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Relationship Between Admission Hypoalbuminemia and Inhospital Mortality in Acute Stroke

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Abstract: This study aims at assessing the relation between hypoalbuminemia and inhospital mortality in patients with acute stroke. In this cross-sectional study, a total of 112 consecutively admitted patients with first acute stroke in Ahvaz Jundishapur Hospital were enrolled. All patients hospitalized for 7-9 days or expired in this period of time. Admission hypoalbuminemia (serum albumin<3.5 mg dL^{-1}) as well as other prognostic factors were determined and compared between the two groups. One hundred and twelve patients, 74 males and 38 females with the mean age of 69.2±12.1 (66-79) years were enrolled. Twenty nine (25.9%) patients expired during the hospitalization. Totally, admission hypoal buminemia was present in 49 (43.8%) patients. 43% of the patients were Hypoalbuminemia. Frequency of patients with admission hypoalbuminemia and is chemic heart disease was significantly higher in the nonsurvivors (75.8- 32.5%, p = 0.001; 34.5 vs. 16.9%, p = 0.047, respectively). The mean Glasgow Coma Scale score was significantly lower in the nonsurvivors (8.1±1.8 vs. 9.4±0.5, p = 0.003). These three parameters remained significant in multivariate analysis. Sex, age, history of hypertension, diabetes mellitus, hypertriglyceridemia, hypercholesterolemia, anemia, heart failure and smoking habit, admission atrial fibrillation, ethnicity and stroke type were comparable between the two groups. In conclusion, hypoalbuminemia is an independent predictor of inhospital mortality in patients with acute stroke.

Key words: Serum albumin, cerebrovascular accident, prognosis, stroke, inhospital mortality

INTRODUCTION

Stroke is the third leading cause of death in the United States. Each year approximately 700000 people are affected by stroke in the West and on average; one patient expires eventually every 3 min (Thom *et al*., 2006; CDC, 2002). The inhospital mortality rate varies between 5-3% according to the type of stroke (ischemic or hemorrhagic) (Liebeskind *et al*., 2006; Gillum and Johnston, 2001). It is generally believed that the early death after stroke is mainly attributable to the disease itself, whereas the death after acute phase is due to the hospitalization and the related complications during this period (Famakin *et al*., 2010). Identifying possible factors in early death after stroke may be useful in designing screenin g programs for early detection of high-risk patients, which in turn would lead to decreased avoidable mortality rate. These etiologies have been extensively evaluated in previous studies and are diverse such as the severity and type of stroke, type of ischemia, volume of hemorrhage, age of patient, level of consciousness, hyperglycemia, etc. However, these factors have been in majority associated with the final outcome; i.e. weeks or months after the first episode of stroke (Cucchiara *et al*., 2004; Frankel *et al*., 2000; Hamidon and Raymond, 2003). Hypoalbuminemia may be an indirect marker of systemic conditions such as malnutrition and patients with low albumin levels may have other underlying chronic medical or neurologic conditions that impair their ability to recover from acute stroke. Alternatively, low albumin levels at the time of acute stroke may simply be indicative of the role of albumin as a negative acute phase reactant whose concentration decreases during acute inflammatory states (Ebersole and Cappelli, 2000). Despite its importance, hypoalbuminemia has not been widely evaluated as a predictor of mortality after acute stroke. In a study by Dziedzic *et al*. (2007) hypoalbuminemia was a frequent finding in acute stroke patients and it was associated with more severe stroke and pro-inflammatory pattern of serum protein electrophoresis. Zuliani *et al*. (2006) also reported that the hypoalbuminemia was an independent risk factor for short-term mortality in patients with acute ischemic stroke. To the best of our knowledge all the studies in

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this regard have been conducted in the West. It is believed that the ethnicity and even demographic factorsmay influence the role of prognostic determinants of stroke (Heuschmann *et al*., 2004). This main aim of this study is to assess the association of hypoalbuminemia in a group of Arab and Azari Iranian patients with stroke with the inhospital outcome.

MATERIALS AND MATHODS

In this cross-sectional study, 184 patients with first acute stroke were recruited during a 12-month period from June 2009 to June 2010 in Ahvaz Golestan and Imam Reza Teaching Hospitals. This hospital is a main referral center for the neurologic diseases in the south-west and north-east of Iran. The study was carried out on 112 cases out of the first 184 patients. Patients' characteristics and basic data including age, sex, ethnicity (Arab, Azari), Glasgow Coma Scale score, smoking status, atrial fibrillation on admission and coexisting disease including previous heart failure, ischemic heart disease, hypertension, diabetes mellitus, hyperlipidemia, hypercholesterolemia and anemia, stroke type (ischemic, hemorrhagic), admission serum albumin and hypoalbuminemia and inhospital death were ascertained. Hypertension was defined as a systolic blood pressure > 140, diastolic blood pressure > 90 mmHg or a positive history of taking antihypertensive medication. Diabetes mellitus was defined as a fasting plasma glucose > 126 mg dL^{-1} or a positive history of taking diabetic medication. Hypertriglyceridemia was defined as a fasting serum triglyceride level > 200 mg dL^{-1} or a positive history of taking lipid-lowering drugs. Hypercholesterolemia was defined as a fasting total serum cholesterol level > 240 mg dL^{-1} or a positive history of taking cholesterol-lowering drugs. Anemia was defined as hemoglobin level<12 mg dL^{-1} in males or <11 mg dL^{-1} in females (Fauci *et al*., 2008). Serum albumin concentration was measured in a blood sample obtained by venipuncture from all participants using a Hitachi 737 Analyzer (Boehringer-Mannheim Diagnostics; USA) (McQuillan *et al*., 1990). Hypoalbuminemia was defined as a serum albumin level<3.5 mg dL^{-1} (Dziedzic *et al*., 2007). All patients were discharged or expired 7-9 days after acute stroke. Patients with conditions other than the parenchymal brain hemorrhage were excluded. The mentioned variables were compared between the survivors and nonsurvivors. This study was approved by the ethics committee of Ahvaz and Tabriz Universities of Medical Sciences. Statistical analysis was performed using the SPSS software (Chicago, IL), version 15.0. Data are presented as mean±standard deviation or frequency (percent). Independent samples t-test, Chi-square test or Fishers' Exact test were used for analysis where appropriate. Logistic regression test was used for multivariate analysis. p-value of <0.05 was considered significant.

RESULTS

One hundred and twelve patients, 74 (66.1%) males and 38 (33.9%) females with the mean age of 69.2±12.1 (66-79) years were enrolled. The mean Glasgow Coma Scale score was 8.8±1.6 (8-10). Regarding the ethnicity, 67 (59.8%) patents were Azari and 45 (40.2%) patients were Arabs. The stroke was is chemic

Table 1: Distribution of patients characteristics and serum albumin status, stratified by patients outcome

Variable	Non-survived (n = 29)	Survived (n = 83)	p-value
Sex			
Male	15 (20.3)	59 (79.7)	0.058
Female	14 (36.8)	24 (63.2)	
Age (years)	71.5±12.1	66.9±12.2	0.085
Glasgow Coma Scale score	8.1±1.8	9.4±0.5	0.003*
Diabetes mellitus	10 (37)	23 (27.7)	0.358
Hypertension	21 (72.4)	58 (71.6)	0.934
Hypertriglyceridemia	5 (17.2)	12 (15)	0.776
Hyperchlostrolemia	6 (20.7)	21 (25.3)	0.617
Anemia	9 (3.33)	22 (28.6)	0.642
Smoking	6 (20.7)	25 (30.9)	0.296
Heart failure	4 (14.3)	4 (5.3)	0.207
Ischemic heart disease	10 (34.5)	14 (16.9)	0.047*
Admission atrial fibrillation	7 (24.1)	10 (12.3)	0.115
Ethnicity			
Azari	13 (44.8)	54 (65.1)	0.056
Arab	16 (55.2)	29 (34.9)	
Stroke type			0.708
Ischemic	22 (75.9)	60 (73.2)	
Hemorrhagic	7 (24.1)	23 (27.7)	
Admission hypoalbuminemia (< 3.5 mg dL^{-1})	22 (75.8)	27 (32.5)	0.001*

Data are shown as mean±standard deviation or frequency (percent). *Statistically significant

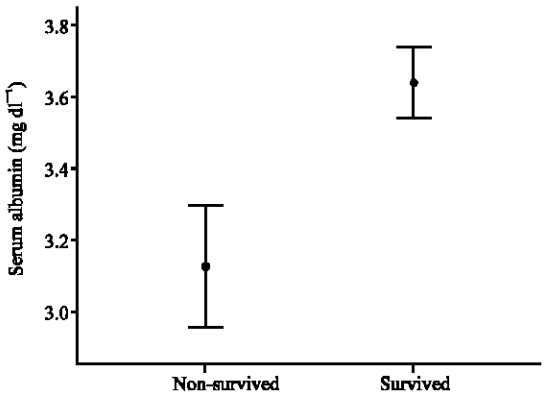

Fig. 1: Error bar of the mean serum level of albumin in survived and non-survived stroke patients.

Type in 82 (73.2%) patients and hemorrhagic type in 30 (26.8%) patients . Positive history of diabetes mellitus was present in 33 (29.5%) patients, hypertension in 79 (70.5%) patients, hyperlipidemia in 17 (15.2%) patients, hypercholesterolemia in 27 (24.1%) patients, anemia in 31 (27.7%) patients, smoking in 31 (27.7%) patients, heart failure in 8 (7.1%) patients, atrial fibrillation in 17 (15.2%) patients and ischemic heart disease in 24 (21.4%) patients. Admission hypoalbuminemia was confirmed in 49 (43.8%) patients. Twenty nine (25.9%) patients expired in hospitalization period and the remaining 83 (74.1%) patients were discharged. Different variables are summarized and compared between the survived and non-survived cases in Table 1. Accordingly, frequency of patients with ischemic heart disease (relative risk = 1.9) and hypoalbuminemia (relative risk = 4.2) was significantly higher in the expired group. The mean Glasgow Coma Scal e score was significantly lower in the expired cases too. There was no significant difference with regard to age, sex, previous history of diabetes mellitus, hypertension, hyperlipidemia, hypercholesterolemia, anemia, smoking , hear t failure and atrial fibrillation, ethnicity and type of stroke between the survivors and non-survivors. The mean level of serum albumin was 3.1±0.4 mg dL^{-1} in the expired patients and 3.6±0.5 mg dL^{-1} in the discharged group. This difference was statistically significant ($p<0.001$) (Fig. 1). The hypoal buminemia was independent risk factor of mortality after adjustment for the presence of heart failure ($p = 0.02$, Exp (B) = 3.2 for hypoalbuminemia; $p = 0.04$, Exp(B) = 1.3 for heart failure, $p = 0.03$, Exp (B) = 1.1 for Glasgow Coma Scale score).

DISCUSSION

In this well-controlled study, independent association of admission hypoalbuminemia with short-term (inhospital) mortality in stroke patients was documented. Albumin concentrations have long been used as a measure of health and disease. Many conditions such as undernutrition, catabolism, and liver and renal disease may reduce serum albumin concentrations. The catabolic state and the associated neuroendocrine response that is likely to follow an acute stroke may lead to altered serum albumin concentrations and there is recent evidence linking the high stress reaction after stroke and undernutrition (Gariballa *et al.*, 1998). Although the data in this regard are scarce in the literature; there are inconclusive, as well. Rordorf *et al.* (2000) did not report hypoalbuminemia among predictors of mortality in stroke patients admitted to the intensive care unit (Rordorf *et al.*, 2000) This is in contrast with our finding. It should be noticed that the above study was conducted in a retrospective manner and so this decreases its value. In another study evaluating predictors of short-term mortality in patients with stroke, hypoalbuminemia was found to be a predictor of mortality in older patients (median age 80 years) in the univariate analysis, but not in the multivariate analysis (Zuliani *et al.*, 2006). The result of this study is also in contrast with ours. Older age of its patients may justify the difference in results. In our study, the mean age of patients was 69.2 years which is much less than 80 years in above investigation. In older age, finding a significant independent contributor to death may be very hard, because there are many risk factors in this regard. In fact, very old patients with acute stroke show a differential clinical profile, different frequency of stroke subtypes, and a poorer outcome compared with stroke patients who are younger (Arboix *et al.*, 2000). On the other hand, in a recent series by Famakin *et al.* (2010) 1477 patients admitted with acute stroke were evaluated. The inhospital death rate was 10%. Univariate analysis showed that mortality was associated with older age, stroke type, Glasgow Coma Scale score less than 9, decreased serum albumin, elevated creatinine, and elevated blood glucose. In the multivariate analysis, independent risk factors for mortality after acute stroke included older age, stroke type, Glasgow Coma Scale score less than 9, and decreased serum albumin. There was no relationship between race and inhospital mortality. The serum level of albumin was less than 3.4 mg dL^{-1} in the expired group. Comparing with our findings, we also did not a relationship between race and mortality. Likewise, the hypoalbuminemia was also an independent predictor of

inhospital mortality. The mean serum level of albumin was 3.1 mg dL^{-1} in nonsurvived patients which is similar to the reported figure in above study. In addition, we did not find any other risk factor for inhospital mortality except for the ischemic heart disease and Glasgow Coma Scale score. This is also in conformity with previous reports (Sweileh, 2008). Dziedzic *et al.* (2007) measured albumin and other serum protein fractions within 36 h after ischemic stroke using electrophoresis. Hypoalbuminemia defined as serum albumin level <3.5 mg dL^{-1} was found in 45.5% of patients. It was associated with more severe stroke and pro-inflammatory pattern of serum protein electrophoresis. The frequency of hypoalbuminemia was 43.8% in our series which is very near to the reported rate in mentioned study. Likewise, the association between hypoalbuminemia and poor outcome of patients with stroke is similar in two studies, as well. Freire *et al.* (2005) showed that o nly severe admission hypoalbuminemia (<2 mg dL^{-1}) is independently associated with poor outcome in patients with acute stroke (Freire *et al.*, 2005). We did not calculate an optimal cut-off point in this regard due to small sample size needed for this propose. Further studies with larger sample sizes may be helping. Gariballa *et al.* (1998) concluded that the serum albumin concentration in the hospital was a strong and independent predictor of mortality at 3 months after acute stroke with hazard ratio of 0.91 for a 0.1 mg dL^{-1} higher serum albumin concentration. They proposed that whether nutritional supplementation with albumin removes or mitigates the hazard of poor outcome associated with undernutrition after acute stroke needs to be determined. Although the relative risk of hypoalbuminemia in prediction of death (4.2) was higher in our study, the result of current study is in line with the mentioned report. It should be noticed that the mortality rate was not determined during the hospitalization period in above study. It is not known whether reversing hypoalbuminemia or maintaining adequate albumin levels in patients with acute stroke will decrease mortality. An ongoing clinical trial of intravenous albumin may shed some light on the effect of treatment of patients with acute ischemic stroke (Ginsberg *et al.*, 2006).

CONCLUSION

In current study, we report hypoalbuminemia as an independent predictor of inhospital mortality for acute stroke in a referral center in Iran. We propose routine serum albumin measurement in management of patients with acute stroke to stratify cases at high risk for inhospital mortality.

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