

Correlation of Sodium and Serum Albumin Levels with the Severity of Acute Ischemic Stroke

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ABSTRACT

Management of acute ischemic stroke patients based on their severity in emergency services is critical. One of the easy, fast, and affordable biochemical markers is serum sodium and albumin, which correlate with the severity of acute ischemic stroke. This research aimed to analyze the correlation of serum sodium and albumin levels with the severity of acute ischemic stroke. This retrospective study used medical record data of 165 acute ischemic stroke patients for the period January 2018-April 2021 at Dr. Wahidin Sudirohusodo Hospital, Makassar. Patients were classified according to the degree of mild, moderate, or severe stroke through the NIHSS score. Examination of serum sodium was done by Electrolyte Analyzer NOVA 5 and albumin with ABX Pentra 400. Data normality test Kolmogorov-Smirnov. The statistical test used the Kruskal-Wallis, Mann-Whitney, and Spearman (significant if $p < 0.05$). There was a negative correlation between serum albumin levels and the severity of stroke patients ($p < 0.001$; $r = -0.327$). There was no significant association between serum sodium and ischemic stroke severity. There was a statistically significant difference in serum albumin levels in patients with mild and moderate stroke ($p = 0.001$), mild and severe ($p = 0.001$). Albumin correlates the outcome of acute ischemic stroke patients ($p < 0.001$), cut-off ≤ 3.25 g/dL (sensitivity 66.7%, specificity 50%). Hypoalbuminemia exacerbates cytotoxic edema by causing water and ions to cross the blood-brain barrier to the astrocytes resulting in further neuron damage. Albumin has a correlation with the NIHSS score ($p < 0.001$; $r = -0.327$). The lower the albumin level, the higher the NIHSS score, indicating the ischemic stroke severity.

Keywords: Ischemic stroke, sodium, albumin

INTRODUCTION

Ischemic stroke is a neurology abnormality caused by a decrease of perfusion to the brain tissue that can cause a cerebral infarct. Ischemic stroke happens in 85% of all stroke cases.¹ Data from World Health Organization (WHO) states that there are 13.7 million new stroke cases and at least 5.5 million deaths due to stroke every year. Riskesdas (basic health research) stated that in 2018, the stroke prevalence in Indonesia rose from 7% in 2013 to 10.9% in 2018. A 71.66% incidence of hyponatremia was found in stroke patients.² Hyponatremic strokes can be caused by Syndrome of Inappropriate Antidiuretic Hormone (SIADH) or Cerebral Salt Wasting Syndrome (CSWS) that causes complications such as seizures or even death.^{3,4} Stroke patients with hyponatremia have a 60% mortality.⁵

Hypoalbuminemia can worsen the prognosis of acute ischemic stroke patients because it could

increase the risk of complications, infection, length of hospitalization, and mortality.⁶ Plasma albumin can be a neuroprotector toward ischemic stroke by decreasing the volume and brain edema, increasing the blood flow to the brain, which is in a perfusion crisis, and increasing microvascular perfusion.^{7,8} The patient neurological status is classified using the National Institute of Health Stroke Scale (NIHSS) scoring system, which is measured immediately at hospital admittance and describes the stroke severity in every patient.^{9,10} Swamy *et al.* showed that an acute ischemic stroke patient with hyponatremia had a higher NIHSS score on the first day, fifth day, and at the end of hospital care.¹¹ Sodium and albumin serum tests can be done in the emergency room on the early onset of acute stroke patients' admittance because the tests are easy to do, fast, and feasible for most health facilities. If the serum sodium and albumin are measured and corrected in the early phase of the disease, the patient will have a better prognosis, decreasing the disease's mortality.^{9,12,13}

Based on what is stated above, the writer wants to analyze the correlation of serum Sodium and albumin with the degree of severity in acute ischemic stroke at Dr. Wahidin Sudirohusodo Makassar.

METHODS

This study's design was a cross-sectional retrospective. We used secondary data from the medical records of Wahidin Sudirohusodo Hospital Makassar patients. The study population was all acute ischemic stroke patients that received care at Dr. Wahidin Sudirohusodo Hospital from January 2018 to April 2021. In addition, the study population was all study populations that had results of serum Sodium on the first day of hospital admission and serum albumin results in the first three days from the onset of stroke. Acute ischemic stroke patients were confirmed using a Head CT scan/MRI and showed signs of cerebral infarct. Exclusion criteria for this study were patients with a history of hemorrhagic or ischemic stroke, chronic kidney failure, and malignancy.

Serum sodium and albumin tests were done at the Dr. Wahidin Sudirohusodo Laboratory, Makassar. Sodium was measured using NOVA 5 electrolyte analyzer using the Ion Selective Electrode (ISE) method with a normal range of 136–146 mmol/L. Albumin was measured using the ABX Pentra 400 with colorimetry method and normal range at 3.5–5.2 g/dL. The levels of sodium and albumin

results were connected with the NIHSS score, a quantitative measure of neurological deficit related to stroke that calculates the severity of stroke. The range for NIHSS score was 0–42 with interpretation as follows: score < 4 (mild), 4–15 (moderate), > 15 (severe).

Data analysis used SPSS. The method used was the calculation of the frequency distribution and statistic tests. Data normality used Kolmogorov-Smirnov. Statistic tests that were used were Kruskal-Wallis, Mann-Whitney, and Spearman tests. Results were statistically significant if $p < 0.05$. In addition, the receiver operating characteristic curve was used to find the cut-off.

The ethical agreement was obtained from the Ethic Committee for Health Research Medical Faculty of Hasanuddin University/Dr. Wahidin Sudirohusodo Hospital with the number 289/UN4.6.4.5.31/PP36/2021.

RESULTS AND DISCUSSION

According to a study conducted by the Medical Record Installation of Dr. Wahidin Sudirohusodo Hospital in May 2021, 165 samples fulfilled the inclusion criteria, that consists of 91 male and 74 female patients. The degree of severity, according to the NIHSS score, was divided into 3, mild (9.1%), moderate (83%), and severe (7.9%). The mean serum sodium concentration was 138.4 mmol/L, and serum albumin was 3.37 mg/dL. The characteristics of the study samples can be seen in Table 1.

Table 1. Characteristics of study samples

Characteristics	N (%)	Mean±SD	Median (min-max)
Age (years old)		60.2±13.2	60 (31-88)
Gender			
Male	91 (55.2)		
Female	74 (44.8)		
Length of hospitalization			
< 7 days	47 (28.5)		
≥ 7 days	118 (71.5)		
Outcome			
Recover	123 (74.5)		
Death	42 (25.5)		
Degree of severity			
Mild	15 (9.1)		
Moderate	137 (83)		
Severe	13 (7.9)		
Comorbid			
Diabetes mellitus	36 (21.8)		
Hypertension	82 (49.7)		
Sodium (mmol/L)		138.4±8.9	139 (107-160)
Albumin (g/dL)		3.37±0.52	3>4 (1.9-4.9)

Source: Secondary Data

Table 2. Relationship of serum sodium with acute ischemic stroke degree of severity according to NIHSS score

		n	Sodium (mmol/L) Median (min-max)	p*
Degree of severity	Mild	15	139 (132-148)	0.532
	Moderate	137	139 (107-160)	
	Severe	13	140 (136-146)	

*Kruskal-Wallis test

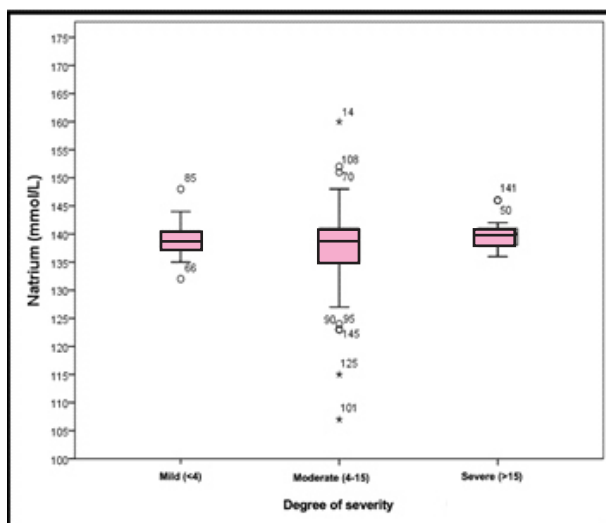
Table 3. Relationship of serum albumin levels with a degree of severity of acute ischemic stroke patients according to the NIHSS score

		n	Albumin (g/dL) Median (min-max)	p*
Degree of severity	Mild	15	3.8 (3.0-4.4)	< 0.001
	Medium	137	3.4 (1.9-4.9)	
	Severe	13	3.3 (2.8-3.8)	

* Kruskal-Wallis test

This study's basic characteristic is that there were more male patients (55.2%) compared to females (44.8%), with a mean age of 31–88 years old. A study by Hashem *et al.* reported that there were more male acute ischemic stroke patients (65%) with a mean age of 46–80.¹⁴ The reason for more male patients than females was explained in a study by Hiraga due to sex hormones. Estrogen can stimulate an immune response when there is an occlusion of the cerebral artery in research rats, causing females to have a lower stroke volume than males. Estradiol also has a potent effect on the endothelium that stimulates dilatation and increases blood flow.^{15,16}

According to Table 2, there was no significant relationship of serum sodium levels with the degree of severity of acute ischemic stroke according to NIHSS score ($p=0.532$) (Figure 1).

**Figure 1.** Serum sodium concentrations according to acute ischemic stroke degree severity

Research by Pradhan *et al.* is in line with this study, where only six patients (9.38%) from 64 ischemic stroke patients had hyponatremia.¹⁷ These findings are not in-line with Mahesar *et al.*, that identified 33 from 132 ischemic strokes with hyponatremia with mean sodium levels of 130-134 mmol/L.¹⁸ Ischemic stroke patients with hyponatremia have a higher NIHSS score on the 5th day compared to normonatremia patients. The results of these studies differ because the previous study did not exclude acute ischemic stroke patients with comorbid or chronic kidney failure and malignancy as confounding factors.¹¹ This research excluded patients with confounding factors such as a history of hemorrhagic or ischemic stroke, chronic kidney disease malignancy, and patients with albumin results > 4 days after the stroke onset.

Table 3 shows a significant relationship between serum albumin and the degree severity of acute ischemic stroke patients according to the NIHSS score ($p<0.001$). Further testing (Post-hoc test) with Mann-Whitney shows a statistically significant difference in serum albumin levels in acute ischemic stroke patients with a mild and moderate ($p=0.001$) degree of severity and mild and severe ($p=0.001$). Still, there was no significant difference between serum albumin levels in moderate and severe degrees of seriousness ($p=0.422$) (Figure 2).

Table 4 shows that according to Spearman tests, there is a negative correlation with a weak correlation between serum albumin levels and NIHSS score ($p<0.001$), meaning the lower the albumin levels, the higher the NIHSS score that calculates the stroke degree of severity. There was no correlation between serum sodium levels and NIHSS score ($p=0.983$).

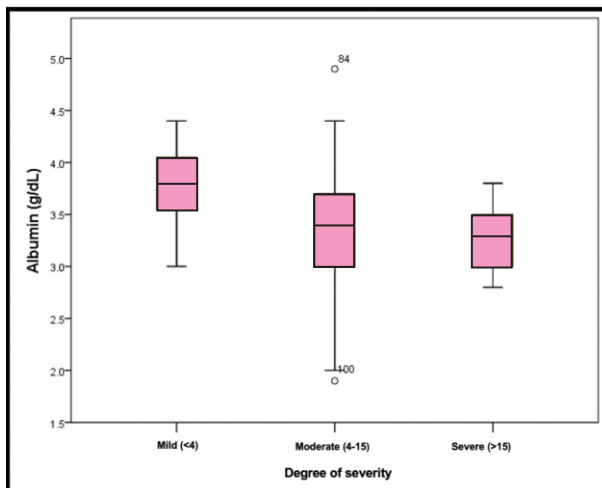


Figure 2. Serum albumin, according to the degree of severity of acute ischemic stroke

Table 4. Correlation of serum sodium and albumin levels with the NIHSS score that was examined on the early onset of stroke

	NIHSS Score		
	n	p*	r
Natrium (mmol/L)	165	0.973	0.386
Albumin (g/dL)	165	<0.001	-0.327

* Spearman test

This research shows that the lower the serum albumin levels, the higher the NIHSS score and degree of severity of the stroke, which is statistically significant ($p < 0.001$; $r = 0.327$). Riana *et al.* found that in acute ischemic stroke patients, there was a significant relationship between serum albumin levels with the NIHSS score on admission ($p = 0.000$; $r = 0.730$). The correlation value (r) was stronger in the previous study because Riana *et al.* excluded patients with congestive heart failure and decompensated

liver cirrhosis comorbidity that could affect the serum albumin levels.⁹ Negative correlation between serum albumin and NIHSS score was also stated by Sandeep *et al.* with significant results ($p = 0.0001$, $r = -0.724$).¹⁹

Table 5 shows a relation between serum albumin levels and the length of hospitalization of patients with acute ischemic stroke. Albumin levels were lower and statistically significant in hospitalized patients > 7 days compared to those < 7 days ($p = 0.015$). There was no relation between serum sodium and the hospitalization length of patients with acute ischemic stroke ($p = 0.454$).

Table 6 shows a relationship between serum albumin and the outcome of acute ischemic stroke patients. Lower albumin levels are statistically significant in patients who died than in those who recovered ($p = 0.049$). There was no relationship between serum sodium levels with the outcome of acute ischemic stroke patients ($p = 0.857$).

Receiver operating characteristic curve analysis of albumin levels in patients with acute ischemic stroke that have passed away can be seen in Figure 3. The area Under Curve (AUC) of Figure 3 is 0.602. Therefore, according to the Youden index, the chosen cut-off of albumin levels < 3.25 g/dL has a 66.7% sensitivity, 50% specificity with a positive predictive value of 100%, and a negative predictive value of 53.84%.

Serum albumin levels significantly affect the length of hospitalization ($p = 0.015$) and outcome ($p = 0.049$) in ischemic stroke patients. This research shows that serum albumin can also predict the outcome of an acute ischemic stroke patient. This result is in line with research by Sandeep *et al.*, where the cut-off point of albumin is < 2.01 g/dL (sensitivity 90.8%; specificity 79.8%).¹⁹ Prognostic value of

Table 5. The relationship between serum sodium and albumin levels with the length of hospitalization in acute ischemic stroke patients

Parameter	Length of Hospitalization		p*
	< 7 days (n=47)	≥ 7 days (n=118)	
Natrium (mmol/L)	140 (115-148)	139 (107-160)	0.454
Albumin (g/dL)	3.5 (2.0-4.4)	3.3 (1.9-4.9)	0.015

*Mann-Whitney test

Table 6. relationship between serum sodium and albumin with the outcome of acute ischemic stroke patients

Parameter	Outcome		p*
	Recovered (n=123)	Death (n=42)	
Natrium (mmol/L)	139 (123-160)	138.5 (107-148)	0.857
Albumin (g/dL)	3.4 (1.9-4.9)	3.25 (2.1-4.4)	0.049

* Mann-Whitney test

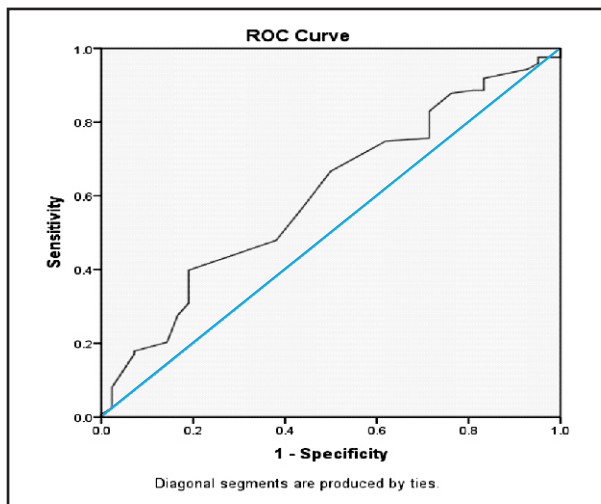


Figure 3. Receiver operating characteristic curve of albumin serum levels in patients with acute ischemic stroke that died (AUC=0.602)

serum albumin level was confirmed by a study by Dash *et al.*, patients with mean serum albumin of < 3.4 g/dL have a worse outcome than patients with albumin > 3.5 g/dL. Patients with better outcomes had a lower NIHSS score and higher albumin during hospitalization.⁸ A cohort study by Zhou *et al.* during three months showed a 1.0 g/dL decrease of serum albumin correlated with a bad outcome (17%) and death (86%) in ischemic stroke patients, the odds ratio of 1.17 (95%CI: 1.01 to 1.35).²⁰ Hypoalbuminemia increases the pneumonia complication that affects the recovery state and health of the patient. These findings indicate a correlation between the severity of the disease course and serum albumin levels on the early onset of stroke. Serum albumin levels can also predict the severity and can be one of the routine markers examined and available in all health care centers.^{19,20}

The limitation of this study was that the NIHSS score could only be done one time at the beginning of admission to the hospital, not periodically as done in the study by Swamy *et al.*, which showed a negative correlation between the NIHSS score and the length of patient care.¹¹

CONCLUSIONS AND SUGGESTIONS

Results of this research can conclude that albumin correlates with NIHSS score. At the same time, sodium levels do not have a significant relationship with the degree of severity of acute ischemic stroke. Serum albumin laboratory results can be a marker of the worsening of a patient's

condition and help choose a specific management strategy for acute ischemic stroke patients in clinical practice. A prospective study is suggested to clarify the results of this study.

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