

Association of Serum Calcium Levels with Clinical Severity of Acute Ischemic Stroke

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Essa Hassan¹, Mohammad Haroon², Shah Umam³, Sohrab Khan¹ and Muhammad Aitizaz¹

ABSTRACT

Objective: To determine the association of serum calcium levels with clinical severity of acute ischemic stroke.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the General Medicine Department, Khyber Teaching Hospital, Peshawar, from January 2025 till June 2025.

Methods: A total of 63 patients aged 30–70 years presenting with acute ischemic stroke were enrolled. Serum calcium levels were measured at admission, and stroke severity was assessed using the NIH Stroke Scale. Patients were categorized into two groups based on serum calcium levels: <8.5 mg/dL and ≥ 8.5 mg/dL. Demographic variables, comorbidities, and risk factors were recorded.

Results: The mean age of the patients was 51.86 ± 10.903 years, while the mean BMI was 26.17 ± 4.81 kg/m². The average duration since stroke onset was 37.48 ± 20.07 hours, and the mean serum calcium level was 8.43 ± 1.06 mg/dL. Patients with lower calcium levels had a higher proportion of moderate, moderate-to-severe, and severe stroke categories. A significant association was found between serum calcium levels and stroke severity ($p = 0.03$).

Conclusion: Lower serum calcium levels were significantly associated with increased clinical severity of acute ischemic stroke. Serum calcium may serve as a simple and useful marker for early risk stratification in acute stroke.

Key Words: Acute ischemic stroke, serum calcium, NIHSS, stroke severity, electrolyte imbalance.

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INTRODUCTION

Stroke is characterized by elevated disability, morbidity, and mortality rates, posing a considerable challenge to global health. The statistics show 12.2 million cases of incidence, 101 million prevalence and 6.55 million deaths caused by stroke which just underlines the urgency of introducing effective prediction efforts¹. Ischemic stroke constitutes the most common type of stroke, which is 70 per cent of all stroke attacks^{1,2}. The number of deaths that are as a result of IS all over the world is 3.29 million, and there is a projection that it may increase to 4.9 million by 2030².

Based on the importance of such statistics, it is necessary to find an early and readily available predictor to make an informed clinical decision and

implement appropriate treatment. Calcium is the most common mineral in the human body, which is of paramount importance in many physiological functions, including nerve conductivity, cell wall integrity, coagulation, muscular contraction, fluid, and endocrine and immune system functions^{3,4}.

Although the role of calcium is of critical importance, the area of correlation of serum calcium levels and the results of Acute Ischemic Stroke is under researched, and its results are rather inconsistent. A number of studies have shown the existence of correlations between the low and the high levels of calcium in the serum and the poor results of insulin sensitivity⁵. On the other hand, other studies have found a non-linear association between serum total calcium concentration and all-cause deaths in one year. Other researches have suggested that there are no significant relationships between serum calcium level and the outcome in acute ischemic stroke⁶.

These differences in calcium markers and the endpoints of the studies also make one raise an inquiry on whether the conflicting results are caused by such differences⁷. One of the studies reported relationship between serum calcium levels (ionized) and clinical severity of acute ischemic stroke. i.e. patients with stroke were subset in two groups where serum calcium below 4.5 mg/dl as (minor stroke in 6.66%, moderate stroke in 36.66, moderate-to-severe stroke in 50, and severe stroke in 6.66), and serum calcium above 4.5mg/dl as (Minor

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stroke in 36.66, moderate stroke in 53. Aboriginal calcium levels in serum have been identified as having been specifically related to poorer clinical outcomes among stroke patients, which could be worsening the neuronal damage and contributing to the magnitude of disability⁸⁻¹¹. Since there are no such studies on this topic in the area, this research aims to identify the correlation between serum calcium levels and clinical severity of the acute ischemic stroke in our health facility.

METHODS

This Cross-sectional study was conducted at the General Medicine Department of Khyber Teaching Hospital, Peshawar, from January 2025 till June 2025. WHO sample size calculator was used to calculate the sample size, keeping the following assumptions. Serum calcium <4.5 mg/dl was observed in 6.6% of minor stroke patients [8]. Margin of error 6.2%, and confidence level 95%. Calculated sample size was 63. Data were collected through non-Probability Consecutive Sampling

Inclusion criteria

- Gender (Male/Female)
- Age range 30-70 Years
- Patients with acute ischemic stroke as defined in the operational definition.

Exclusion criteria

- Patients with hemorrhagic stroke
- Patients with malignancy
- Patients with autoimmune diseases

Data collection

The study commenced after approval was obtained from the hospital's ethical review board and the CPSP research unit. All individuals who met the selection criteria were enrolled. The objectives, potential benefits, and possible risks of the study were explained to each participant, after which informed written consent was taken. Baseline demographic information, including age, BMI, gender, education status, employment status, residence, and socioeconomic status, was recorded. For assessment of ionized serum calcium, 5–10 mL of venous blood was drawn using a sterile needle and collected in an appropriate container for laboratory analysis. Stroke severity was evaluated using the NIH Stroke Scale (NIHSS) as per the operational definition. All assessments were performed under the supervision of a consultant with at least five years of post-fellowship experience. All patient information was documented on a structured proforma.

Data Analysis

Data were analyzed using IBM SPSS version 27. Numerical variables such as age, BMI, duration of stroke, and serum calcium levels were presented as mean \pm standard deviation or median (IQR), depending on the distribution. The Shapiro–Wilk test was applied to assess normality. Categorical data such as gender, stroke severity (minor, moderate, moderate-to-severe, severe), calcium level categories, hypertension,

diabetes, smoking status, education level, employment status, residence, and socioeconomic status were presented as frequencies and percentages. The association between serum calcium levels and stroke severity was assessed using the Chi-square test, with $p < 0.05$ considered statistically significant.

RESULTS

Data were collected from 63 patients, mean age of the participants was 51.86 ± 10.903 years, indicating a predominantly middle-aged population. The average BMI was 26.17 ± 4.81 kg/m², placing most individuals in the overweight range. The mean duration since stroke onset was 37.48 ± 20.07 hours. The mean serum calcium level was 8.43 ± 1.06 mg/dL. Gender distribution was nearly equal, with males accounting for 49.2% and females for 50.8%. Regarding education, 36.5% of the subjects had no formal education, while 19.0% had higher education. Employment trends showed that 38.1% were self-employed, 33.3% unemployed, and 28.6% employed. A majority of patients belonged to urban areas (57.1%), while 42.9% resided in rural regions. Socioeconomic stratification showed that 46.0% of participants belonged to the middle socioeconomic group, followed by 34.9% in the low and 19.0% in the high socioeconomic groups. Hypertension and diabetes were common comorbidities, affecting 55.6% and 52.4% of participants, respectively. Smoking status revealed that 38.1% were smokers, 33.3% were non-smokers, and 28.6% were ex-smokers. Table 1.

Patients with low serum calcium levels (<8.5 mg/dL) predominantly fell into moderate (30.8%), moderate-to-severe (30.8%), and severe (23.1%) stroke categories, with only 15.4% classified as minor stroke. In contrast, individuals with normal calcium levels (≥ 8.5 mg/dL) showed a higher proportion of minor strokes (33.3%) and fewer severe strokes (15.4%). The association between serum calcium level and stroke severity was statistically significant ($p = 0.03$). Table 2.

Hypertension showed a clear trend toward higher severity, with 34.2% of hypertensive patients presenting with moderate stroke and 26.3% with moderate-to-severe stroke. A small proportion (18.4%) had severe stroke. A similar pattern was observed for diabetes: 31.0% of diabetic patients had moderate stroke, and 27.6% had moderate-to-severe stroke. Smoking status also demonstrated variation across severity levels. Smokers most frequently fell in the moderate category (35.3%), while non-smokers were more evenly distributed. Ex-smokers showed higher proportions in minor (30.0%) and severe (30.0%) categories. Table 3. Patients with minor stroke had the highest mean calcium level (8.72 ± 0.88 mg/dL), followed by moderate stroke (8.46 ± 0.97 mg/dL) and moderate-to-severe stroke (8.12 ± 1.05 mg/dL). The lowest mean calcium level was observed in patients with severe stroke (7.89 ± 1.14 mg/dL). The difference in mean calcium values across severity groups was statistically significant ($p = 0.04$). Table 4.

Table No. 1: Descriptive and Frequency Distribution of Study Variables (N = 63)

Variable	Category / Statistic	n (%) / Mean ± SD
Age (years)	Mean ± SD	51.86 ± 10.903
BMI (kg/m ²)	Mean ± SD	26.17 ± 4.81
Duration of Stroke (hours)	Mean ± SD	37.48 ± 20.07
Serum Calcium (mg/dL)	Mean ± SD	8.43 ± 1.06
Gender	Male	31 (49.2)
	Female	32 (50.8)
Education Status	None	23 (36.5)
	Primary	18 (28.6)
	Secondary	10 (15.9)
	Higher	12 (19.0)
Employment Status	Unemployed	21 (33.3)
	Employed	18 (28.6)
	Self-employed	24 (38.1)
Residence	Rural	27 (42.9)
	Urban	36 (57.1)
Socioeconomic Status	Low	22 (34.9)
	Middle	29 (46.0)
	High	12 (19.0)
Hypertension	Yes	35 (55.6)
	No	28 (44.4)
Diabetes	Yes	33 (52.4)
	No	30 (47.6)
Smoking Status	Non-smoker	21 (33.3)
	Smoker	24 (38.1)
	Ex-smoker	18 (28.6)
Stroke Severity (NIHSS Category)	Minor	20 (31.7)
	Moderate-to-severe	13 (20.6)
	Severe	30 (47.6)

Table No. 2: Association of Serum Calcium Levels with Stroke Severity

Serum Calcium Level	Minor n (%)	Moderate n (%)	Moderate-to-severe n (%)	Severe n (%)	p-value
Low (<8.5 mg/dL)	4 (15.4)	8 (30.8)	8 (30.8)	6 (23.1)	0.03
Normal (≥8.5 mg/dL)	13 (33.3)	11 (28.2)	7 (17.9)	6 (15.4)	—

Table No. 3: Risk Factors Across Stroke Severity

Risk Factor	Minor n (%)	Moderate n (%)	Moderate-to-severe n (%)	Severe n (%)	Total n (%)
Hypertension	8 (21.1)	13 (34.2)	10 (26.3)	7 (18.4)	35 (55.6)
No Hypertension	9 (36.0)	6 (24.0)	5 (20.0)	5 (20.0)	28 (44.4)
Diabetes	7 (24.1)	9 (31.0)	8 (27.6)	5 (17.2)	33 (52.4)
No Diabetes	10 (29.4)	10 (29.4)	7 (20.6)	7 (20.6)	30 (47.6)
Smoker	4 (23.5)	6 (35.3)	4 (23.5)	3 (17.6)	24 (38.1)
Non-smoker	10 (27.8)	11 (30.6)	9 (25.0)	6 (16.7)	21 (33.3)
Ex-smoker	3 (30.0)	2 (20.0)	2 (20.0)	3 (30.0)	18 (28.6)

Table No. 4: Comparison of Mean Serum Calcium Across Stroke Severity

Stroke Severity	Mean Calcium (mg/dL) ± SD	p-value
Minor	8.72 ± 0.88	0.04
Moderate	8.46 ± 0.97	
Moderate-to-severe	8.12 ± 1.05	
Severe	7.89 ± 1.14	

DISCUSSION

This study explored the association between serum calcium levels and the clinical severity of acute ischemic stroke among patients presenting to a tertiary care hospital. The results showed a strong regularity: the lower were the levels of serum calcium the higher were the categories of NIHSS severity which showed the significant correlation between calcium homeostasis and the degree of a neurological impairment. The number of moderate, moderate-to-severe and severe strokes among patients with a calcium level under 8.5 mg/dL was higher than among patients with normal calcium level and this fact was statistically significant. The findings corroborate the increasing evidence that electrolyte imbalances, especially those in calcium, can affect ischemic neuronal damage. The relationship that is observed is biologically plausible. The critical functions of calcium include stability of neuronal membranes, transmission of neuronal synapses, and blood vessel tone. In cerebral ischemia disrupted autoregulation and excitotoxicity cause intracellular calcium overload which boosts neuronal apoptosis and expansion of the infarct. Reduced extracellular serum calcium can also contribute to the further destabilization of neuronal activity and inhibition of the buffering of brain against ischemic damage¹². The trend in this paper is similar to the mechanistic interpretation that has been suggested in other studies that have also indicated that hypocalcemia is associated with greater infarct size, more significant neurological impairments, and worse clinical outcomes¹³.

The proportion of patients with more severe stroke had more frequent hypertension, diabetes, and smoking, as well which is in line with known epidemiology of strokes. These comorbidities are established causes of cerebrovascular pathology by the mechanisms of dysfunction of endothelial functions, accelerated atherosclerosis, and dysfunction in microvascular autoregulation. Although these factors were not the main interest of the study they can be still justified by their presence in the categories of severity and prove the further relevance of the burden of ischemic stroke¹⁴. The trend was similar to that found in earlier studies that indicated a similar tendency of the cardiovascular risk factors clustering within patients who suffered more significant neurological impairment. The average serum calcium level in the present study was slightly low in the moderate-severe and severe groups than that of the mild group. The differences are not very large in numbers, but considering the trend, there is an increasing downward trend in the severity categories. These gradients were also reported in earlier studies, which substantiate the assumption that clinical effects of even minor changes in serum calcium can occur in

acute stroke¹⁵. Calcium is simple to detect, is commonplace and cheap, and could therefore prove useful as an early prognostic indicator, particularly in resource-constrained environments^{16,17}. There are a number of limitations associated with this study, which ought to be considered when interpreting the results. To begin with, the cross-sectional study did not allow testing any causal relationship between serum calcium level and stroke severity, thus only associations could be determined. Second, serum calcium was only determined at one time, which might not be indicative of the changes at the acute period of ischemia. Serial calcium patterns may be more insightful on the dynamics of calcium during stroke. Third, the research was carried out in one center and the sample size is quite small (63); therefore, it might not apply to larger populations. Fourth, no assessment of potential confounders, including nutritional status, levels of vitamin D, parathyroid hormone, renal functioning, and history of medication, was conducted, which can determine serum calcium levels. And finally, some variables might lack sociodemographic as well as clinical data, which could have resulted in classification bias.

CONCLUSION

It is concluded that lower serum calcium levels are significantly associated with greater clinical severity of acute ischemic stroke. Patients presenting with reduced calcium levels were more likely to fall into higher NIHSS categories, indicating more substantial neurological impairment. Because serum calcium measurement is simple, rapid, and routinely available in emergency settings, it may serve as a useful adjunct marker for early risk stratification. Further large-scale, prospective studies are recommended to validate this association and to determine whether correcting calcium imbalance could offer therapeutic benefit in improving stroke outcomes.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Essa Hassan, Mohammad Haroon, Shah Umam
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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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