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THE EFFECT OF SERUM MAGNESIUM AND CALCIUM LEVELS ON THE SEVERITY OF ACUTE ISCHEMIC STROKE IN PATIENTS HOSPITALIZED FOR LESS THAN 7 DAYS

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ABSTRACT
Stroke ranks as the second leading cause of death worldwide, with an annual mortality of approximately 5.5 million. Stroke is classified into ischemic stroke and hemorrhagic stroke, the latter including intracerebral hemorrhage and subarachnoid hemorrhage. Ischemic stroke, caused by arterial occlusion, accounts for the majority of stroke cases. This study aims to evaluate the effect of serum magnesium and calcium levels on the severity of acute ischemic stroke in patients hospitalized for less than 7 days at the Stroke Unit of Adam Malik Hospital. This study was an analytical research with a cross-sectional design, which involved measuring multiple variables at a single point in time. Data were collected from 50 patients admitted to the Stroke Unit of Adam Malik Hospital. Sampling was conducted consecutively for all patients who met the inclusion criteria. The data were analyzed using the Shapiro-Wilk test to assess the normality of the distribution. From a total of 50 study participants, the majority (54%) were male. The average age of the subjects was 58.42 years, with an age range of 29 to 80 years. Most patients had a high school education (42%). The mean NIHSS (National Institutes of Health Stroke Scale) score was 7.58, indicating a moderate level of stroke severity, with NIHSS scores ranging from 5 to 19. The average serum magnesium and calcium levels in patients with acute ischemic stroke were within normal limits, recorded at 2.01 mg/dL and 9.25 mg/dL, respectively. There was no significant association between serum magnesium and calcium levels and the severity of acute ischemic stroke based on NIHSS scores, with p-values of 0.499 and 0.504, respectively.

Keywords: acute ischemic stroke; calcium; magnesium

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INTRODUCTION

Stroke is defined by the World Health Organization (WHO) as a clinical syndrome characterized by rapidly developing clinical signs of focal (or global in cases of coma) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than a vascular origin. Although still widely used, the WHO definition heavily relies on clinical symptoms and is now considered outdated by the American Heart Association (AHA) and American Stroke Association (ASA). This is due to significant advancements in the understanding of the nature, timing, clinical recognition of stroke and its mimics, as well as neuroimaging findings, all of which necessitate an updated definition (Coupland et al., 2017; Chugh C, 2019).

Stroke is generally classified into three categories: ischemic stroke, hemorrhagic stroke, and subarachnoid hemorrhage. Ischemic stroke occurs due to a blockage of blood vessels that restricts blood supply to the brain, whereas hemorrhagic stroke results from a ruptured blood vessel causing bleeding into the intracranial space. Depending on the site of bleeding, hemorrhagic stroke can be

further classified into intracerebral or subarachnoid hemorrhage. Approximately 60–80% of all strokes are ischemic (Chugh C, 2019). Ischemic stroke is defined as an episode of neurological dysfunction caused by focal infarction in the brain or retina, with symptoms lasting more than 24 hours (Parmar P, 2018).

Magnesium is an essential metallic element in the human body, ranking fourth in abundance after calcium, sodium, and potassium. It plays a crucial role in regulating various physiological functions, including glucose metabolism, protein synthesis, nucleic acid production, and muscle and nerve function. Magnesium deficiency has been linked to an increased risk of several diseases such as hypertension, diabetes, metabolic syndrome, coronary artery disease, and stroke. A study by Kuldeep et al. (2024) reported that stroke patients had significantly lower serum magnesium levels at admission (1.79 ± 0.54 mg/dL) compared to controls (2.02 ± 0.48 mg/dL, P = 0.002), and on day 3 (1.98 ± 0.52 mg/dL vs. 2.19 ± 0.40 mg/dL, P = 0.001). Lower serum magnesium levels were associated with higher NIHSS scores, indicating greater neurological deficit (Kuldeep J, et al., 2024).

Calcium is the most abundant mineral in the body. In addition to being a structural component of bones, calcium is critically important in blood coagulation, intracellular signaling, muscle contraction, and nervous system function. However, it is also associated with certain pathological processes, such as atherosclerotic plaque formation and soft tissue calcification (Ding C, et al., 2022). A study by Ding C. et al. (2022) stated that current findings on the association between serum calcium levels and stroke risk remain inconclusive. A community-based prospective study involving 552 stroke cases with a 12.6-year follow-up found a significant positive association between serum calcium levels and stroke risk (per SD increase—hazard ratio [HR]: 1.16; 95% CI: 1.07, 1.26), particularly among adults with higher average baseline corrected calcium levels (10.3 mg/dL). Another post hoc analysis from a randomized controlled trial involving 7,259 postmenopausal women with osteoporosis reported that higher baseline serum calcium levels were associated with an increased incidence of stroke (per SD increase—HR: 1.22; 95% CI: 0.99, 1.49; P = 0.06). The aim of this study was to analyze the effect of serum magnesium and calcium levels on patients with acute ischemic stroke who were admitted within 7 days to the Stroke Unit of Adam Malik General Hospital.

METHOD

This was an analytical study with a cross-sectional design, which measured several variables at a single point in time. The study was conducted at the Clinical Pathology Sub-Installation of the Faculty of Medicine, Universitas Sumatera Utara (FK USU)/Adam Malik General Hospital Medan, in collaboration with the Department of Neurology FK USU/Adam Malik Hospital, from December 2024 to June 2025. Samples were taken consecutively from all eligible patients in the stroke unit of Adam Malik Hospital who met the inclusion criteria. A total of 50 respondents were included in this study. Subject characteristics were presented in tabular form and described accordingly. The association between serum magnesium and calcium levels with the severity of acute ischemic stroke was analyzed using simple linear regression. A p-value of <0.05 was considered statistically significant. Sampling was conducted consecutively for all subjects who met the study criteria, namely patients diagnosed with ischemic stroke by a neurologist, ischemic stroke patients admitted to the stroke unit within 7 days, patients aged >18 years, and those who provided informed consent either personally or through their family. This study was conducted after obtaining ethical approval from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara, Medan, with approval number 202/KEPK/USU/2025.

RESULT

Table 1.
Characteristics of Study Subjects

Subject Characteristics	Subjects (n = 50)
Age, Years	
Mean (SD)	58,42 (12,34)
Median (Min-Max)	58,50 (29-80)
Sex, n (%)	
Female	23 (46%)
Male	27 (54%)
Educational level, n (%)	
Elementary School (SD)	2 (4,0%)
Junior High School (SMP)	10 (20,0%)
Senior High School (SMA)	21 (42,0%)
	1 (2,0%)
Diploma (D3)	16 (32%)
University Degree	
NIHSS Score	
Mean (SD)	7,58 (2,87)
Median (Min-Max)	7,00 (5-19)
Onset of Stroke (Hours)	
Mean (SD)	34,56 (11,10)
Median (Min-Max)	24,00 (24-46)

Table 2.
Serum Magnesium and Calcium Levels

Parameter	Subjek (n=50)
Magnesium, mg/dL	
Median (Min-Max)	2,01 (1,81-2,45)
Kalsium, mg/dL	
Median (Min-Max)	9,25 (8,37-9,87)

Table 3.
Simple Linear Regression Analysis of the Effect of Magnesium and Calcium Levels in Acute Ischemic Stroke Patients Admitted Within 7 Days at the Stroke Unit of Adam Malik Hospital

Variable	R	B (Regression Coefficient)	p-value	95% Confodence Interval (CI)
Magnesium	0,098	1,711	0,499	-3,336 s.d. 6,757
Kalsium	0,097	-0,653	0,504	–2,603 s.d. 1,297

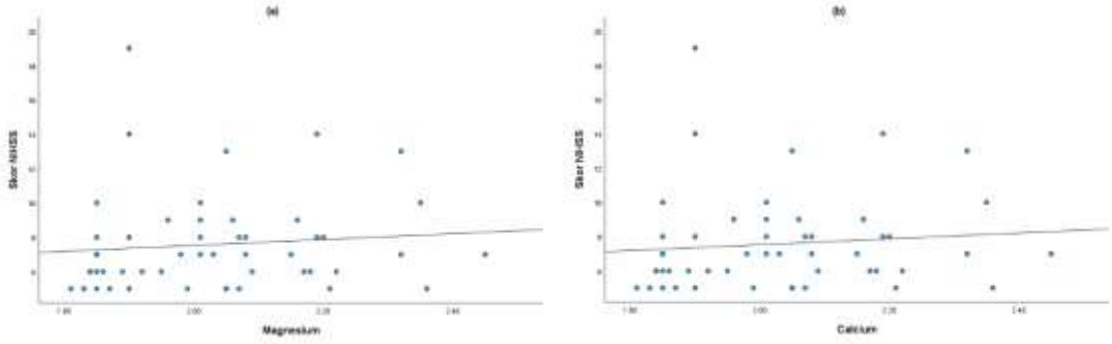

Figure 1. Scatter Plot Graphs Showing the Relationship Between Serum Levels and Stroke Severity:
(a)Scatter plot of magnesium levels and NIHSS score
(b) Scatter plot of calcium levels and NIHSS score

The results of the simple linear regression analysis showed no significant association between serum magnesium levels and the severity of acute ischemic stroke, as indicated by a p-value of 0.499. The regression coefficient (B) was 1.711 with a 95% confidence interval ranging from –3.336 to 6.757, suggesting a positive trend that was not statistically significant. Similarly, serum

calcium levels were not significantly associated with stroke severity, with a p-value of 0.504. The regression coefficient (B) was –0.653, and the 95% confidence interval ranged from –2.603 to 1.297, indicating no clear effect of calcium levels on stroke severity in this population.

DISCUSSION

Based on the study subjects, the mean age of patients was 58.42 years, with a median age of 58.50 years and an age range of 29 to 80 years. According to Kalita et al. (2023), the highest prevalence of stroke (3.69%) was found in the age group of 75 years and older, while the prevalence in the 45–59 years group was 0.75%. Similarly, Imoisili et al. (2024) reported that stroke prevalence was highest among adults aged ≥65 years (7.7%), and lowest among those aged 18–44 years (0.9%) (Kalita J et al., 2023; Imoisili OE et al., 2024). Regarding sex distribution, the study found that 23 subjects (46%) were female and 27 subjects (54%) were male, indicating that acute ischemic stroke occurred more frequently in males. This is consistent with a study by Peters et al. (2020), which showed that the incidence rate of ischemic stroke per 10,000 people per year was 6.06 (5.75–6.38) in women and 11.35 (10.88–11.84) in men. Data from the Global Burden of Disease (GBD) 2021 also reported that new ischemic stroke cases in men reached 4.02 million (95% UI: 3.44–4.67 million), compared to 3.78 million (95% UI: 3.25–4.34 million) in women (Peters SAE et al., 2020; Hou S et al., 2024).

Men are exposed to several risk factors such as smoking and alcohol consumption. In contrast, women have specific risk factors including pregnancy, menopause, and the use of estrogen-containing oral contraceptives, which are associated with a threefold increased risk of venous thrombosis compared to non-users. Cerebral hemodynamic studies have shown significantly reduced cerebral reactivity in postmenopausal women compared to premenopausal women of similar age. The late perimenopausal and postmenopausal stages are also associated with increased levels of total cholesterol, low-density lipoprotein (LDL), and lipoproteins. Smoking contributes to atherosclerosis development, lowers HDL-C levels, and raises blood pressure. The 2018 Indonesian Basic Health Survey (Riskesdas) reported that the stroke prevalence was 11 per thousand in males and 10.9 per thousand in females, suggesting that gender alone is not a protective factor (Soto-Cámara R et al., 2020; Riset Kesehatan Dasar, 2018).

The highest educational level among subjects was senior high school (SMA), reported in 21 participants (42.0%). A study by Wen et al. (2020) found that individuals with only basic education had the highest risk of stroke (log-rank test, $P < 0.001$). Participants with intermediate and higher education levels showed a 17% reduction in stroke risk (Xiuyun W et al., 2020). The mean NIHSS score in this study was 7.58, with a median of 7.00, and scores ranging from 5 to 19, indicating a moderate level of stroke severity. The NIHSS is widely used as an initial assessment tool to determine stroke severity and predict patient prognosis. Based on the results of the simple linear regression analysis, serum magnesium levels showed a p-value of 0.499, indicating no statistically significant association. Similarly, serum calcium levels yielded a p-value of 0.504, which was also not statistically significant. These findings suggest that there is insufficient evidence to conclude that serum magnesium or calcium levels influence the severity of ischemic stroke as measured by the NIHSS score.

The mean onset time of acute ischemic stroke in this study was 34.56 hours, with a range of 24 to 46 hours. During the early phase of ischemic stroke (0–48 hours), the body enters an acute condition characterized by cellular stress responses, tissue damage, and initial inflammation. In this phase, disruption of cerebral blood flow causes metabolic dysfunction, including disturbances in electrolyte balance—particularly calcium. Although excessive calcium influx into brain cells may occur, this is not immediately reflected as elevated serum calcium levels. Between 72 and 96 hours after stroke onset, the body enters the subacute phase, characterized by increased systemic inflammatory response, progressing tissue necrosis, and the release of ions from damaged cells—

including calcium that was previously sequestered intracellularly. The observed elevation in serum calcium levels during this phase is likely due to calcium being released from injured brain tissue, in conjunction with systemic inflammation reaching its peak. Ovbiagele et al. (2008) reported that elevated serum calcium levels at 72 to 96 hours post-ischemic stroke were independently associated with mid-term functional outcomes, whereas calcium levels measured at very early time points (e.g., upon hospital admission) did not appear to have significant prognostic value.

Albumin-corrected calcium is a crucial parameter for assessing true calcium status in the body, especially in acute conditions like ischemic stroke. The majority of calcium in the bloodstream is bound to albumin, with only a small portion existing as free (ionized) calcium, which is physiologically active. In cases of severe stroke, serum calcium levels may increase due to the release of calcium from necrotic brain tissue, disrupted cellular metabolism, impaired ionic homeostasis, and activation of cellular stress responses—such as mitochondrial damage leading to calcium leakage. In the present study, total serum calcium levels in acute ischemic stroke patients appeared within normal limits. This can be explained by the acute inflammatory state during stroke, which is often associated with reduced serum albumin levels. As albumin is the primary binding protein for calcium, a decline in albumin can result in a relative increase in ionized calcium, which is not reflected in total calcium measurements. Therefore, relying solely on total serum calcium without considering albumin levels may misrepresent the physiological calcium status.

Correcting calcium values for albumin is essential to uncover elevations in physiologically active calcium that may contribute to stroke pathophysiology, including excitotoxicity, neuronal death, and infarct expansion. These findings reinforce that albumin-corrected calcium provides superior prognostic value compared to total serum calcium in assessing the severity of acute ischemic stroke. A study by Chung et al. (2015) further supports this, showing that albumin-corrected calcium has significant prognostic implications for early neurological outcomes and long-term mortality following acute ischemic stroke. Moreover, in our study, albumin-corrected calcium demonstrated a clearer association with clinical outcomes than unadjusted total serum calcium levels.

A significant decline in serum magnesium levels in patients with ischemic stroke typically begins to be detectable between 24 to 48 hours after stroke onset, becoming more pronounced after 48 hours. This means that within the first 24 hours (hyperacute phase), serum magnesium levels generally remain within the normal range; during the early acute phase (24–48 hours), levels may begin to decrease gradually, depending on stroke severity; and in the subacute phase (≥48 hours), the reduction in magnesium becomes more evident and statistically significant, particularly in patients with severe strokes.

In the present study, most patients with acute ischemic stroke had serum magnesium levels within the normal range. This finding may be attributed to the timing of blood sample collection, which was performed within 72 hours of stroke onset—corresponding to the hyperacute to early acute phase. During this period, intracellular magnesium changes resulting from cerebral ischemia may not yet be fully reflected in serum magnesium concentrations. Hence, more substantial fluctuations are likely to emerge in the subacute or chronic phases. Moreover, factors such as stable hydration status, adequate nutrition, and preserved renal function in most participants may have contributed to the maintenance of normal serum magnesium levels.

A study by Cojocaru et al. (2007) assessed serum magnesium levels at hospital admission and again 48 hours after the onset of ischemic stroke. Neurological deficits were evaluated using the NIHSS score on day one and at 48 hours. Statistical analysis using the Student's t-test revealed a significant association between low serum magnesium levels at 48 hours and the severity of neurological deficits. A study by Yueqi et al. (2024) found that higher serum calcium levels were associated with increased stroke severity. This suggests that serum calcium levels may serve as an early indicator to

predict the severity and initial outcomes of acute ischemic stroke (Zhang Y et al., 2024). Therefore, although this study did not find a statistically significant association, monitoring electrolyte levels remains essential as part of comprehensive stroke management, since electrolyte imbalances can affect the clinical condition of patients.

CONCLUSION

There was no significant association between serum magnesium and calcium levels and the severity of acute ischemic stroke. The timing of sample collection within 72 hours of stroke onset and the absence of albumin correction for calcium may have contributed to these findings.

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