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Relationship of serum albumin with the severity and outcomes of stroke

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Abstarct

Objectives: To investigate the relationship of serum albumin with severity and outcome of stroke in Pakistani population

Material and methods: A prospective cross-sectional study was conducted in Medical Units of Khyber Teaching Hospital (KTH), Peshawar, KPK, Pakistan, during a 3-month period from 8th November 2010 to 8th Feb 2011. Patients, who were admitted to hospital for acute attack of stroke, were included in this study. Data regarding serum albumin, lipid profile and cerebrovascular risk factors were collected. Stroke severity was analyzed by NIHSS (National Institutes of Health Stroke Scale) while functional outcomes were evaluated on mRS (modified Rankin Scale).

Results: Total 62 stroke-patients' data were available during the study period, among which 44 patients were included on the basis of inclusion criteria. Hypertension was the most prevalent cerebrovascular risk factor followed by a concurrent heart disease. The mean pre hospitalization NIHSS score of the patient's with serum albumin below 4.5gm/dl was found to be 17.75 while post hospitalization score was 10.6. For this group, mean pre hospitalization mRS was found to be 4.6 while post hospitalization score was 3.4. These results show that low serum albumin levels were associated with greater stroke severity and poor functional outcomes. Similarly higher serum albumin levels were associated with decreased stroke severity, shorter hospitalization stay and better functional outcomes. Average serum albumin level was significantly higher in patients with good outcomes as compared to patients with poor outcomes (4.89 gm/dl versus 4.21 gm/dl; p-value = 0.01).

Conclusion: Higher serum albumin levels in stroke patients were associated with lesser stroke severity, shorter hospitalization stay and better functional outcomes. Larger studies are required to further investigate the role of albumin in the prognosis of stroke.

Key words

Stroke severity, stroke outcome, albumin, National Institutes of Health Stroke Scale (NIHSS), modified Rankin Scale (mRS)

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Introduction

Stroke is a clinical syndrome of rapid onset of focal cerebral deficit, lasting more than 24 hours or leading to death, with no apparent cause other than a vascular one [1]. Stroke is a major cause of disability worldwide and it is the 2nd most prevalent cause of death globally [2]. Because of the aging population and current smoking trend in developing countries, the stroke mortality burden is expected to increase greatly during the coming years [3]. In a recently conducted study, the prevalence of stroke in Pakistan is 6.4% and this is expected to rise because of the increased prevalence of risk factors that lead to stroke [4].

Stroke causes neuronal cell injury which arises from destructive biochemical substances released from a variety of sources. Serum albumin is a multifunctional protein which along with other properties also offers neroprotective effects. In some experimental studies on animal models of acute stroke, marked reduction in cerebral infarction and improvement of the neurological functions after external albumin therapy was observed [5]. Some studies reported positive correlation between serum albumin and prognosis of stroke, but further work is suggested to demonstrate this relationship [6-9]. It has also been pointed out that such studies are limited in various ethnic groups [10]. To the best our knowledge, no data are available about the relationship between serum albumin and prognosis of stroke in Pakistani population. Therefore, the purpose of this work was to investigate the relationship of serum albumin with severity and outcome of stroke in Pakistani population.

Materials And Methods

Study design, setting and study population

This was a prospective cross-sectional study conducted in Medical Units of Khyber Teaching Hospital (KTH), Peshawar, KPK, Pakistan, which is a tertiary-care hospital. This study included patients who were admitted to hospital for an acute attack of stroke during a three-month period, from 8th November 2010 to 8th Feb 2011. Patients with recurrent stroke and those who contracted aspiration pneumonia were excluded from the study.

Definition and classification of stoke

Stroke was defined as rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than of vascular origin [1]. Stroke was classified as either ischemic or hemorrhagic on the basis of the findings of the CT-scan.

Data collection and evaluation

The data collection team composed of two physicians and one pharmacist. The team prospectively collected patients' relevant information for the study that included: brain CT-scan (performed 24 hour after stroke), serum albumin, ESR (erythrocyte sedimentation rate), lipid profile and blood glucose (24 hour after acute phase of stroke). Cerebrovascular risk factors were recorded for each patient included hypertension, diabetes mellitus, hyperlipidemia, smoking and heart diseases (coronary artery disease, arthrosclerosis, myocardial infarction and atrial fibrillation). Hypertension was diagnosed when its presence was documented in medical records or when at least two readings of blood pressure were ≥140 mm of Hg (systolic) or ≥90 mm of Hg (diastolic) after acute phase of stroke. Diabetes mellitus was diagnosed if its presence was shown in medical records or when patient was taking oral hypoglycemic or insulin. Heart disease was diagnosed on the basis of medical history. Hyperlipidemia was diagnosed when it was present in medical record or when it was confirmed from the lipid profile of the patient after the acute phase of stroke. Patient was defined as smoker when there was history of smoking in the past 5 years. A pilot run was performed on six cases to determine the validity of data collection form to capture all the information required for data analysis.

Neurological function and stroke severity were measured with the National Institutes of Health Stroke Scale (NIHSS) [11]. The NIHSS is a widely used tool for measurement of stroke severity with established validity. It is a 15-item instrument addressing the severity of cerebral damage. The score represents observed levels of wakefulness, vision, sensation, movement, language function and perception. Total scores can range between 0 – 42 with higher scores indicative of increased severity. NIHSS was scored at the time of admission (pre hospitalization) and at the time of discharge (post hospitalization) by the data collection team. When the NIHSS score was between 1-4, stroke was ranked as mild stroke; when it was from 5-15, stroke was ranked as moderate; when the score was from 16-20, it was ranked as moderate-severe and when the score was from 21-42, it was ranked as severe stroke.

Functional outcomes were operationalized using the modified Rankin Scale (mRS) [12]. The mRS is a stroke-specific measure of level of functional independence as compared with pre stroke activity. A score of 0 – 5 is assigned with scores indicating the stroke survivor's disability level from "no symptoms" (0) to "severe disability" (5) while death is scored as six.

Statistical analysis

Data were presented in the form of frequencies and percentages, where appropriate. Difference in the means of two variables was determined using student t-test. P-value of 0.05 or less was considered statistically significant. SPSS version 16 was used for all statistical analyses.

Results

During the study period, a total of 62 stroke-patients were evaluated. Ten patients of recurrent stroke & eight patients with aspiration pneumonia were excluded and the remaining 44 patients were included in the study. Table 1 shows patients' demographics and cerebrovascular risk factors. In total of 44 patients, 34 (72.3%) patients were having ischemic stroke while 10 (27.72%) patients were having hemorrhagic stroke. Hypertension was the most prevalent cerebrovascular risk factor followed by a concurrent heart disease.

In order to assess the impact of serum albumin on various stroke variables, patients were divided into 3 groups on the basis of their serum albumin levels: (1) below 4.5 gm/dl, (2) from 4.5 gm/dl to 5.0 gm/dl, and (3) more than or equal to 5.1 gm/dl. Various stroke variables of each group were then analyzed (Table 2). The mean pre hospitalization NIHSS score of the patient's with serum albumin below 4.5gm/dl was found to be 17.75 while post hospitalization score was 10.6. The average hospital stay for this group was 8 days. The mean pre hospitalization mRS was found to be 4.6 while post hospitalization score was 3.4. The stroke variables of the second group (albumin level 4.5-5.0 gm/dl) were found to be significantly changed from first group. The mean NIHSS pre hospitalization score was 18.58 while post hospitalization score was 8.16. The average hospital stay was 7.75 days. Pre hospitalization mRS score was 4.91 while post hospitalization mRS score was 3.33. For the third group the mean pre hospitalization NIHSS score was 7.66 and the post hospitalization score was 1.6. The average hospital stay for this group was 5.75 days. Pre hospitalization mRS score was 4.16 while post hospitalization score was 1.5. The results show that low serum albumin levels were associated with greater stroke severity, longer hospital stay and poor functional outcomes while higher albumin levels were associated with decreased stroke severity, shorter hospital stay and better functional outcomes (Table 2).

To evaluate the impact of albumin on the functional outcomes of the stroke, the study population was divided into two groups: poor outcome and good outcome. Poor

outcome group patients were those whose mRS score at discharge was from 4 to 6 showing bad prognosis and physical dependency while the good outcome group patients were those whose mRS score at discharge was from 0 to 3. Albumin level was 4.21 gm/dl (rang: 3.3- 5) in poor outcome group, while 4.89 gm/dl (rang: 4-7) in good outcome group. Statistically, albumin level was significantly higher in the patient with good outcome ($p = 0.01$).

To further assess the importance and the impact of various factors towards the stroke outcome, the study population was divided into three groups on the basis of mRS at discharge: 0-1, 2-3 and 4-6 (Table 4).The mean age of the three groups were found to be different from each other. The group having the best outcome (0-1) had the lowest mean age (56 years) while mean age of the patients with poorest outcome (4-6) was 63.5 years. Thus it can be concluded that increased age had a negative impact on the stroke outcome. Hypertension and diabetes were more prevalent in the group with poor outcome. Mean albumin was highest in the first group having best functional outcomes at discharge and it was lowest in the group with poorest outcome showing that higher albumin is associated better outcomes (Table 4).

Discussion

Results of this study suggest that patients with higher serum albumin levels were having lesser stroke severity and good functional outcome than those with lower serum albumin. The higher the serum albumin, the better was the prognosis of stroke. These findings are consistent with many other studies. Cho et al. reported that higher serum albumin was associated with better functional outcomes in stroke patients [7]. In another study by Dziedzic et al. positive correlation was observed between albumin and stroke outcome [6]. Similar findings have been reported by some other researchers as well [8, 9].

Various mechanisms are proposed to explain the effect of serum albumin on stroke outcome. It is suggested that albumin decreases the hematocrit levels, impedes erythrocyte aggregation and reduces the erythrocyte sedimentation [8]. Albumin also antagonize thrombosis, stagnation and leukocyte adhesion within the postcapillary microcirculation in early reperfusion phase of stroke thus offering neuro protection in stroke patients [9]. In one experimental study, albumin therapy was administered to rats with experimentally induced stroke and observed for response to albumin therapy. It was found that albumin reduced the hematocrit acutely by 25% to 30%. This is similar to one previous study, in which albumin therapy produced an acute reduction in hematocrit from 40% to 23%. These studies reinforce the claim that albumin has hemodilutaroy effect [6]. Apart from hemodilutary effects albumin have effects on microcirculation. It is suggested that the free sulfhydryl group of albumin reacts with nitrogen oxides to form stable *S*-nitrosothiol. This *S*-nitrosothiol exerts actions like that of endothelium-derived relaxing factor which leads to improved microcirculation through vasodilatation and antiplatelet aggregation effects [13, 14]. Albumin maintained normal microvascular permeability by binding the endothelial glycocalyx. Albumin has metabolic effects on the brain. It generates calcium waves in the brain and also acts as a major regulator of pyruvate dehydrogenase [5, 15]. Pyruvate dehydrogenase is inhibited in cerebral ischemia and leads decreased metabolic activity and substrate entry into the neurons [16].

This study is limited by its small sample size. Therefore it should be considered a preliminary work in Pakistani stroke-population. It is suggested that further larger studies, preferably multi-center, should be conducted to investigate the relationship of albumin with stroke severity and outcome.

Conclusion

Higher serum albumin levels in stroke patients were associated with lesser stroke severity, shorter hospitalization stay and better functional outcomes. Larger studies are required to further investigate the role of albumin in the prognosis of stroke.

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Table 1 Patients' demographics and cerebrovascular risk factors

Variable	Frequency	Percentage
Men	26	59.0
Women	18	41.0
Ischemic stroke	34	77.3
Hemorrhagic stroke	10	22.7
Deaths	4	9.0
Hypertension	23	52.3
Diabetes	19	43.2
Dyslipidemia	14	31.8
Heart disease	20	45.5
Smoking	9	20.5

Table 2 Stroke variables of study population according to albumin levels

Variables		Groups on the basis serum albumin (gm/dl)		
		< 4.5 (n = 20)	4.5-5.0 (n = 12)	≥5.1 (n = 12)
NIHSS score	Pre hospitalization	17.75(4-31)	18.58(10-31)	7.66(4-14)
	Post hospitalization	10.6 (0-42)	8.16 (1-42)	1.6 (0-4)
mRS score	Pre hospitalization	4.6 (4-5)	4.91 (4-5)	4.16 (4-5)
	Post hospitalization	3.4 (1-6)	3.33 (2-4)	1.5 (1-3)

Table 3 Serum albumin and clinical outcome*

Outcome**	Mean serum albumin (gm/dl)	P-value
Good	4.89	0.01***
Poor	4.21	

*This table presents comparison of mean serum-albumin level of patient with good outcome and mean serum-albumin level of patient with poor outcomes.
**Outcome is based on modified Rankin Scale (mRS). For Good outcomes, mRS score = 0-3; while for poor outcomes, mRS score = 4-6.
***Difference is statistically significant.

Table 4 Main traits of the study population according to the functional outcome at discharge

Variables	mRS at discharge		
	mRS 0-1(n=10)	mRS 2-3 (n=18)	mRS 4-6 (n=16)
Age (mean)	56 (45-60)	61.7 (50-75)	63.5 (55-70)
Male(n)	8	9	7
Female (n)	2	9	9
NIHSS (admission mean)	6.5 (4-10)	11.55 (4-21)	24.8 (15-31)
NIHSS (discharge-mean)	1.5 (0-3)	2.8 (0-6)	16.5 (4-42)
Ischemic (n)	9	13	12
Hemorrhagic (n)	1	5	4
Hypertension (n)	4	10	9
Diabetes (n)	2	9	8
Smoking (n)	5	1	3
Dyslipidemia (n)	3	5	6
Heart Disease (n)	2	10	8
Albumin (mean)	5.2 (3.8-6.2)	4.7 (3.4-7)	4.2 (3.3-5)