malignancies were excluded from the study. Diagnosis of ischemic stroke is based on clinical observation confirmed by radiological imaging.

Prior to the commencement of the study, ethical clearance was obtained from Institutional Human Ethical Committee. The selected patients were briefed about the nature of the study and written informed consent was obtained from them in regional language. Patients were examined clinically in detail and the severity of stroke was assessed by National Institute of Health stroke scale (NIHSS) at baseline. Blood samples for assessment of albumin were collected at admission within 36 hours after stroke onset. Serum albumin estimation was done using Bromo Cresol Green (BCG) end point method. Functional outcome was measured 1 week post admission and after 3 months during follow up using

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modified Rankin scale (mRs). This scale runs from 0-6, running from perfect health without symptoms to death. A score of mRs: 0-3 was taken as favourable score and mRs: 4-6 was taken as unfavourable score. Serum albumin level <3.5 g% is considered as low.

The data were reported as the mean +/- SD or the median, depending on their distribution. The differences in quantitative variables between groups were assessed by means of the unpaired t test. Comparison between groups was made by the non-parametric Mann- Whitney test. ANOVA was used to assess the variables. The chi square test was used to assess the difference in categoric variables between groups.

Statistical analysis and interpretation of the data was done by using SPSS version 20. P value of <0.05 using two tailed test was taken as being of significance for all statistical tests

RESULTS

Among the study population of 50 patients, 44(88%) were males and 6(12%) were females. Out of 50 patients, 3 patients (1 male, 2 females) lost to follow-up. Number of patients with NIHSS score less than or equal to 10 was 41 and more than 10 was 9. Among those with NIHSS more than 10, there were seven males and two females. NIHSS score of 10 or less than 10 was seen in high numbers in 56-65 and >65 years age group. The risk factors of the study population and the nature of the ischemic stroke were tabulated in Figure 1and Figure 2 respectively.

Among the 47 patients, number of patients who had significant disability was 15. Among them 6 were in the age group of 56 to 65. Number of patients who had mild disability was 32.Among them about 11 patients were in the age group more than 65. After 3 months, number of patients with significant disability were 4 and number of patients with mild disability were 43.Significant improvement was seen in the age group of 56 to 65 (9 to 13).

Out of the 43 male patients, 14 patients had significant disability (mRs >3) and 29 patients had mild disability (mRs ≤3). Among the 14 with significant disability, 3 had death as outcome. Out of the 4 female patients, 1 had significant disability and died during the first week. Remaining 3

Serum albumin g/dl	NIHSS score		Total	P value
	≤10	>10		
3-3.4	0	1	1	
3.5-3.9	10	3	13	
4-4.4	24	3	27	0.124
>4.4	7	2	9	
Total	41	9	50	

Table-1: Serum Albumin with NIHSS Score

Serum albumin g/dl	mRs at 1 week		Total	P value	mRs at 3 months		Total	P value
	≤3	>3			≤3	>3		
<3.5	0	1	1		1	0	1	
≥3.5	32	14	46	0.319	41	5	46	
Total	32	15	47		42	5	47	0.894

Table-2: Serum Albumin with mRs score

mRs at 1 week	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	P value
					Lower Bound	Upper Bound			
≤3	32	5.5948	12.00600	2.12238	1.2662	9.9234	.11	52.54	
>3	14	26.5182	26.47135	7.07477	11.2341	41.8023	.30	81.60	
Total	46	11.9628	19.91184	2.93584	6.0497	17.8759	.11	81.60	0.001

Table-3: Volume of Infarct in CT scan with mRs after 1 week

mRs at 3 months	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	P value
					Lower Bound	Upper Bound			
≤3	42	10.6385	17.63608	2.72131	5.1428	16.1343	.11	62.70	0.146
>3	4	25.8675	37.60486	18.80243	-33.9702	85.7052	1.57	81.60	
Total	46	11.9628	19.91184	2.93584	6.0497	17.8759	.11	81.60	

Table-4: Volume of Infarct in CT Scan with mRs after 3 months

Study	No of Patients	Mean Albumin	P Value
Idicula et al[18]	444	3.76	<0.05
Dziedzic et al[7]	759	3.55	<0.01
Gaurav et al[19]	50	3.81	<0.001
Present study	50	3.85	0.894

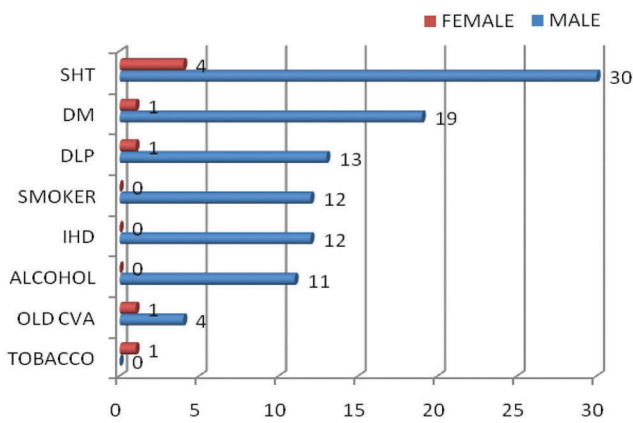**Table-5:** Comparison with other studies

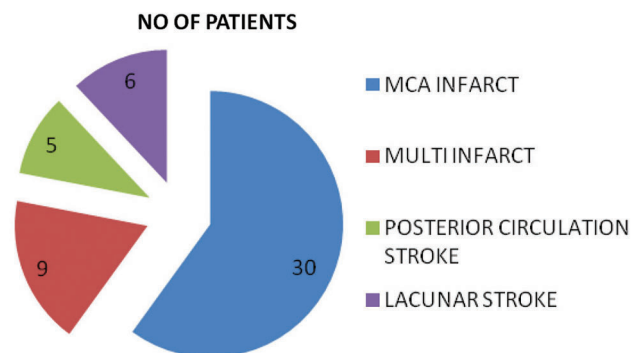**Figure-1:** Risk factors of stroke in the study population

Figure-2: Frequency of lesion in MRI / CT brain

patients had mild disability. At 3 months follow-up, among the male patients, number of patients with significant disability dropped from 14 to 4. In the female group, the 3 patients with mild disability had improvement in the mRS score and didn't worsen.

Among 50 patients, only one patient in the age group of 46 - 55 had low serum albumin levels (<3.4 g/dl)). Mean albumin was 3.8. Majority of patients had albumin levels between 4 and 4.4. Both males and females showed similarity in this.

Table 1 showed that out of 9 patients with NIHSS score >10, only one patient had low serum albumin level<3.5 g/dl. The remaining 41 patients with a NIHSS score of less than 10 had serum albumin level above 3.5 g/dl.

On co-relating serum albumin level with mRS score at 1 week after stroke onset, while all the 32 patients with mRS ≤3 had serum albumin levels ≥3.5 g/dl, only one out of 15 with mRS > 3 had low serum albumin levels, the rest had serum albumin levels ≥3.5 g/dl. P value was 0.319. Hence there was no significant correlation. (Table 2) On co-relating serum albumin level with mRS score at 3 months after stroke, it was noted that out of 14 patients with high albumin levels who initially had mRS > 3 at 1 week, 9 had clinical improvement and the remaining 5 persisted to have mRS > 3 at 3 months post stroke. Also, a single patient with serum albumin <3.5 had an improvement in mRS score from baseline.

Out of 47 patients, volume of infarct could not be calculated for one patient. In the rest, the mean volume of infarct is significantly higher in those with mRs >3 than those ≤3 score

at 1 week after stroke. (P value was 0.001) The results are tabulated in Table 3

The volume of infarct and mRS scale was compared during 3rd month using ANOVA method. P value was 0.146. This showed there was no correlation between volume of infarct and outcome during 3rd month. (Table 4)

DISCUSSION

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.[12-14] It reduces hematocrit level and also plays a vital role in aggregation of erythrocytes[15] by increasing low shear viscosity and decreasing erythrocyte sedimentation under no-flow conditions. Albumin has a good antioxidant property. Other neuroprotective effect of albumin in stroke includes Prevention of thrombosis and Prevention of leukocyte adhesion within post capillary microcirculation in the early reperfusion phase.

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. Based on the above said properties it was postulated that albumin infusion post ischemic stroke may be beneficial in long term outcome.

Experimental studies in rats done by Belayev et al. showed that high-dose human albumin therapy, if administered within 2 to 4 hours after stroke onset, is highly effective in improving neurological status and in reducing infarction volume and extent of brain swelling.[16]

Based on all the evidences human trial known as ALIAS (Albumin In Acute Ischemic Stroke) was conducted. It showed that treatment with intravenous albumin 25% at 2 g/kg was not associated with improved outcome at 90 days and was associated with increased incidence of intracerebral haemorrhage and pulmonary oedema. Further research is required to come to conclusive evidence that human albumin infusion can improve the clinical outcome of stroke patients as there were good results in rat models of stroke.

The mean age group of the study population was 53 years, predominantly middle aged group which is a decade lower than the peak age group of stroke in western countries.[17]

In the present study, male patients had more severe stroke compared to female patients. Most common risk factors noticed in this study were diabetes mellitus and systemic hypertension.

Around 42 patients had good outcome in this study and only 5 patients had poor outcome. Most of the previous studies showed that patients with good outcome had lower NIHSS

score and high serum albumin level on admission and those with worst outcome showed high NIHSS score and low serum albumin level. In our study also patient with low NIHSS and high albumin had good neurological outcome. Only one patient had low albumin and high NIHSS score had unfavourable mRs score after 1 week; however his mRs score improved after 3 months

The studies which were done earlier didn't take volume of infarct into account. The patients with poor outcomes had a mean volume of infarct of around 26.51 and those with good outcome had a mean volume of infarct of around 5.59. Even though there was significant correlation between volume of infarct and mRS score at 1 week there was no significant correlation between them at 3 months

In this study, most patients with a good outcome had lower NIHSS score, low mRS score, high albumin and low volume of infarct. Those with worst outcome had higher NIHSS, high mRS and high volume of infarct. The one patient with low serum albumin also had a good outcome in 3 months. It is not only serum albumin but volume of infarct also do play a role in the final outcome of the patient which was not considered in other studies. Those who had poor outcome had a mean volume of infarct of around 25 cm^3 and also there was statistical significance between volume of infarct and mRS at 1 week. Even though clinically most of the patients had good outcome after 3 months based on mRS score, statistically P value was not significant. Hence this study is contrary to the evidence that serum albumin is a long term predictor of ischemic stroke outcome. The disadvantage of this study was that not enough number of patients could be obtained with low serum albumin levels.

CONCLUSION

Though the risk of stroke increases with age, our patients were predominantly in the middle aged group. Male patients had more severe stroke compared to female patients. Most common risk factors noticed in this study were diabetes mellitus and systemic hypertension. Most patients with a good outcome had lower NIHSS score, low mRS score, high albumin and low volume of infarct. Those with worst outcome had higher NIHSS, high mRS and high volume of infarct. The one patient with low serum albumin also had a good outcome in 3 months. It is not only serum albumin but volume of infarct also does play a role in the final outcome of the patient.

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