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Association of Serum Albumin with Short-Term Outcome of Ischemic Stroke

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Abstract

Background: Serum albumin is proved to be a neuroprotective substance in experimental studies in focal cerebral ischemia. **Objective:** The aim of this study was to find out any association of serum albumin with the short term outcome of ischemic stroke. **Methodology:** This observational study was conducted in the Department of Neurology and Department of Internal Medicine at Dhaka Medical College Hospital, Dhaka from January 2011 to December 2011. A total of fifty consecutive patient with first ever ischemic stroke were included. Short term outcome was measured on day 7 using the modified Rankin Scale (mRS) and poor outcome was defined as mRS score 4 to 6 or death. Serum albumin was measured within 24 hours of onset of stroke. **Result:** Serum albumin was found to be significantly associated with the short-term outcome of ischemic stroke [P-value of Chi square (df = 1) was 0.010]. On logistic regression analysis, SA level [p = 0.018, Odds Ratio (OR) =5.817; 95% confidence interval: 1.348 to 25.106] remained significantly and positively associated with the short-term outcome of ischemic stroke. **Conclusion:** Serum albumin is significantly associated with the short-term outcome of ischemic stroke and lower level predicts poor outcome and higher level predicts good outcome. *[Journal of National Institute of Neurosciences Bangladesh, 2019;5(2): 101-105]*

Keywords: : Ischemic stroke; albumin; short-term outcome; neuroprotection

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Introductio

Serum albumin (SA) is one of the several substances that are being investigated for their potential neuroprotective effect[1-3]. Experimental studies have shown that albumin therapy substantially improves neurological function, markedly reduces the volume of cerebral infarction, and eliminates brain swelling in animals with acute stroke[4-5]. It is proved that sufficient serum albumin levels improve the plasma viscosity, microcirculation and oxygen transport capacity[5-7]. It was reported that the low dose,

cold albumin infusion locally in the ischemic areas exerts neuroprotective effects[8].

Serum albumin increases the collateral perfusion in the ischemic areas which has been suggested as one of the neuroprotective mechanisms[6]. In addition to these preclinical and clinical trials a few studies also investigated the association of SA with outcome of ischemic stroke apparently to help clinical trials gain stronger ground. This current study is one among them which is intended to find out the association of SA on admission with outcome of ischemic stroke on day 7 of onset.

Methodology

This observational study was conducted in the Department of Neurology and Department of Internal Medicine at Dhaka Medical College Hospital, Dhaka from January 2011 to December 2011 for a period of one (01) year. Adult patients with the age more than 18 years admitted in the hospital within 24 hours of first ever ischemic stroke confirmed by CT-scan or by MRI were included in the study. Patients having previous history of stroke or TIA or known to be suffering from comorbidities like cancer, liver disease, renal failure, and protein loosing enteropathies were excluded from this study.The size of the infarct was designated as large when the sum of the largest transverse and sagittal diameters divided by 2 was more >1.5 cm and small when it was ≤ 1.5 cm[9]. The measurements were done by a consultant radiologist. Patients of ischemic stroke (confirmed by CT/MRI) fulfilling the inclusion and exclusion criteria were assessed by the investigator. The Scandinavian Stroke Scale (SSS) was used to assess stroke severity on admission[10]. The patients were divided into 2 groups based on the stroke severity on admission: An SSS score of ≤25 was designated as severe and above this level was designated as 'not severe'[9]. Functional outcome was measured on day 7 using modified Rankin Scale (mRS) and this was designated as short-term functional outcome[10]. Short-term functional outcome was divided into poor outcome and good outcome. An mRS score of 4-6 or death was defined as poor outcome and 0-3 was defined as good outcome[2,9]. The mRS scoring was carried out by a trainee doctor who was blinded about the SSS score on admission. In this study baseline serum albumin was defined as the serum albumin level measured within 24 hours of onset of stroke. Baseline SA levels were divided into two groups as ≤35 gm/L and >35 gm/L arbitrarily[2]. The research protocol was accepted by the Ethical Review Committee of Dhaka Medical College prior to beginning of the study and informed consent was obtained from all the patients. For all the variables, statistically significant association with SA on admission was tested by running chi square test to find out any confounder affecting the SA. In the next step, statistically significant association with mRS was tested for all the variables by running chi square again. Finally, based on the above analyses, theoretical background and specification of statistical modeling, the logistic regression analyses were performed. Values of p of less than 0.05 was considered significant. All the analyses were done by the statistical software SPSS version 18.0.

Results

Fifty consecutive patients of first ever ischemic stroke fulfilling the inclusion and exclusion criteria were recruited. Four patients expired before the 7th day from stroke onset depicting the 7day mortality of 8.0%. The mean (±SD) age of the respondents was 63.64 ± 13.228 years ranging from 30 to 100 years, with a male/female ratio of 2.85:1.The normal level of SA was found in 24% of the patients and the mean (±SD) of SA was 36.06 (±4.474) (Table 1).

Table 1:Basic characteristics of the respondents of the study

Sample Size		50
Expired (number %)		4 (8%)
SA	No. with normal value (%)	24 (48%)
	No. with value lower than normal (%)	26 (52%)
	mean (±SD) gm/L	36.06 (±4.474)
	Range gm/L	26 – 46
mRS score (mean ± SD)		3.74 (±1.575)
SSS (mean ± SD)		17.92 (±10.919)
Size of lesion mean (± SD)		3.585 (±2.31168)
Age in yrs	mean (± SD)	63.64 (±13.228)
	Range	30 – 100
Male (number %)		37 (74%)
HTN (number %)		30 (60%)
Ht Disease (number %)		11 (22%)
DM (number %)		14 (28%)
Smoking (number %)		27 (54%)
Married		50 (100%)
Rural residence (number %)		33 (66%)

SD=Standard deviation, HTN=Hypertension, Ht disease = either atrial fibrillation or ischaemic heart disease, mRS = Modified Rankin Scale, SSS = Scandinavian Stroke Scale, Normal value of SA = 35 – 50 gm/L[19]

The unadjusted association between various variables and stroke outcome was measured. Among these eleven

variables infarct size, and SA level were significantly associated with short-term outcome (mRS score) of ischemic stroke (Table 2).

Table 2: Presence of Co-morbidities in Study Groups

Variables		Outcome		P value
		Good	Poor	
Age	<65	9(18%)	20(40%)	0.390
	≥65	9(18%)	12(24%)	
Sex	M	16(32%)	21(42%)	0.072
	F	2(4%)	11(22%)	
HTN	No	9(18%)	11(22%)	0.279
	Yes	9(18%)	21(42%)	
DM	No	12(24%)	24(48%)	0.529
	Yes	6(12%)	8(16%)	
Smoking	No	8(16%)	15(30%)	0.869
	Yes	10(20%)	17(34%)	
Ht Disease	AF or IHD	3(6%)	8(16%)	0.495
	No	15(30%)	24(48%)	
SSS	Not severe (≥25)	7(14%)	7(14%)	0.198
	Severe (<25)	11(22%)	25(50%)	
Size	Small (≤1.5)	9(18%)	6(12%)	0.021
	Large(>1.5)	9(18%)	26(52%)	
Serum	>35 g/L	13(26%)	11(22%)	0.010
Albumin	≤35 g/L	5(10%)	21(42%)	
Income	Middle to High	12(24%)	24(48%)	0.529
Status	Low	6(12%)	8(16%)	
Lesion Side	Left	13(26%)	18(36%)	0.264
	Right	5(10%)	14(14%)	

p-value = p-value of chi square, DM = Diabetes mellitus, Ht Dis = history of either ischaemic heart disease or atrial fibrillation, HTN = hypertension, mRS-modified Rankin Scale score on day 7 of ischaemic stroke onset, Size = size of the infarct, SSS = Scandinavian Stroke Scale score on admission

On logistic regression analysis SA level [p = 0.018, Odds Ratio (OR) =5.817] and size of infarct (p = 0.036, OR = 4.932) were found to be significantly associated with the mRS score that is the outcome in ischemic stroke (Table 3).

Table 3: Results of Logistic Regression Analysis

Variables	OR	P value	95% CI	
			Lower	Upper
Age	0.642	0.544	0.153	2.689
Albumin	5.817	0.018	1.348	25.106
Size of infarct	4.932	0.036	1.113	21.854
SSS	3.303	0.130	0.705	15.488

P value = P value of logistic regression study, SSS = Scandinavian Stroke Scale score, OR = Odds ratio

Discussion

This study performed in a cohort of 50 consecutive first ever ischemic stroke patients demonstrates that a high level of serum albumin is associated with a better short-term (7 day) functional outcome. In one previous prospective study on albumin in ischemic stroke, high serum albumin was associated with good outcome[9]. Similar results were found in other studies as well[2].This result might suggest a neuroprotective effect of albumin in ischemic stroke.

The neuroprotective effect of albumin is exerted by several mechanisms. First, albumin is a high-molecular-weight protein that reduces the blood-brain barrier permeability and brain edema following ischemia. Second, albumin increases the plasma oncotic pressure without increasing the plasma osmolality, which in turn leads to an expansion of intravascular blood volume and a better microvascular circulation. Third, under low-flow conditions, albumin decreases red blood cell sedimentation and viscosity which might favor reperfusion[11]. Fourth, albumin reverses stagnation and thrombosis in the postcapillary microcirculation during the recanalization phase[5]. Fifth, albumin is shown to have a prothrombolytic effect explained by its capability to maintain vascular patency after successful thrombolysis or by preventing post-thrombolytic reocclusion[12-13]. Sixth, oxidative stress and inflammation are major factors that lead to further neuronal damage following acute ischemia. Albumin is recognized as an important antioxidant in plasma which might play a beneficial role during the delayed phase of neuronal death[14]. Seventh, it is also speculated that albumin might exert neuroprotection by binding to lysophosphatidylcholine (lyso PC)[15]. Free lyso PC upregulates leukocyte adhesion molecules and thereby induces pro-inflammatory action on vascular endothelium. Free lyso PC also augments apoptotic cell death at high concentration. Thus, if administered at high dose, albumin may bind to free lyso PC and provide neuroprotection by reducing inflammation and apoptosis.

The general objective of this study was to assess the association of baseline serum albumin with short-term outcome of ischemic stroke. Multiple logistic regression analysis of serum albumin in this study revealed that the estimated odds ratio (OR) was 5.817, which means that patients with low serum albumin level have odds to have poor stroke outcome 5.817 times as great as that of the patients with high serum albumin level and this was significant at a p-value of 0.018. For SA, this study draws inference that higher

SA level on admission is more likely to have good short-term outcome in ischaemic stroke patients than lower SA level.

On previous studies, high SA was found to be independently associated with better outcome (OR = 1.12, 95% CI = 1.05-1.2, p = 0.001)[2] and lower SA level was found to be an independent predictor of poor outcome (OR=0.43, 95% CI = 0.26-0.70) of ischaemic stroke[9]. Similarly, it was found that SA was significantly correlated with the functional outcome measured as modified Barthel Index (MBI) gain [(adjusted R^2=0.062, F=8.250, p=0.001) and (t=2.743, p=0.008)][16]. Other studies also found lower SA to be an independent predictor of mortality in all stroke patients[17]. Clearly, all of these above mentioned previous studies directly support the finding of current study.

It is noteworthy that albumin is thought to be a negative acute phase protein. So, one may expect that the level of albumin after stroke may be found reduced from the premorbid level due to the acute stress response. But this is not likely to happen if it is measured within 24 hours of stroke onset as SA has a long half-life[18]. On the other hand, SA is acknowledged to be a marker of nutritional status[9], so SA measured within 24 hours of onset of stroke may be affected by the premorbid nutritional status which is again attributable to its long half-life[16]. In this study, diseases that may affect the SA level were excluded so that influence on SA from premorbid disease condition might be minimized and, on the other hand, SA was measured within 24 hours of onset of stroke so that the level of SA might not be affected by the stress resulting from stroke.

The mean (±SD) SA level was 36.06 (±4.474) gm/L in the present study. Likewise, the mean SA was 37 (±0.60)[16] and 42.7 (±4.3) gm/L[2] in previous two studies. The mean is slightly lower in the present study. The SA level ranged from 26 to 42 gm/L and 26 (52%) patients had SA level below the normal range (35-50 gm/dl)[19] and 24 (48%) patients had SA level within the normal range. This may reflect an overall malnourishment in the current study population, though, the investigator could not find any previous data regarding the population's normal range or mean of SA level.

In the current study, size of the infarct was also significantly associated (p=0.036, OR = 4.932, 95% CI = 1.113-21.854) with the short-term outcome of ischemic stroke which was also found in other similar studies[9]. On the other hand, another study found volume of infarct not to be correlated significantly with functional outcome[16]. Overall, in all of the studies including the current one, SA was either a predictor of or was associated or correlated with functional outcome of ischaemic stroke.

Conclusion

This study has revealed that the SA level within 24 hours of onset of ischemic stroke is independently associated with short-term functional outcome. Lower SA is associated with poor outcome and higher SA with good outcome. This is suggestive of a profound neuroprotective effect of SA. This conclusion conforms not only with the current study but also with the prior observational studies and preclinical and clinical trials. The other variable that is also independently associated with functional outcome is the size of infarct.

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