Section: General Medicine

Original Research Article

ASSOCIATION OF SERUM CALCIUM LEVELS WITH INFARCT SIZE IN ACUTE ISCHEMIC STROKE: AN OBSERVATIONAL STUDY

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ABSTRACT

Background: Acute ischemic stroke (AIS) is a leading cause of mortality and long-term disability worldwide. Calcium plays a critical role in the pathophysiology of cerebral ischemia through its involvement in neuronal injury and the ischemic cascade. Previous studies have suggested that serum calcium levels may correlate with stroke severity and outcome. This study aimed to evaluate the association between serum calcium levels and infarct size in patients with acute ischemic stroke. **Materials and Methods:** A hospital-based observational study was conducted at CSI Kalyani General Hospital, Chennai, over a period of 18 months. Sixty-two patients aged 40 years and above presenting within 48 hours of onset of acute ischemic stroke were included. Serum total calcium, serum albumin, and albumin-corrected calcium levels were measured on admission. Infarct size was assessed using computed tomography (CT) of the brain. Correlation analyses were performed to determine the relationship between serum calcium levels and infarct size. **Results:** A significant negative correlation was observed between corrected serum calcium levels and infarct size ($p < 0.001$). Total serum calcium levels also demonstrated a significant inverse correlation with infarct size ($p < 0.001$). Patients with lower serum calcium levels had larger infarcts compared with those having normal calcium levels. In addition, serum triglyceride and total cholesterol levels showed significant positive correlations with infarct size, whereas HDL cholesterol demonstrated a significant negative correlation. Smoking was associated with larger infarct size. **Conclusion:** Lower serum total calcium and albumin-corrected calcium levels are significantly associated with larger infarct size in patients with acute ischemic stroke. Corrected serum calcium may serve as a simple, inexpensive, and readily available biomarker for assessing stroke severity and prognosis. Further large-scale prospective studies are warranted to validate its role as a prognostic indicator in acute ischemic stroke.

INTRODUCTION

Stroke is one of the leading causes of mortality and long-term disability worldwide and represents a major public health challenge, particularly in low- and middle-income countries.[1] Acute ischemic stroke (AIS), resulting from interruption of cerebral blood flow, accounts for approximately 85% of all stroke cases.[1] Despite advances in acute stroke management, predicting stroke severity and outcome at the time of presentation remains an important clinical challenge. Early identification of reliable prognostic biomarkers may facilitate risk stratification and guide therapeutic decision-making. Calcium plays a pivotal role in the pathophysiology of cerebral ischemia. During ischemic injury, depletion of cellular energy stores leads to failure of membrane ion pumps, neuronal depolarization, and excessive influx of calcium ions into neurons. Intracellular calcium accumulation activates a cascade of enzymatic processes, including phospholipase activation, free radical generation, mitochondrial dysfunction, and apoptotic pathways, ultimately resulting in neuronal death and expansion of the infarcted area.[10-14] Consequently, serum calcium levels may reflect the extent of ischemic injury and have potential value as a prognostic marker in acute ischemic stroke.

Several studies have demonstrated an association between serum calcium levels and stroke severity. Lower serum calcium concentrations have been linked to larger infarct volumes, higher neurological

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deficit scores, and poorer functional outcomes.[2,4,5] Conversely, higher serum calcium levels have been associated with smaller infarct sizes and improved recovery following ischemic stroke.[3,4] Albumin-corrected calcium has been suggested to be a more reliable indicator than total serum calcium because a substantial proportion of circulating calcium is protein-bound, predominantly to albumin.[1,2]

Although previous studies have reported an inverse relationship between serum calcium levels and infarct size,[1-5] evidence from the Indian population remains limited. Furthermore, the utility of serum calcium as an easily available and cost-effective prognostic biomarker in routine clinical practice requires further evaluation.[6,7,9] Therefore, the present study was undertaken to assess the association between serum calcium levels, including albumin-corrected calcium, and infarct size in patients presenting with acute ischemic stroke.

Aim

To determine the correlation between serum calcium levels and infarct size in patients with acute ischemic stroke.

Objectives

1. To estimate serum total calcium and albumin-corrected calcium levels in patients with acute ischemic stroke.
2. To measure infarct size using computed tomography (CT) of the brain.
3. To evaluate the correlation between serum calcium levels and infarct size.
4. To assess the potential role of serum calcium as a prognostic indicator in acute ischemic stroke.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based observational study was conducted in the Department of General Medicine, CSI Kalyani General Hospital, Chennai, over a period of 18 months. The study was designed to evaluate the association between serum calcium levels and infarct size in patients presenting with acute ischemic stroke.

Study Population

The study included patients admitted to the emergency department with a diagnosis of acute ischemic stroke. A total of 62 consecutive patients who fulfilled the eligibility criteria were enrolled during the study period.

Inclusion Criteria

1. Age ≥40 years.
2. Both male and female patients.
3. Presentation within 48 hours of onset of stroke symptoms.
4. Diagnosis of acute ischemic stroke based on clinical examination and confirmation by computed tomography (CT) of the brain.

Exclusion Criteria

1. Known malignancy.
2. Clinical or laboratory evidence of active infection.
3. Previous history of transient ischemic attack (TIA) or reversible ischemic neurological deficit.
4. Hemorrhagic stroke, subarachnoid hemorrhage, or cerebral venous sinus thrombosis confirmed by neuroimaging.
5. Recent major surgery or trauma.
6. Chronic hepatic disease or renal disease that could affect serum calcium or albumin levels.

Data Collection

After obtaining informed consent, eligible patients presenting with acute ischemic stroke were enrolled consecutively in the study. Detailed demographic information, clinical history, presenting symptoms, vascular risk factors, and associated comorbidities were recorded using a structured proforma. Blood samples were collected at admission for the estimation of serum total calcium, serum albumin, total cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol levels. Albumin-corrected calcium levels were calculated from the measured serum calcium and albumin values. All patients underwent non-contrast computed tomography (CT) of the brain within 48 hours of admission to confirm the diagnosis and assess infarct size. Clinical, biochemical, and radiological findings were systematically documented and analyzed to evaluate the association between serum calcium levels and infarct size in patients with acute ischemic stroke.

Neuroimaging Assessment

All patients underwent non-contrast computed tomography (CT) of the brain within 48 hours of admission to confirm the diagnosis of acute ischemic stroke and to exclude intracerebral hemorrhage or other intracranial pathologies. CT imaging was performed using a 128-slice multidetector CT scanner. The location and extent of cerebral infarction were assessed by an experienced radiologist. Infarct size was estimated from CT images using the method described by Sims et al., which is considered a reliable technique for measuring infarct volume in acute ischemic stroke. The largest lesion slice was identified, and the maximum longitudinal diameter, maximum perpendicular diameter, and lesion depth were measured to estimate infarct volume. The radiological findings were documented and correlated with serum calcium levels to evaluate their association with infarct size and stroke severity.

Outcome Measures

The primary outcome measure of the study was the association between serum calcium levels (total serum calcium and albumin-corrected calcium) and infarct size in patients with acute ischemic stroke. Infarct size, as determined by computed tomography (CT) of the brain, was used as an indicator of stroke severity. Secondary outcome measures included the relationship between infarct size and demographic characteristics, clinical presentation, vascular risk

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factors, blood pressure, smoking status, alcohol consumption, diabetes mellitus, serum albumin levels, and lipid profile parameters. These measures were evaluated to identify factors associated with increased stroke severity and to assess the potential role of serum calcium as a prognostic marker in acute ischemic stroke.

Ethical Considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee of CSI Kalyani General Hospital, Chennai. Written informed consent was obtained from all participants or their legally authorized representatives prior to enrollment in the study. Patient confidentiality and privacy were strictly maintained throughout the study, and all data were anonymized before analysis. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and Good Clinical Practice guidelines.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the independent Student's *t*-test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. Pearson's correlation analysis was used to assess the relationship between serum calcium levels and infarct size. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 62 patients with acute ischemic stroke were included in the study. The demographic characteristics, clinical profile, biochemical parameters, and radiological findings were analyzed to determine the association between serum calcium levels and infarct size.

Baseline Characteristics

A total of 62 patients with acute ischemic stroke were included in the study. The majority of patients belonged to the elderly age group, with most subjects in the low serum calcium group being between 71 and 80 years of age. Male patients constituted a higher proportion of the study population and were more likely to have lower corrected calcium levels compared to females. Diabetes mellitus and dyslipidemia were the most common vascular risk factors observed among patients with low serum calcium levels. Although a higher proportion of smokers, hypertensives, and alcohol consumers was observed in the low calcium group, these associations were not statistically significant.

Table 1: Baseline Characteristics of the Study Population

Variable	Findings
Total sample size	62
Predominant age group	71–80 years
Gender predominance	Male
Common risk factors	Diabetes mellitus, Dyslipidemia
Smoking prevalence	Higher in low calcium group
Hypertension prevalence	Higher in low calcium group
Alcohol consumption	Higher in low calcium group

Note: Baseline demographic and clinical characteristics of the 62 patients with acute ischemic stroke included in the study. Data are presented as frequency (n) and percentage (%). The table describes the distribution of age, sex, and major vascular risk factors among the study participants.

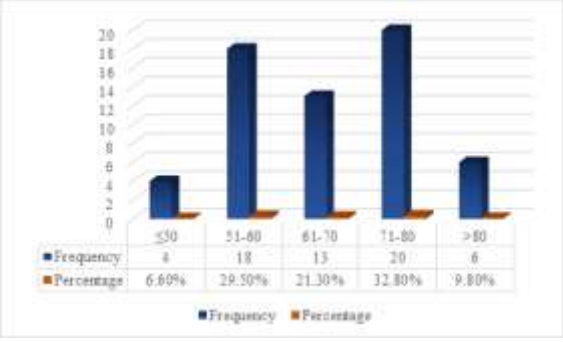

Figure 1: Distribution of Study Participants According to Age Group

Figure Note: Figure 1 illustrates the distribution of study participants according to age group. A higher proportion of patients belonged to the older age categories, indicating that the occurrence of acute ischemic stroke increased with advancing age in the study population.

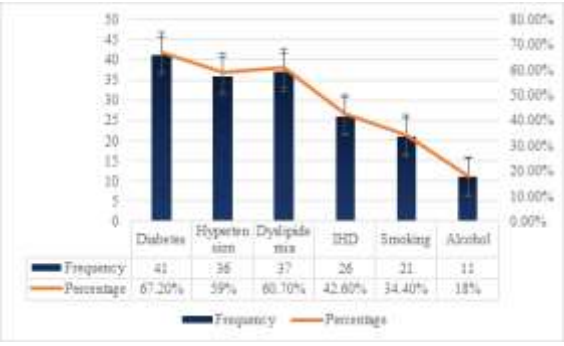

Figure 2: Distribution of Vascular Risk Factors Among Patients with Acute Ischemic Stroke (N = 61)

Figure Note: Figure 2 illustrates the distribution of major vascular risk factors among patients with acute ischemic stroke. Diabetes mellitus, hypertension,

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dyslipidemia, smoking, and alcohol consumption were the most commonly observed risk factors in the study population, highlighting their potential contribution to the development and severity of ischemic stroke.

Figure 3: Distribution of Vascular Territory Involvement Among Patients with Acute Ischemic Stroke (N = 61)

Figure Note: Figure 3 illustrates the distribution of cerebral vascular territories involved in acute ischemic stroke among the study participants. The middle cerebral artery (MCA) territory was the most frequently affected vascular territory, followed by the posterior cerebral artery (PCA) and anterior cerebral artery (ACA) territories.

Clinical and Radiological Characteristics

Weakness of limbs was the most common presenting symptom among patients with acute ischemic stroke. Radiological assessment revealed that the middle cerebral artery (MCA) territory was the most frequently involved vascular territory, followed by the posterior cerebral artery (PCA) and anterior cerebral artery (ACA). Although ACA territory infarcts demonstrated larger mean infarct sizes, the difference among vascular territories was not statistically significant.

Table 2: Clinical and Radiological Characteristics

Variable	Findings
Most common presenting symptom	Weakness of limbs
Most commonly involved territory	MCA
Other territories involved	PCA, ACA
Largest mean infarct size	ACA territory
Statistical significance	Not significant

Note: Clinical and radiological characteristics of patients with acute ischemic stroke. Data include presenting symptoms, vascular territory involvement, and neuroimaging findings as assessed by CT brain imaging.

Comparison of Infarct Size According to Clinical Variables

Male patients demonstrated significantly larger infarct sizes compared to female patients. Smokers also had significantly larger infarct sizes when compared to non-smokers. Although differences in infarct size were observed among patients with diabetes mellitus, hypertension, and alcohol consumption, these associations did not reach statistical significance.

Table 3: Comparison of Infarct Size According to Clinical Variables

Variable	Association with Infarct Size	Statistical Significance
Male gender	Larger infarct size	Significant
Smoking	Larger infarct size	Significant
Diabetes mellitus	No significant association	Not significant
Hypertension	No significant association	Not significant
Alcohol consumption	No significant association	Not significant

Note: Table 3 compares infarct size across different clinical variables, including gender, smoking status, diabetes mellitus, hypertension, and alcohol consumption. The association between these clinical factors and infarct size was evaluated to identify variables associated with increased stroke severity.

Association Between Serum Calcium Levels and Infarct Size

A significant negative correlation was observed between serum calcium parameters and infarct size. Lower albumin-corrected calcium levels were associated with larger infarct sizes. Similarly, lower total serum calcium levels were significantly associated with increased infarct size, suggesting that reduced serum calcium concentrations may be indicative of greater stroke severity.

Table 4: Association Between Serum Calcium Levels and Infarct Size

Parameter	Correlation with Infarct Size	p-value
Total serum calcium	Negative	<0.001
Albumin-corrected calcium	Negative	<0.001

Note: Table 4 shows the correlation between serum calcium parameters and infarct size in patients with acute ischemic stroke. Total serum calcium and albumin-corrected calcium levels were analyzed to determine their relationship with infarct size measured on CT imaging. A negative correlation

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indicates that lower serum calcium levels are associated with larger infarct size and increased stroke severity.

Association of Lipid Profile Parameters with Infarct Size

Serum triglyceride levels demonstrated a significant positive correlation with infarct size. Total cholesterol levels also showed a significant positive association with infarct size. In contrast, HDL cholesterol exhibited a significant negative correlation, indicating that lower HDL levels were associated with larger infarcts.

Table 5: Association of Lipid Profile Parameters with Infarct Size

Parameter	Correlation with Infarct Size	p-value
Total cholesterol	Positive	<0.001
Triglycerides	Positive	<0.001
HDL cholesterol	Negative	<0.001

Note: Table 5 presents the correlation between lipid profile parameters and infarct size in patients with acute ischemic stroke. Serum total cholesterol, triglyceride, and HDL cholesterol levels were analyzed to assess their association with infarct size measured on CT imaging. Positive correlation indicates that higher lipid levels are associated with larger infarct size, whereas negative correlation indicates an inverse relationship with stroke severity.

Association of Blood Pressure with Infarct Size

Systolic blood pressure demonstrated a negative correlation with infarct size, whereas diastolic blood pressure showed a positive correlation. However, neither association was statistically significant.

Table 6: Association of Blood Pressure with Infarct Size

Parameter	Correlation with Infarct Size	p-value
Systolic blood pressure	Negative	0.971
Diastolic blood pressure	Positive	0.578

Note: Table 6 presents the association between blood pressure parameters and infarct size in patients with acute ischemic stroke. The correlation of systolic and diastolic blood pressure measured at admission with infarct size was analyzed to evaluate their relationship with stroke severity. A positive correlation indicates increasing infarct size with higher blood pressure values, whereas a negative correlation indicates an inverse relationship.

Summary of Correlation Analysis

Correlation analysis revealed that lower total serum calcium and albumin-corrected calcium levels were significantly associated with larger infarct sizes in patients with acute ischemic stroke. Higher triglyceride and total cholesterol levels were associated with increased infarct size, whereas higher HDL cholesterol levels were associated with smaller infarcts. Blood pressure parameters did not demonstrate a statistically significant relationship with infarct size.

Table 7: Summary of Correlation Analysis Between Biochemical Parameters and Infarct Size

Parameter	Direction of Correlation	Statistical Significance
Total serum calcium	Negative	Significant
Albumin-corrected calcium	Negative	Significant
Total cholesterol	Positive	Significant
Triglycerides	Positive	Significant
HDL cholesterol	Negative	Significant
Systolic blood pressure	Negative	Not significant
Diastolic blood pressure	Positive	Not significant

Note: Table 7 summarizes the correlation between biochemical parameters and infarct size in patients with acute ischemic stroke. The direction and statistical significance of the correlations were evaluated to identify laboratory markers associated with stroke severity. Lower serum calcium and HDL cholesterol levels were associated with larger infarct sizes, whereas higher total cholesterol and triglyceride levels were associated with increased infarct size.

DISCUSSION

The present study evaluated the association between serum calcium levels and infarct size in patients with acute ischemic stroke. The principal finding of this study was the significant negative correlation between both total serum calcium and albumin-corrected calcium levels and infarct size. Patients with lower serum calcium levels had larger infarct sizes, suggesting that serum calcium may serve as a useful marker of stroke severity, as reported by Kasundra et al. and Prabhakar et al.[1,2]

In the present study, the majority of patients belonged to the older age groups, reflecting the increased incidence of ischemic stroke with advancing age. Male predominance was observed among the study participants, which is consistent with previous epidemiological studies reporting a higher prevalence of vascular risk factors among men.[3,4]

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Smoking was associated with significantly larger infarct sizes, emphasizing its role as an important modifiable risk factor for ischemic stroke.

A significant inverse relationship was observed between serum calcium levels and infarct size. Lower albumin-corrected calcium levels were associated with larger infarcts, indicating more severe cerebral ischemic injury. Similar findings have been reported by Sri Parna et al., who demonstrated significant negative correlations between total calcium, albumin-corrected calcium, and infarct size in patients with acute ischemic stroke.[1] Likewise, Prabhakar et al. reported significant negative correlations between total, corrected, and ionized calcium levels and infarct size as well as stroke severity assessed using the National Institutes of Health Stroke Scale (NIHSS).[2]

The biological explanation for this association may be related to the role of calcium in the ischemic cascade. During cerebral ischemia, failure of cellular energy metabolism leads to membrane depolarization and excessive influx of calcium ions into neurons. Elevated intracellular calcium activates phospholipases, proteases, and free radical pathways, resulting in neuronal injury and cell death.[10-14] Consequently, lower extracellular serum calcium levels may reflect increased intracellular calcium accumulation and greater ischemic damage.

The findings of the present study are also consistent with the work of Ovbiagele et al., who reported that higher serum calcium levels were associated with improved functional outcomes following ischemic stroke.[4] Similarly, Gaurav et al. demonstrated that higher calcium levels were associated with smaller infarct sizes and better neurological recovery.[1] These observations support the potential role of serum calcium as a prognostic biomarker in acute ischemic stroke.

Among the lipid profile parameters evaluated, serum triglyceride and total cholesterol levels demonstrated significant positive correlations with infarct size, whereas HDL cholesterol showed a significant negative correlation. These findings suggest that dyslipidemia may contribute not only to the occurrence of ischemic stroke but also to the severity of cerebral infarction. Elevated triglyceride and cholesterol levels may accelerate atherosclerosis and impair cerebral perfusion, resulting in larger infarcts, while HDL cholesterol may exert protective vascular effects through its anti-inflammatory and antioxidant properties.[15]

No significant association was observed between blood pressure parameters and infarct size in the present study. Although systolic blood pressure demonstrated a negative correlation and diastolic blood pressure a positive correlation with infarct size, neither relationship reached statistical significance. Similar variability has been reported in previous studies, suggesting that blood pressure at presentation may not reliably reflect the extent of cerebral infarction.[8]

The findings of this study have important clinical implications. Serum calcium estimation is inexpensive, widely available, and routinely performed in clinical practice. The observed association between lower serum calcium levels and larger infarct size suggests that serum calcium, particularly albumin-corrected calcium, may serve as a useful adjunctive marker for early assessment of stroke severity and prognosis.[5,6,9]

However, the present study has certain limitations. The sample size was relatively small, ionized calcium levels were not measured, and serial calcium measurements were not performed. In addition, established stroke severity scales such as the NIHSS and Barthel Index were not included in the analysis. Further large-scale prospective studies incorporating functional outcome measures are warranted to validate the prognostic value of serum calcium in acute ischemic stroke.[2,7]

In conclusion, the present study demonstrated a significant inverse association between serum calcium levels and infarct size in patients with acute ischemic stroke. Lower total serum calcium and albumin-corrected calcium levels were associated with larger infarcts, supporting the potential role of serum calcium as a marker of stroke severity and prognosis.[1-4]

Limitations

The present study has several limitations. First, the sample size was relatively small and was derived from a single-center study, which may limit the generalizability of the findings. Second, total serum calcium and albumin-corrected calcium levels were measured instead of ionized calcium, the physiologically active form of calcium. Third, serum calcium and albumin levels were assessed only at admission, and serial measurements were not performed to evaluate temporal changes during the course of stroke. Fourth, the time interval between stroke onset and blood sample collection varied among patients, which could have influenced serum calcium levels. Fifth, only patients with acute ischemic stroke were included, precluding assessment of the relationship between serum calcium levels and other stroke subtypes. Finally, established stroke severity and functional outcome measures, such as the National Institutes of Health Stroke Scale (NIHSS) and Barthel Index, were not incorporated into the study, limiting comprehensive evaluation of neurological outcomes.

CONCLUSION

The present study demonstrated a significant inverse association between serum calcium levels and infarct size in patients with acute ischemic stroke. Both total serum calcium and albumin-corrected calcium levels showed significant negative correlations with infarct size, indicating that lower calcium levels were associated with larger cerebral infarctions and greater stroke severity. In addition, serum triglyceride and

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total cholesterol levels were positively correlated with infarct size, whereas HDL cholesterol exhibited a negative correlation. These findings suggest that serum calcium, particularly albumin-corrected calcium, may serve as a simple, inexpensive, and readily available biomarker for assessing stroke severity in patients with acute ischemic stroke. Further large-scale prospective studies are warranted to validate its prognostic utility and explore its role in predicting functional outcomes following stroke.

Conflict of Interest: The authors declare no conflict of interest.

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