Correlation of electrolytes with falling risk, cognitive function, and functional outcome in acute ischemic stroke patient

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ABSTRACT

Stroke outcome is determined on multiple factors. However, there are limited studies discussing the impact of electrolyte imbalance on stroke outcome. In this study, we analyzed sodium, calcium, and potassium level in acute ischemic stroke, and compare their risk of falling, cognitive function, and functional outcome. This was a cross-sectional study in Dr. Moewardi General Hospital, Indonesia between January and June 2023. Patient with acute ischemic stroke were enrolled in this study. Cognitive function was assessed with mini mental state examination (MMSE) and the Indonesian version of montreal cognitive assessment (MoCA-Ina). National Institutes of Health Stroke Scale (NIHSS), Modified Rankin Scale (MRS) and Morse Fall Score (MFS) were used to assessed stroke severity, disability, and risk of falling, respectively. Pearson correlation was then performed to evaluate the correlation of electrolytes level with MMSE, MoCA-Ina, NIHSS, MRS, and MFS. Furthermore, we also analyzed the odds ratio of increasing risk of falling, cognitive function deterioration, and worse functional outcome. A p-value of <0.05 is considered statistically significant. On univariate analysis, natrium is correlated with MMSE (r=0.174; p=0.042), NIHSS (r=-0.412; p=0.011), MRS (r=-0.174; p=0.042), and MFS (r=-0.304; p=0.042). Potassium is correlated with MMSE (r=0.344; p=0.044), MoCA-INA (r=0.341; p=0.048), NIHSS (r=-0.572; p=0.019), (MRS r=-0.376; p=0.017), and MFS (r=-0.612; p=0.031). Calcium is correlated with NIHSS r=-0.348 (p=0.018), MRS r=-0.256 (p=0.036). On odds ratio analysis, low natrium level increased the risk of deteriorating cognitive function, and low level of potassium increased the risk of falling. Electrolyte imbalances correlates with risk of falling and deteriorating cognitive function.

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1. INTRODUCTION

Stroke, also known as cerebrovascular attack, is an acute focal or general neurological deficit of brain, spinal cord, or retina by a vascular cause that lasted for more than 24 hours. Generally, stroke could be classified as ischemic stroke, where blood flow is blocked due to thrombus or emboli, and hemorrhage stroke, where a vessel is ruptured and blood seeps into brain parenchyma or subarachnoid space [1]. Stroke is leading cause of death and disability in Indonesia. Indonesian health survey done by Indonesian Ministry of Health, the prevalence of stroke in Indonesia has increased from 7 per 1,000 population in 2013 to 10.9 per 1,000 population in 2018 [2]. Stroke is a devastating condition and often result in physical and mental impairment [2], [3].

Stroke patient has higher risk of falling, due to several factors that can affect balance, coordination, and muscle strength, which are essential for maintaining stability while walking or performing daily activities. Stroke also have significant effects on cognitive function, including acquiring, processing, storing, and using information due to the damage in cortical area of the brain. Furthermore, stroke survivors also struggle to perform daily activity independently [4].

Electrolyte imbalance is one of comorbidities often found in patients with acute stroke. Electrolyte imbalance refers to a disruption in the normal levels of electrolytes in the body, which are crucial for various physiological functions. Electrolytes, such as sodium, potassium, calcium, and magnesium, play vital roles in maintaining fluid balance, conducting nerve impulses, regulating muscle contractions, and supporting cellular function. Electrolyte imbalance, either due to excessive loss or inadequate intake, can lead to significant health complications. Electrolyte imbalance can have significant implications in the context of stroke. Stroke can disrupt the delicate balance of electrolytes in the body, leading to further complications and impairing the recovery process. The brain relies heavily on a stable electrolyte environment to function optimally, and any disruption can have detrimental effects [5].

Managing electrolyte balance is an important aspect of stroke management. Sodium is crucial for blood pressure regulation and maintaining fluid balance, thus greatly affect brain physiology on stroke. On the other hand, hyponatremia can also occur as stroke complication because of disturbance of anti-diuretic hormone (ADH) secretion. Potassium is another important electrolyte that plays a crucial role in human physiology, including nerve function, muscle contraction, and vessel regulation. Low potassium levels or hypokalemia can contribute to vasoconstriction, impairing blood flow and potentially induced hypoperfusion. Potassium level is also substantial for muscle contraction. Low potassium levels can contribute to muscle weakness, fatigue, and arrythmia. These symptoms can affect a stroke survivor's ability to participate in rehabilitation and regain function [5], [6].

Stroke outcome is determined on several factors. Age, sex, initial stroke severity, and time needed from onset to admission is often studied as predictors of stroke outcome [4]. However, there are limited studies discussing the impact of electrolyte imbalance on stroke outcome. In this study, we analyzed sodium, calcium, and potassium level from patients with acute ischemic stroke, and compare their risk of falling, cognitive function, and functional outcome.

2. METHOD

2.1. Patients and study design

This was a cross sectional study done in Dr. Moewardi General Hospital, Surakarta, Indonesia. Patients with acute ischemic stroke in neurology ward between January and June 2023 were enrolled in this study. Participants were selected by purposive sampling, where all patients that met the inclusion and exclusion criteria were included until minimum number of samples were reached. Written informed consent was signed and the study design was approved by the local institutional review board, Dr. Moewardi General Hospital health research ethics committee through ethical clearance number 208/III/HREC/2023.

Inclusion criteria for this study were confirmed diagnosis of ischemic stroke by computed tomography-scan (CT-scan) or magnetic resonance imaging (MRI), have sufficient cognitive and language abilities to understand and comply with study procedures and assessments, and agree to participate in this study and signed informed consent. To control the confounding variable, we established the exclusion criteria for this study, i.e., patient with unknown stroke onset, older patients aged ≥65 years, patients with other comorbidities, i.e., diabetes mellitus, atrial fibrillation and history of ischemic heart disease, and patients with history of neurobehavior disorders. Patient who met the inclusion and exclusion criteria then included in this study, had history taken and took physical examination.

Cognitive function was assessed with mini mental state examination (MMSE) and the Indonesian version of montreal cognitive assessment (MoCA-Ina). National Institutes of Health Stroke Scale (NIHSS), Modified Rankin Scale (MRS) and Morse Fall Score (MFS) were used to assessed stroke severity, degree of disability, and risk of falling, respectively. According to the cross-sectional sample size formula based on previous research [5], a minimum sample of 80 patient is required in this study.

2.2. Data analysis

Data obtained was analyzed with Kolmogorov Smirnov test to determined data distribution, with $p>0.05$ considered normal distribution. Pearson correlation was then performed to evaluate the correlation of sodium, potassium, and calcium level with MMSE, MoCA-Ina, NIHSS, MRS, and MFS. Furthermore, we also analyzed the odds ratio of increasing risk of falling, cognitive function deterioration, and worse functional outcome. A p-value of <0.05 is considered statistically significant.

3. RESULTS AND DISCUSSION

Ninety patients with acute ischemic stroke were enrolled in this study. Forty-nine patients (54.33%) were male, and the average age of the research subjects was 58.71±9.65 years ranging from 36 to 83 years. Patients' demographic characteristic on this study is presented on Table 1.

Table 1. Patients' demographic

Subject characteristics		Total (percentage)
Age (years)	36–45	9 (10%)
	46–55	56 (62.22%)
	>55	25 (27.78%)
Gender	Male	49 (54.33%)
	Female	41 (45.67%)
Body mass index (kg/m^2)	<18.5	4 (4.44%)
	18.5–24.9	46 (51.11%)
	25–29.9	38 (42.23%)
	≥30	2 (2.22%)
Hypertension	Yes	71 (78.89%)
	No	19 (21.21%)
Diabetes mellitus	Yes	67 (74.44%)
	No	23 (25.56%)
Dyslipidemia	Yes	54 (60.00%)
	No	36 (40.00%)

The sodium levels ranged from 120–150 mmol/L with an average of 134.33±4.56 mg/dL. The potassium levels ranged from 2.7–6.6 mmol/L with an average of 3.72±0.62 mg/dL. And the serum calcium levels of the study subjects ranged from 0.45–2.65 mmol/L with an average of 1.16±0.20 mg/dL.

Cognitive function was assessed using the MMSE and MoCA-INA instruments, and the results showed MMSE score average of 26.44±4.38, ranging from 3–30, and MoCA-INA score average of 26.20±5.14, ranging between 5–30. Stroke severity was assessed using NIHSS, with score mean was 6.19±3.351 ranging between 1–21, and MRS, with score mean of 2.15±1.154, ranging from 1–4. The risk of falling was assessed using the MFS with average score of 37.16±19.48, ranging between 0–90. Univariate analysis between electrolytes level and MMSE, MoCA INA, NIHSS, MRS, and MFS were presented in Table 2. We further do odds ratio analysis on parameter that was statistically significant on univariate analysis. Odds ratio of electrolytes imbalance on risk of falling and decreased cognitive function were depicted in Figures 1 and 2.

Table 2. Univariate analysis of electrolytes level and MMSE, MoCA INA, NIHSS, MRS, and MFS

	MMSE	MoCA INA	NIHSS	MRS	MFS
Sodium	0.174 (p=0.042)	0.213 (p=0.41)	-0.412 (p=0.011)	-0.283 (p=0.023)	-0.304 (p=0.042)
Potassium	0.344 (p=0.044)	0.341 (p=0.048)	-0.572 (p=0.019)	-0.376 (p=0.017)	-0.612 (p=0.031)
Calcium	0.049 (p=0.055)	0.027 (p=0.061)	-0.348 (p=0.018)	-0.256 (p=0.036)	-0.142 (p=0.073)

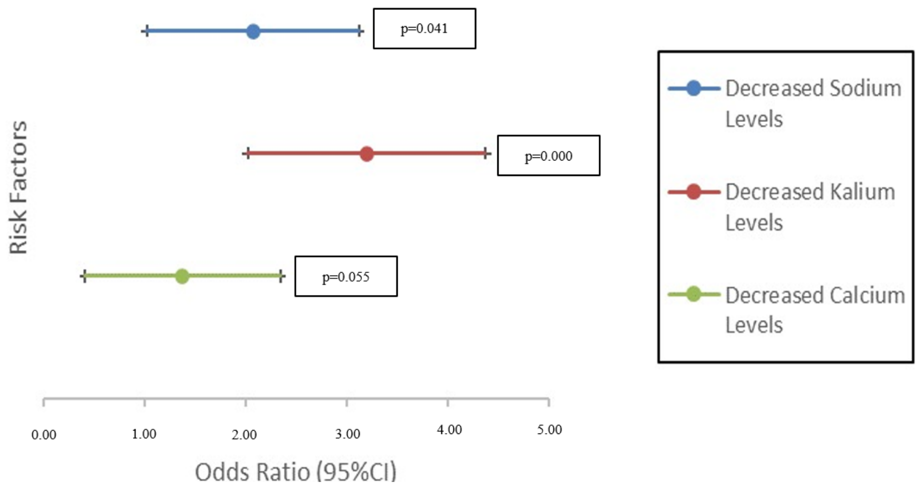

Figure 1. Odds ratio of electrolyte level and deterioration of cognitive function

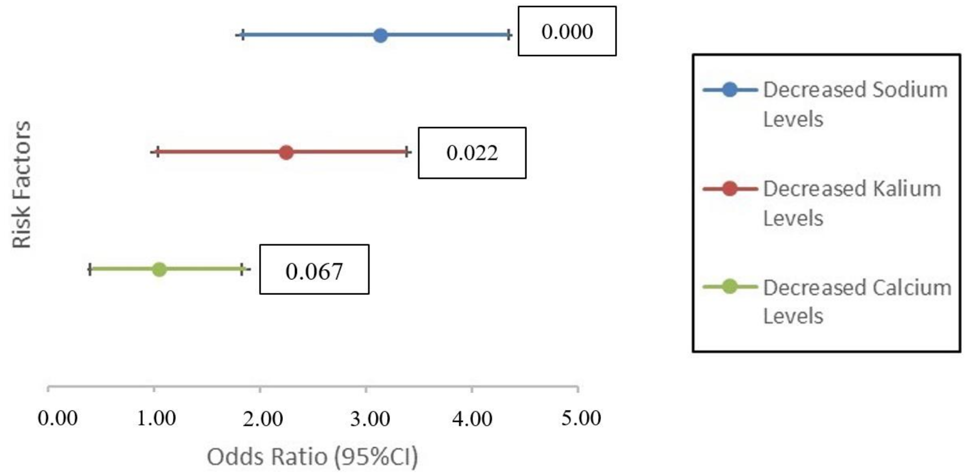

Figure 2. Odds ratio of electrolyte level and deterioration of risk of falling

This study is conducted analyzed sodium, calcium, and potassium level from patients with acute ischemic stroke, and compare their risk of falling, cognitive function, and functional outcome. Cognitive function was assessed with MMSE and MoCA-Ina. MMSE evaluate seven domains of cognitive function, i.e., orientation, visuospatial, language, attention, working dan recall memory, and executive functioning. MMSE has high sensitivity (100%) and sensitivity (98.5%) to detect patient with cognitive impairment [7]. On the other hand, MoCA-Ina was developed based on English version of MoCA examination for Indonesian population. MoCA-Ina is also valid and reliable to examine patient cognitive function in wide range of disease, including stroke [8].

This study used NIHSS, MRS and MFS were used to assessed stroke severity, disability, and risk of falling, respectively. NIHSS is standardized scoring assessment of stroke severity that is widely used. Minimum and maximum possible score of NIHSS is 0 and 42, with higher score indicates more severe stroke [9]. MRS is a seven-level scale to measuring the disability of stroke patients. MRS is one of the most used scales to measure disability in stroke clinical trials [10]. MFS is simple method to evaluate patient's likelihood of falling. MFS has been shown to have good predictive validity and interrater reliability [11].

In this study, we observed a significant positive correlation between sodium level and MMSE, and significant negative correlation between sodium level and NIHSS, MRS, and MFS, indicating that low sodium level is correlated with more severe stroke and disability, higher rate of cognitive deterioration, and higher risk of falling. Further analysis also revealed that the odds of risk of falling is increased on patient with more severe hyponatremia. The correlation between hyponatremia and stroke severity arises from the physiological impact of altered sodium levels on brain function and fluid balance. When hyponatremia occurs during a stroke, it can exacerbate cerebral edema, leading to increased intracranial pressure and neurological damage. Additionally, hyponatremia may hinder the brain's ability to regulate water content, further contributing to cerebral swelling and worsening stroke outcomes. Studies have shown that hyponatremia at the time of stroke onset is associated with larger infarct volumes, increased disability, and higher mortality rates [12], [13]. The correlation between hyponatremia and fall risk arises from the impact of altered sodium levels on various physiological processes that influence balance and coordination. Sodium plays a crucial role in maintaining proper nerve and muscle function, including those involved in postural control. When sodium levels are low, it can lead to muscle weakness, dizziness, confusion, and impaired cognition, all of which contribute to an increased risk of falls. Additionally, hyponatremia can affect the body's fluid balance, leading to fluid shifts that impact blood pressure regulation and further compromise stability. Studies have demonstrated that older adults with hyponatremia are more susceptible to falls, with an elevated incidence of fractures and other fall-related injuries [14]. More severe stroke in patient with hyponatremia may also alter patient's cognitive function. Studies have shown that individuals with chronic hyponatremia may experience symptoms such as confusion, impaired attention, memory problems, and slower cognitive processing. Severe cases of hyponatremia have been associated with more severe neurological manifestations, including seizures and coma [15], [16].

Hyponatremia could also occur as stroke complications, which attributed to several mechanisms. Firstly, stroke-induced damage to the brain can affect the hypothalamus, a region responsible for regulating sodium and water balance. Disruption of this regulatory mechanism may lead to the development of hyponatremia. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) and cerebral salt-wasting syndrome (CSWS) are two distinct syndromes that can occur in as stroke complication and have implications for sodium and fluid balance. Secondly, stroke-related impairments in swallowing and thirst sensation can contribute to inadequate fluid intake, further exacerbating the risk of hyponatremia. Additionally, certain stroke treatments, such as the administration of intravenous fluids or medications, can potentially contribute to electrolyte disturbances, including hyponatremia. It is important to monitor and manage hyponatremia in stroke patients promptly, as it can impact their overall clinical course and prognosis [12], [14], [17]–[19].

Similarly, we also observed significant positive correlation between potassium level and MoCA-INA and MMSE, and negative correlation between potassium level and NIHSS, MRS, and MFS. Further analysis also revealed that the odds of risk of cognitive deterioration is higher in patient with hypokalemia. Potassium is an essential mineral that plays a vital role in maintaining proper nerve and muscle function, including the muscles of the heart. It helps regulate heart rhythm, blood pressure, and the balance of fluids in the body. When potassium levels are too low, it can lead to irregular heart rhythms (arrhythmias) and other cardiovascular complications. While hypokalemia itself may not directly cause more severe strokes, it is possible that low potassium levels could contribute to an individual's overall health condition and increase the risk of complications. For instance, if patients with hypokalemia have underlying heart disease or high blood pressure, these conditions can increase the risk of stroke severity [19]–[23]. When potassium levels are low, it can lead to muscle weakness and fatigue, compromising one's ability to maintain stability and increasing the likelihood of falls. A study published in the Journal of the American Geriatrics Society found that hypokalemia was associated with an increased risk of falls among older adults, emphasizing the importance of monitoring and managing potassium levels to prevent falls and related injuries [24].

Hypokalemia, while less common than other electrolyte imbalances, it can have notable effects on cognitive function and overall brain health. Studies have suggested a potential link between low potassium levels and lower cognitive function. Hypokalemia can lead to neuronal hyperexcitability, affecting neurotransmission and synaptic activity in the brain. This disturbance in neural signaling may contribute to cognitive impairments, including memory problems, difficulty concentrating, and slowed cognitive processing. One study examined the relationship between hypokalemia and cognitive function in elderly patients found that lower potassium levels were associated with cognitive decline and increased risk of dementia in this population [25], [26].

The relationship between calcium levels and stroke severity is not as extensively studied as other factors such as blood pressure or cholesterol. However, there is some evidence suggesting that abnormal calcium levels may have an impact on stroke severity. One study examined the association between serum calcium levels and stroke outcomes. The study found that higher serum calcium levels on admission were associated with more severe strokes and poorer functional outcomes among ischemic stroke patients. However, it is important to note that this study focused specifically on ischemic strokes and does not provide a comprehensive understanding of the relationship between calcium levels and stroke severity [27]. Another study explored the association between calcium levels and hemorrhagic stroke, specifically intracerebral hemorrhage (ICH). The study found that lower levels of serum ionized calcium were associated with larger hematoma volumes, indicating a potential link between low calcium levels and greater hemorrhage severity in ICH patients. Again, this study specifically examines hemorrhagic stroke and does not cover all types of strokes [28].

Numerous studies have established the strong connection between hypocalcemia and stroke incidence, emphasizing the role of calcium in maintaining vascular health and blood clotting mechanisms [29]. Additionally, hypocalcemia has been identified as a significant risk factor for falls among older adults, leading to an increased susceptibility to fractures [30]. A study highlighted the association between low calcium levels and the increased risk of falling, further emphasizing the importance of maintaining adequate calcium levels to prevent fall-related injuries [31]. Fracture risk is also heightened in individuals with hypocalcemia due to the adverse effects on bone density and bone mineralization. Li *et al*. [32] demonstrated a clear link between low calcium levels and an increased risk of fractures, particularly in postmenopausal women. Similarly, a study supported these findings, establishing hypocalcemia as a significant predictor of fracture risk across diverse populations [33]–[35].

4. CONCLUSION

Electrolyte imbalances correlates with risk of falling and deteriorating cognitive function. This finding suggests that in the future, electrolyte can be one of prognosis predictor of cognitive function deterioration and risk of falling, thus early prevention can be applied in risk group population. Further study with bigger number of samples and risk factor analysis is still needed to ensure the validity and reliability of our study.

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