e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(9); 147-150

Original Research Article

A Correlational Study of Serum Calcium with Size of Infarct and Clinical Outcome in Acute Ischemic Stroke

Suvarna Sathri[1], Changala Soujanya[2], V E Rama Naidu Mopada[3], K Rambabu[4], R Vikram Vardhan[5], K. Yoshitha Meenakshi[6], Sugandhi Adabala[7], Kethavath Husya Naik[8], Pediredla Sailaja[9], Harika Routu[10], Pinniboyana Siva Sai[11], Reddy Deekshitha[12]

[1]Assistant Professor, Department of General Medicine, Andhra Medical College, Visakhapatnam
[2]Assistant Professor, Department of General Medicine, Andhra Medical College, Visakhapatnam
[3]Assistant Professor, Department of General Medicine, Andhra Medical College, Visakhapatnam
[4]Professor, Department of General Medicine, Andhra Medical College, Visakhapatnam
[5]Associate Professor, Department of General Medicine, Andhra Medical College, Visakhapatnam
[6]Senior Resident, Department of Neurology, Christian Medical College, Vellore
[7]3rd Year Post Graduate, Department of General Medicine, Andhra Medical College, Visakhapatnam
[8]3rd Year Post Graduate, Department of General Medicine, Andhra Medical College, Visakhapatnam
[9]2nd Year Post Graduate, Department of General Medicine, Andhra Medical College, Visakhapatnam
[10]2nd Year Post Graduate, Department of General Medicine, Andhra Medical College, Visakhapatnam
[11]1st Year Post Graduate, Department of General Medicine, Andhra Medical College, Visakhapatnam
[12]1st Year Post Graduate, Department of General Medicine, Andhra Medical College, Visakhapatnam

Received: 02-07-2025 / Revised: 01-08-2025 / Accepted: 02-09-2025
Corresponding Author: Dr. K Rambabu
Conflict of interest: Nil

Abstract:

Introduction: Stroke is a leading cause of death and disability, with ischemic stroke being most common. Calcium overload during ischemia contributes to neuronal injury and infarct expansion. This study evaluates serum calcium levels in acute ischemic stroke and correlates them with infarct size and severity using CT imaging and NIHSS scoring.

Methods: This one-year observational study at Andhra Medical College included patients >35 years with CT-confirmed acute ischemic stroke within 48–72 hours of onset. Exclusions included hemorrhagic stroke and comorbid conditions. Serum calcium, infarct size (ABC/2 method), and NIHSS scores were assessed. Thrombolysis was not administered to any participant.

Results: In this study of 100 stroke patients, males predominated (65%). Diabetes, hypertension, and CAD were more prevalent in men. Females had lower calcium levels, larger infarcts, and higher NIHSS scores. Hypocalcemia was common in ages 40–60. Lower calcium correlated significantly with increased infarct volume and stroke severity ($P < 0.05$).

Conclusion: Lower serum calcium levels in acute ischemic stroke patients were significantly associated with larger infarcts and higher NIHSS scores, indicating worse outcomes. Hypocalcemia may serve as a prognostic biomarker and therapeutic target. These findings underscore the potential importance of monitoring calcium levels in the acute management of stroke.

Keywords: Ischemic stroke, serum calcium, infarct size, NIHSS score, hypocalcemia

Introduction

Stroke is a major public health concern globally, ranking as the second leading cause of death and a primary cause of long-term disability [1]. Among the two major types, ischemic stroke accounts for the majority of cases and is characterized by a sudden onset of neurological deficit due to impaired cerebral blood flow. In ischemic stroke, deprivation of oxygen and glucose leads to a rapid decline in ATP levels, triggering neuronal injury and death [2]. A key mediator in this pathophysiological process is calcium, which accumulates within neurons during ischemia, contributing to excitotoxicity and cytotoxic edema.

Calcium plays a crucial role in the cascade of neuronal damage during ischemic events [3]. Ischemia-induced energy failure disrupts membrane ion pumps, causing depolarization and the release of glutamate. This excitatory neurotransmitter stimulates postsynaptic receptors, leading to excessive calcium influx. The resulting calcium

overload activates several downstream pathways including calcium-sensitive enzymes such as calcineurin, which exacerbate neuronal injury. Moreover, cytotoxic edema and disruption in calcium homeostasis contribute to the enlargement of infarcted areas. Several clinical studies have observed an association between serum calcium levels and stroke severity, suggesting that calcium imbalance may influence infarct size and neurological outcomes [4, 5]. The present study aims to evaluate the serum calcium levels at the time of presentation in patients with acute ischemic stroke. It further seeks to calculate the size of cerebral infarcts using CT imaging and to correlate these findings with the clinical severity of stroke as assessed by the National Institutes of Health Stroke Scale (NIHSS).

Methods

It was an observational study, conducted in department of General Medicine, Andhra Medical College, Visakhapatnam. Study was conducted from December 2022 to November 2023, 1 year. Study protocol was approved by Institutional Ethics committee. An informed written consent was taken from the study members.

Patients > 35 years presenting within 48–72 hours of stroke onset, clinically diagnosed and CT-confirmed as acute ischemic stroke, were included. Patients were excluded if they were < 35 years, presented > 72 hours after symptom onset, or had a previous history of stroke; hemorrhagic stroke, stroke secondary to tuberculoma, tumor, trauma, or subarachnoid hemorrhage, renal or hepatic diseases, malignancy, or pancreatitis were also excluded. Additionally, individuals on calcium supplementation or presenting with fever and active infections were not included in the study.

Patients were selected using a simple random sampling technique. Data collection was carried out using a structured proforma, which included sociodemographic details, clinical history, and biochemical investigations. A detailed clinical, neurological, and general physical examination was performed for each patient. A standardized questionnaire was administered to gather relevant patient information. All patients underwent essential laboratory investigations including serum calcium estimation, complete blood picture (CBP), liver function tests (LFT), renal function tests (RFT), and serum proteins. Serum calcium levels were measured at the time of admission.

The diagnosis of ischemic stroke was confirmed using brain CT. The clinical severity of stroke was assessed using the NIHSS at admission. Infarct size was calculated using the ABC/2 method, a validated formula where 'A' represents the greatest diameter of the infarct, 'B' is the diameter perpendicular to A, and 'C' is the number of CT slices on which the infarct appears, multiplied by the slice thickness. The resulting value (A×B×C)/2 provided an estimate of the infarct volume in cubic centimeters. The participant's data were recorded in the standard proforma. Patients were managed using standardized treatment protocols for acute ischemic stroke. Notably, none of the patients received thrombolytic therapy during the course of this study, thereby eliminating its potential influence on outcomes.

Statistical analysis: The data was analysed using SPSS version 20. For significance, multivariate analysis, Pearson correlation analysis, and the chi-square test were used. P less than 0.05 was considered statistically significant.

Results

Total 100 patients were included in the study, of whom 65 were male. The mean age of the participants was 62.37 ± 9.43 years. Among them, 34 (64.1%) males and 19 (35.4%) females had diabetes mellitus (DM). Hypertension was seen in 31 (59.6%) males and 21 (40.3%) females. Coronary artery disease (CAD) was more prevalent in males (64.1%) compared to females (35.9%). The mean serum calcium levels were 9.027 ± 0.46 mg/dL in males and 8.697 ± 0.44 mg/dL in females. Hypocalcemia was more common in the 40–60 year group, while normal calcium levels were more frequently observed in those aged 71–90 years.

Among patients with aphasia, 54.10% were women and 45.90% were men. The mean infarct size was 26.71 ± 17.68 cm^3 in males and 36.52 ± 17.84 cm^3 in females. The mean NIHSS score was higher in females (22.68 ± 9.69) compared to males (16.01 ± 10.18). A significant negative correlation ($p < 0.05$) was observed between serum calcium levels and both NIHSS score and infarct volume, indicating worse outcomes with lower calcium levels.

Discussion

In this study involving 100 acute ischemic stroke patients, 65% were male, with a mean age of 62.37 ± 9.43 years. The findings reflect a male predominance in stroke incidence, aligning with previous literature that suggests men have a higher risk of stroke at a younger age compared to women, potentially due to higher exposure to risk factors such as smoking, alcohol consumption, and cardiovascular disease [6]. DM was observed in 53% of participants, with a higher prevalence in males (64.1%) than females (35.4%). This is consistent with evidence that diabetes significantly increases the risk of stroke and is more common in males among stroke cohorts [7]. Hypertension, a major modifiable risk factor for stroke, was found in 52% of the participants—59.6% of males and 40.3% of females—again indicating a greater burden

among men. CAD was also more prevalent in males (64.1%) than females (35.9%), supporting previous reports that males are at increased risk of concurrent cardiovascular disease, which can compound stroke risk and severity [8]. These findings highlight the importance of aggressive risk factor control, especially in male populations, to prevent stroke and its complications. Gender-based differences in comorbidities such as diabetes, hypertension, and CAD emphasize the need for targeted screening and individualized management strategies in stroke prevention.

The mean serum calcium level was higher in males (9.027 ± 0.46 mg/dL) compared to females (8.697 ± 0.44 mg/dL). This gender disparity in calcium levels may be attributed to hormonal differences, dietary calcium intake, and age-related bone metabolism variations. Estrogen deficiency in postmenopausal women leads to reduced calcium absorption and increased bone resorption, which may partly explain lower calcium levels among female [9]. Additionally, hypocalcemia was more commonly observed in patients aged 40–60 years, while normal calcium levels predominated in the elderly population (71–90 years). This finding is somewhat unexpected, as calcium levels often decline with age due to impaired vitamin D metabolism and decreased intestinal absorption [10]. However, it is possible that elderly patients receiving regular medical care may be more likely to have their calcium levels monitored and supplemented, leading to better maintenance of normal calcium levels.

Hypocalcemia has been recognized as a potential risk factor in stroke, influencing both neuronal excitability and infarct size. Calcium plays a key role in the pathophysiology of ischemic injury, and lower systemic calcium levels have been associated with poorer neurological outcomes [11]. The negative correlation between serum calcium and infarct size or NIHSS score in this study further supports this association. Thus, identifying and correcting hypocalcemia early in the course of stroke may have prognostic significance and therapeutic implications.

In this study, aphasia was more common among women, affecting 54.10% compared to 45.90% of men. Aphasia, a language disorder caused by damage to the brain's speech centers, is a common manifestation of large hemispheric strokes. The observed female predominance may reflect the higher NIHSS scores and infarct volumes in female patients. Previous studies have demonstrated that women often present with more severe strokes and worse outcomes than men, possibly due to older age at presentation, comorbidities, and biological differences in cerebrovascular regulation [12]. Moreover, hormonal changes post-menopause, including reduced estrogen levels, may contribute to increased stroke severity in women [13].

The mean infarct size in this study was significantly larger in females (36.52 ± 17.84 cm^3) than in males (26.71 ± 17.68 cm^3), and the mean NIHSS score—a validated scale measuring stroke severity—was notably higher in females (22.68 ± 9.69 vs. 16.01 ± 10.18). Larger infarct volumes are associated with greater neurological deficits and worse outcomes. These findings are consistent with prior research suggesting that sex-related differences influence infarct volume and neurological status at admission and discharge [14]. The higher NIHSS scores in females may reflect the larger infarct size, but may also be influenced by variations in pre-stroke functional status and response to ischemia. Moreover, the presence of aphasia can inflate NIHSS scores disproportionately in patients with left hemispheric infarcts, possibly contributing to higher scores among females with language-dominant hemisphere involvement [15].

A significant negative correlation was identified between serum calcium levels and both infarct volume and NIHSS score ($p < 0.05$). Patients with lower serum calcium levels at admission had larger infarcts and more severe neurological deficits. Calcium plays a central role in cellular excitotoxicity and neuronal injury during ischemic stroke. Intracellular calcium overload, mediated by glutamate excitotoxicity and failure of ATP-dependent ion pumps, contributes to cellular damage [16]. Previous studies have shown that hypocalcemia is associated with worse stroke outcomes, including higher mortality and functional impairment [17]. Lower systemic calcium may reflect a disruption in neurovascular homeostasis and impaired synaptic transmission, both of which exacerbate ischemic injury. Thus, serum calcium may serve as a potential biomarker for predicting infarct size and severity in acute ischemic stroke patients. Correcting hypocalcemia could be explored as an adjunctive strategy to improve outcomes in selected patients.

Conclusion: This study demonstrated a significant negative correlation between serum calcium levels and both NIHSS scores and infarct volume in patients with acute ischemic stroke. Lower serum calcium levels were associated with larger infarct sizes and greater neurological deficits, particularly among female. Hypocalcemia was more common in the 40–60 year age group and was linked to poorer clinical outcomes. These findings suggest that serum calcium may serve as a useful biomarker for predicting stroke severity and prognosis. Early identification and potential correction of hypocalcemia could improve stroke outcomes, warranting further research into calcium's role in cerebrovascular disease management.

References

1. Behera DK, Rahut DB, Mishra S. Analyzing stroke burden and risk factors in India using data from the Global Burden of Disease Study. Sci Rep. 2024; 14: 22640.
2. Salaudeen MA, Bello N, Danraka RN, Ammani ML. Understanding the Pathophysiology of Ischemic Stroke: The Basis of Current Therapies and Opportunity for New Ones. Biomolecules. 2024; 14(3): 305.
3. Vikrant Rahi, Ravinder K. Kaundal. Exploring the intricacies of calcium dysregulation in ischemic stroke: Insights into neuronal cell death and therapeutic strategies. Life Sciences. 2024; 347: 122651.
4. Hou J, Huang Z, Zeng W, et al. Serum calcium is associated with sudden cardiac arrest in stroke patients from ICU: a multicenter retrospective study based on the NICU collaborative research database. Sci Rep. 2024; 14: 1700.
5. Nayak RR, Narayanaswamy S. Association of serum calcium levels with infarct volume and stroke scores in acute ischemic stroke patients: An observational study. Caspian J Intern Med. 2022; 13(4):780 – 5.
6. Abdu H, Seyoum G. Sex Differences in Stroke Risk Factors, Clinical Profiles, and In-Hospital Outcomes Among Stroke Patients Admitted to the Medical Ward of Dessie Comprehensive Specialized Hospital, Northeast Ethiopia. Degener Neurol Neuromuscul Dis. 2022; 12: 133 – 44.
7. Mosenzon O, Cheng AY, Rabinstein AA, Sacco S. Diabetes and Stroke: What Are the Connections? J Stroke. 2023; 25(1): 26 – 38.
8. Nathaniel J. Glasser, Jacob C Jameson, Elbert S Huang, et al. Male gender expressivity and diagnosis and treatment of cardiovascular disease risks in men. JAMA Netw Open. 2024; 7(10): e2441281
9. Cheng CH, Chen LR, Chen KH. Osteoporosis Due to Hormone Imbalance: An overview of the effects of estrogen deficiency and glucocorticoid overuse on bone turnover. Int J Mol Sci. 2022; 23(3): 1376.
10. Fleet JC. Vitamin D-Mediated regulation of intestinal calcium absorption. Nutrients. 2022; 14(16):3351.
11. Vijay Prabhu SN, Tripathi BK, Agarwal Y, et al. Association of serum calcium levels with clinical severity of ischemic stroke at the time of admission as defined by NIHSS score: A cross-sectional, observational study. J Family Med Prim Care. 2022; 11(10): 6427 – 32.
12. Gall SL, Donnan G, Dewey HM, Macdonell R, et al. Sex differences in presentation, severity, and management of stroke in a population-based study. Neurology. 2010; 74(12): 975 – 81.
13. Reeves MJ, Bushnell CD, Howard G, Gargano JW, et al. Sex differences in stroke: epidemiology, clinical presentation, medical care, and outcomes. Lancet Neurol. 2008; 7(10): 915 – 26.
14. Bushnell C, Howard VJ, Lisabeth L, Caso V, Gall S, Kleindorfer D, Chaturvedi S, Madsen TE, Demel SL, Lee SJ, Reeves M. Sex differences in the evaluation and treatment of acute ischaemic stroke. Lancet Neurol. 2018; 17(7): 641 – 50.
15. Tilling K, Sterne JA, Rudd AG, Glass TA, Wityk RJ, Wolfe CD. A new method for predicting recovery after stroke. Stroke. 2001; 32(12): 2867 – 73.
16. Szydlowska K, Tymianski M. Calcium, ischemia and excitotoxicity. Cell Calcium. 2010; 47(2): 122 – 9.
17. Gu F, Zhao W, Duan X, Zhang Y, Luo X, Chen G, Jin X, Pan H, Gao F, Wu H. Association of hypocalcemia with in-hospital mortality in critically ill patients with intracerebral hemorrhage: A retrospective cohort study. Front Neurol. 2023; 13: 1054098.