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Relationship between Serum Sodium level and Impairment and Disability in Stroke Patients

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ABSTRACT

Background and Objective: Hyponatremia is associated with adverse outcomes and increased mortality in acute stroke patients. However, the role of hyponatremia as a negative prognostic indicator has been controversial. This study was conducted to determine the relationship between serum sodium level and impairment and disability in stroke patients in Babol, northern Iran.

Methods: This cross-sectional study was conducted in 6 months on 125 stroke patients admitted to Ayatollah Rouhani Hospital in Babol. The National Institutes of Health Stroke Scale and the Modified Rankin Scale were used to determine the impairment and disability caused by stroke. Venous blood was collected to determine the serum concentrations of sodium. The normal ranges were defined as 135-145 mEq/L.

Findings: Of 125 stroke patients, 108 cases (86.4%) were ischemic stroke. Eighty-two cases (65.5%) had hyponatremia. The type of stroke showed statistically significant difference with hyponatremia in 14 hemorrhagic stroke cases (17%) versus 68 ischemic stroke cases (83%) (p=0.01). Furthermore, the difference in gender showed statistically significant difference with hyponatremia in 49 women (59%), and 33 men (41%) (p=0.02). In hyponatremic patients, the severity of impairment at admission (p=0.01) and disability at discharge time (p=0.02) was higher than patients with normal sodium serum level. In patients with a history of smoking, 9 cases (21%) had normal sodium level while 33 cases (79%) had hyponatremia (p=0.03).

Conclusion: The results of the present study showed that the severity of impairment and disability at the time of discharge in stroke patients is related to serum sodium level. Therefore, paying attention and correcting serum sodium level should be considered more in acute stroke patients.

Keywords: *Stroke, Ischemic Stroke, Hemorrhagic Stroke, Hyponatremia, Disability Evaluation*.

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Introduction

Stroke is one of the leading causes of death worldwide (1-4). Among the most debilitating neurological diseases, stroke is the leading cause of serious long-term disability (5, 6). Two-thirds of all strokes occur in developing countries despite their preventable nature (7). In addition to high mortality rate, it is one of the most important healthcare issues which imposes a lot of financial burdens on families and countries (8).

Stroke patients frequently develop electrolyte disturbances in their clinical course, of which hyponatremia is especially a trigger that exacerbates neurological symptoms. It is the most common electrolyte imbalance in patients with acute cerebrovascular insults (9). In addition, it can exacerbate the outcomes and increase mortality. It is frequently observed in patients with stroke either on admission (3.9-45.3%) or during their hospitalization (40-45%) (10). When the level of sodium in the blood is low, it could cause cerebral edema, seizures, and disturbance of consciousness. In addition, low sodium status may cause volume depletion leading to cerebral ischemia and cerebral infarction. In a meta-analysis by Shima et al., the association between hyponatremia and poor outcomes in patients was confirmed. The patients with post-stroke hyponatremia were 1.7 times more likely to die within 90 days and had high mortality during hospitalization (11, 12). Hyponatremia is an independent predictor of 3-year mortality in first-ever ischemic stroke (13).

As has been reported in some studies, despite this evidence, there is still no consensus on how the mechanism of hyponatremia affects the prognosis of stroke patients (14). The serum sodium level to determine the prognosis of stroke (13), and the difference in prevalence in populations based on disease subtypes, show the disagreement about the role of hyponatremia in different diseases (15). It is necessary to raise the awareness of relevant authorities in this regard (16).

Considering this issue, the prognostic significance of hyponatremia has not been sufficiently examined and data on electrolyte changes in neurological disorders like stroke is insufficient in Iran. This study aims to determine the relationship between hyponatremia and impairment and disability of these patients along with other related variables to take the appropriate preventive and therapeutic measures.

Methods

This cross-sectional study was conducted on 125 stroke patients admitted to Ayatollah Rouhani Hospital in Babol within six months after approval by the Ethics Committee of Babol University of Medical Sciences with the code MUBABOL.HRI.REC.1395.55. This hospital is the main stroke treatment center in the north of Iran. According to the incidence of stroke in Babol, which is 50 per 100,000 people, the sample size was determined based on a previous study (17) and consultation with a biostatistician. Informed consent was obtained from each participant or their kin before the interview or neurological examination.

Inclusion criteria were all admitted stroke patients who were higher than 18 years and less than 24 hours passed their admission. Exclusion criteria were transient ischemic attack (TIA), hemiparesis or any focal neurological findings resulting from head trauma, metabolic encephalopathy, brain mass lesions such as brain tumor or brain abscess, hemiplegic migraine attack, and postictal of seizures. In addition, patients with renal failure, liver failure and patients under treatment of corticosteroid drug were excluded. Moreover, patients who had pneumonia or used antihypertensive drugs, and diuretics as possible causes of hyponatremia, were excluded in the study.

Diagnosis of stroke was based on standards of the American Heart Association-American Stroke Association (18). The stroke in this study was divided into ischemic and hemorrhagic types; the ischemic stroke (IS) included thrombotic and embolic (cardiac origin and artery to artery) and according to TOAST

classification, it was divided into five groups as large vessel occlusion, small vessel occlusion, cardiac emboli, the stroke of other determined etiology, and the stroke of undetermined etiology. The hemorrhagic stroke (HS) was divided into intra cerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH) subtypes. Stroke was diagnosed by a neurologist, based on the patient's history, neurological examination and neuroimaging studies which were performed for all consecutive stroke patients. The severity of impairment at admission was determined on the basis of NIH Stroke Scale (NIHSS) criteria (i.e., scores≤8 showed mild stroke; scores 9-15 showed moderate stroke; and scores≥ 16 showed severe stroke) (14). The disability of patients to be discharged was determined based on the modified Rankin Scale as mild, moderate and severe (18). In this study, mild disability included patients with a score of 2 or less, cases with a score of 3 were considered as moderate disability, and a score of 4 was considered as severe injury.

Blood sample was collected during the first 24 hours after the onset of stroke. The venous blood (0.5ml) was taken and sodium serum level was analyzed based on latex particle agglutination test by Hitachi 912 auto analyzer. Patients based on sodium serum level were divided into two groups. The serum sodium concentration<135 mmol/L (135 mEq/L) was considered as hyponatremic and 135 to 145 mmol/L was defined as normal serum level (19).

The data were recorded through a checklist, which included age, gender, time of stroke onset and hospitalization time, type of stroke and stroke severity score at the time of admission and the degree of stroke disability at the time of hospitalization and discharge (3 to 7 days after admission).

The history of risk factors in stroke survivors such as hypertension (HTN), ischemic heart disease (IHD), diabetes mellitus (DM), hyperlipidemia (HLP) and smoking were recorded. The systolic blood pressure less than 140 mmHg and diastolic less than 85 mmHg were considered as normal. Fasting blood sugar greater than 126 mg/dl was considered as diabetes. Triglycerides higher than 150 mg/dl were considered as high triglycerides, HDL less than 40 mg/dl in men and 50 mg/dl in women was considered as low HDL and LDL higher than 130 mg/dl was considered as a high LDL (20). History of ischemic heart disease was obtained from background information history of cardiac medications and electrocardiogram. Smoking (cigarettes) was defined as a daily intake of at least 5 cigarettes for at least a year earlier. Patients with at least one major risk factor were considered as a positive risk factor.

The study data were compared using SPSS version 23 and Independent Samples T Test and chi-square test, and $p<0.05$ was considered significant.

Results

Out of 125 stroke patients included in the study, 82 cases (65.6%) of stroke patients had hyponatremia during hospitalization. The difference with hyponatremia based on gender was statistically significant (49 women [60%] versus 33 men [40%]) (p=0.02). According to the TOAST classification of ischemic stroke patients, 42 cases (49%) of large vessel occlusion, 28 cases (26%) of small vessel occlusion, 11 cases (10%) of cardiac embolism, and 27 cases of occlusion (15%) with other known or unknown causes.

Of 17 hemorrhagic patients (13.6%), 12 cases (70.6%) were ICH and 5 cases (29.4%) were SAH. The difference based on the type of stroke with hyponatremia was statistically significant (68 IS cases [82%] vs. 14 HS cases [17%]) (p=0.01). The frequency of different types of stroke and demographic variables in patients with hyponatremia in comparison with normal serum sodium level were shown in Table 1. History of smoking as a stroke risk factor was present in 42 stroke patients (33.60%), among which 9 cases (21%) had normal sodium level and 33 cases (79%) were hyponatremic (p=0.03). The stroke risk factors such as HTN, IHD, DM and HLP were seen in 104 cases (83.2%), among which 66 cases (63.5%) had hyponatremia, and 38 cases (36.5%) had normal serum level of sodium (p=0.36).

The difference in the National Institutes of Health Stroke Scale between hyponatremic vs. normal serum sodium level stroke patients was statistically significant (p=0.01). Thus, only 4 cases (14%) of normal sodium level vs. 24 cases (86%) of hyponatremic patients were seen in the severe impairment category. The difference in the degree of disability (mRS) of stroke patients at discharge in 5 cases (15%) with normal sodium level vs. 28 cases (85%) with hyponatremia were seen in severe disability category (p=0.02). Unfortunately, the mortality rate was 12 cases (9.6%) in stroke patients after hospitalization; 4 cases (33.3%) in patients with normal sodium level vs. 8 cases (66.7%) in hyponatremic patients. The mortality in hyponatremic patients was twice as normal sodium level patients. So, there was clinically significant difference in mortality rate between the two groups (p=0.93).

Table 1. Stroke types, risk factors, severity, and early prognosis in stroke patients with or without Hyponatremia in Babol

Variable	Normal Sodium* Number(%)	Hyponatremia Number(%)	Total Number(%)	p-value**
Gender				
Female	21(30)	49(70)	70(56)	0.02
Male	22(40)	33(60)	55(44)	
Ischemic				
Thrombotic	31(36)	54(64)	85(68)	0.81
Embolic	9(40)	14(60)	23(18.40)	
TOAST Definition				
Large vessel occlusion	16(38)	26(62)	42(49)	0.76
Small vessel occlusion	10(36)	18(64)	28(26)	
Cardiac emboli	4(36)	7(64)	11(10)	
Other and undetermined	10(37)	17(63)	27(15)	
Hemorrhagic				
Subarachnoid	1(20)	4(80)	5(29.40)	0.87
Intracerebral	2(17)	10(83)	12(70.60)	
Severity (NIHSS) at admission*				
Mild	16(34)	31(64)	47(37.60)	0.01
Moderate	23(46)	27(54)	50(40)	
Severe	4(14)	24(86)	28(22.40)	
Smoking				
Yes	9(21)	33(79)	42(33.60)	0.03
No	34(41)	49(59)	83(66.40)	
Risk factors				
Yes	38(36.50)	66(63.50)	104(83.20)	0.36
No	16(76)	5(24)	21(16.80)	
Disability (mRS) at discharge*				
Mild	16(41)	23(59)	39(34.50)	0.02
Moderate	18(44)	23(56)	41(36.20)	
Severe	5(15)	28(85)	33(29.20)	
Mortality				
No	39(34.50)	74(65.50)	113(90.40)	0.93
Yes	4(33.30)	8(66.70)	12(9.60)	

***The serum sodium concentration ([Na^+])< 135 mmol/L (135 mEq/L) was considered as Hyponatremia and 135 to 145 mmol/L was defined as normal serum levels. Serum level assessment was performed with Latex particle agglutination test with Hitachi 912 auto analyzer in Ayatollah Rouhani Hospital Laboratory.**

****Chi-square or Fisher exact test were used between demographic and clinical variable with sodium serum levels.**

*****Abbreviations: National Institute of Health Stroke Scale (NIHSS), Modified Rankin Scale (mRS).**

Discussion

Based on the findings of this study, the difference in the severity of disorder during hospitalization in stroke patients with hyponatremia compared to the normal serum sodium level was statistically significant, and it was more severe in cases of hyponatremia, which was similar to the study of Rodrigues et al., who concluded that the severity of disorder increased during hospitalization until discharge in the hyponatremia group (12). On the other hand, in the study of Badikillaya et al., no correlation was observed between the severity of stroke and hyponatremia (21). In addition, in the study of Kembuan et al., no association was observed between blood sodium abnormalities and acute stroke severity, although electrolyte abnormalities were common during hospitalization (22). If the association between hyponatremia and stroke severity is confirmed, the question arises as to whether hyponatremia leads to severe stroke or does more severe stroke lead to more hyponatremia. Our findings also showed that hyponatremia is associated with an increase in impairment during hospitalization and inability to discharge, which is consistent with the results of Rodrigues. How and through what mechanisms hyponatremia aggravates the disorder needs further investigation.

In the present study, there was no statistically significant difference between the mortality rate of stroke patients with hyponatremia and the control group, but in some studies, the mortality rate of stroke patients with electrolyte imbalance was higher than that of patients with normal levels. In addition, in the study of Soiza et al. in Brazil, patients with hyponatremia aged less than 75 years showed a significant difference in mortality prognosis (13). In the study by Huang et al., they concluded that hyponatremia was a predictor of three-year mortality in first stroke, indicating that hyponatremia can be a strong prognostic factor for the acute phase (23). Despite these results, our findings did not confirm that hyponatremia is a strong predictor of increased mortality in the acute phase of hospitalized patients. In justifying the lack of relationship between hyponatremia and premature mortality rate in our study, we can mention the short prognostic period of hospitalization (up to one week) in this study. Differences in health care, medical and nursing services, and avoiding excessive fluid therapy, along with many other factors, were also involved in the premature death rate of these patients.

The frequency of hyponatremia in stroke patients in Babol in this study was 66%, which is high compared to other studies. In the study of Soiza et al. in Brazil, of 8540 stroke patients, the prevalence of hyponatremia was 14% (13). In the study of Rodrigues et al., of 3585 patients with ischemic stroke, the prevalence of hyponatremia was 16%, and in the study of Saleem et al., the prevalence of hyponatremia was 35% (12, 24). The reasons for the large difference between the low frequency (14-35%) of hyponatremia in these studies and our study (66%) could be due to different study methods (25), for example, due to the small sample size. In addition, it can be due to different lifestyles and differences in health policies in controlling risk factors.

Based on the serum sodium level in stroke patients, the frequency of stroke risk factors in the two groups did not show a statistically significant difference, but smoking in cases of hyponatremia was higher compared to stroke patients with normal serum sodium level. According to this finding, smoking as a risk factor should be taken for granted considering the relationship between smoking history in the past in hyponatremic stroke patients. Regarding the association of stroke risk factors with hyponatremia, in a study by Huang et al., diabetes mellitus was more conspicuous in cases of stroke with hyponatremia during hospitalization (23). Maybe some of these risk factors for hyponatremia will be confirmed in future studies, and these findings may be useful in the prevention or treatment of these patients.

Based on the findings of this study, the ratio of hyponatremia cases to normal serum sodium level cases was higher in patients with hemorrhagic stroke than in ischemic patients. In the study of Alam et al., 23% of hemorrhagic patients and 21% of ischemic patients had hyponatremia (26). Furthermore, in some other

studies such as Saleem et al., hyponatremia was seen more in hemorrhagic patients (24). The study of Babaliche et al. showed that hyponatremia is more common in hemorrhagic strokes (27). The strength of our study is that it examined the impact of hyponatremia on various aspects of stroke such as types, risk factors, prognosis, disability and mortality after stroke. The limitations of this study were the small sample size, lack of control group, and the short follow-up period.

The results of the present study showed that there is a significant relationship between the increase in the severity of the impairment from hospitalization to disability at the time of discharge in hyponatremic patients. The prevalence of hyponatremia in patients with acute cerebral stroke was high and it can be considered as a predictor of severity of impairment during hospitalization and disability during discharge. Therefore, paying more attention and correcting the serum sodium level should be well considered in acute stroke patients.

Conflict of interest: The authors declare that there is no conflict of interest.

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