ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 3, 2025

ASSOCIATION BETWEEN CALCIUM AND TRIGLYCERIDE GLYCEMIC INDEX IN DETERMINING THE SEVERITY OF ACUTE ISCHEMIC STROKE –A CASE CONTROL STUDY

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ABSTRACT:

Introduction: The sudden cessation of blood supply to the brain, known as acute ischaemic stroke (AIS), is a serious worldwide health issue that can cause neurological impairments and perhaps permanent disability.

In order to predict the risk of an acute ischaemic stroke, this study sought to examine the asso ciation between calcium levels and the triglyceride-glucose (TyG) index as biomarkers.

Methodology: A case-control study was conducted at a tertiary care hospital over six months, enrolling 80 participants (40 Acute ischemic stroke cases and 40 age- and sex-matched controls). The diagnosis of AIS was confirmed through clinical evaluation and neuroimaging. Data collection included demographic details, clinical examination findings, and laboratory investigations. The TyG index was calculated as the logarithm of the product of fasting triglycerides and glucose divided by two.

Results: The study found that AIS patients had significantly higher TyG index compared to controls. Elevated TyG index was associated with increased stroke severity, as measured by the National Institutes of Health Stroke Scale (NIHSS). Serum calcium levels measured in cases and controls was not stastically significant .

Conclusion: The findings suggest that both the TyG index and serum calcium levels may serve as valuable biomarkers in assessing the risk of acute ischemic stroke. These biomarkers could enhance clinical decision-making and contribute to the early identification of patients at high risk for adverse outcomes following ischemic stroke. Further research is warranted to explore the underlying mechanisms linking these biomarkers to stroke pathophysiology.

Keywords: Ischemic Stroke, Triglycerides, Glucose, Calcium, Insulin Resistance

INTRODUCTION:

Acute ischaemic stroke (AIS), a serious worldwide health concern, is defined by an abrupt cessation of blood supply to the brain, which can result in neurological impairments and possibly permanent disability. Ischaemic stroke is a major cause of long-term disability globally and carries a heavy burden, contributing to high rates of morbidity and mortality.

Finding biomarkers that can predict the risk and prognosis of ischaemic stroke has gained more attention in recent years, with a focus on calcium levels and the triglyceride-glucose (TyG) index.

An accurate surrogate marker for insulin resistance (IR) is the triglyceride-glucose (TyG) index, which is computed as the product of fasting triglycerides and glucose divided by two(1).The pathogenesis of several metabolic disorders, such as obesity, type 2 diabetes, and cardiovascular diseases, all of which are linked to an elevated risk of stroke, depends critically on insulin resistance.

TyG may be useful as a predictive indicator for stroke outcomes, as recent research has shown that a higher TyG index is associated with a higher incidence of ischaemic stroke(2).

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 3, 2025

Elevated TyG index values were linked to a considerably greater risk of ischaemic stroke as well as unfavourable clinical outcomes, such as mortality and recurrent strokes, according to a systematic review and meta-analysis.[3]

The pathophysiology of ischaemic stroke has also been linked to calcium, a mineral th at is vital to human health.

During ischaemic episodes, a disruption in calcium homeostasis can cause neuronal damage a nd death[4].Serum calcium levels may be a significant biomarker for predicting the severity an d prognosis of strokes, according to studies.

In the treatment of acute ischaemic stroke, elevated calcium levels have been linked to worse functional outcomes in patients after an ischaemic event, suggesting that calcium may have a predictive role[5].

By starting a chain of cytotoxic events, intracellular calcium buildup causes harm to neurons. The various processes of cerebral ischaemia involve calcium ions.[6]

For example, calcium rapidly moves from the extracellular to intracellular regions of cerebral tissues in response to ischaemia and hypoxia.[7,8]

An new field of study examines the relationship between calcium levels and the TyG index in the setting of acute ischaemic stroke.

Clinicians may gain important insights by comprehending the relationships between these bio markers and how each one affects stroke risk and prognosis.

In order to determine their possible roles in forecasting stroke outcomes and directing therape utic measures, this study intends to examine the association between calcium and triglyceride glycaemic index as indicators in acute ischaemic stroke.

Two interesting biomarkers that could improve our knowledge of the risk variables linked to acute ischaemic stroke are the TyG index and calcium levels.

This study aims to add to the increasing amount of data demonstrating the utility of biochemi cal markers in the clinical treatment of ischaemic stroke by clarifying their connections with s troke outcomes. Severity stratification is objectified by these biological markers.

To increase validity, composite scores can be created by identifying multiple such parameters .By creating such composite ratings, prognostication will be improved and predictive models for acute ischaemic stroke outcome can be formed.

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 3, 2025

METHODOLOGY:

Study Design and Population

This study employed a case-control design to investigate the role of the calcium and triglyceride glycemic index (TyG index) as markers in acute ischemic stroke (AIS). The study was conducted at a tertiary care hospital over a period of six months. A total of 80 participants were enrolled, consisting of 40 cases diagnosed with acute ischemic stroke and 40 age- and sex-matched controls without a history of stroke or transient ischemic attack. The diagnosis of acute ischemic stroke was confirmed through clinical evaluation and neuroimaging, primarily using computed tomography (CT) or magnetic resonance imaging (MRI). Informed consent was obtained from all participants, and ethical approval was granted by the Institutional Review Board prior to the study commencement.

Data Collection

Data were collected using a structured case record form that included several key domains:

1. Patient Demographic Details: Information such as age, gender, and medical history was recorded to characterize the study population. This included details regarding comorbidities such as hypertension, diabetes mellitus, and hyperlipidemia.
2. Clinical Examination Findings: A thorough clinical examination was performed on all participants. Neurological assessments were conducted using the National Institutes of Health Stroke Scale (NIHSS) to evaluate the severity of the stroke in cases.
3. Laboratory Investigations: Blood samples were drawn from all participants within 24 hours of admission for cases and during the same timeframe for controls. The TyG index was calculated using the formula: TyG index = (fasting triglycerides (mg/dL) / fasting glucose (mg/dL) . Additionally, serum calcium levels were measured using standard laboratory techniques. Other laboratory parameters, including complete blood counts, lipid profiles, and renal function tests, were also assessed to provide a comprehensive metabolic profile.

Definition of Outcomes

The primary outcomes of interest were the levels of the TyG index and serum calcium in relation to the diagnosis of acute ischemic stroke. The cases were compared to controls to determine the significance of these biomarkers in predicting stroke occurrence. The secondary outcomes included the assessment of stroke severity based on NIHSS score.

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 3, 2025

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 25. Descriptive statistics were computed for demographic and clinical characteristics, with continuous variables expressed as mean ± standard deviation and categorical variables presented as frequencies and percentages. The differences between cases and controls were assessed using independent t-tests for continuous variables and chi-square tests for categorical variables. Logistic regression analysis was performed to evaluate the association between the TyG index, serum calcium levels, and the risk of acute ischemic stroke, adjusting for potential confounders such as age, gender, and comorbidities. A p-value of less than 0.05 was considered statistically significant.

RESULTS:

The study included 80 participants, with 40 cases diagnosed with AIS and 40 age- and sex-matched controls.

Table 1 explores the correlation between the TyG index and the severity of Acute Ischemic Stroke (AIS) among participants. A positive correlation here suggesst that higher TyG index values are associated with more severe AIS. This relationship highlights the interconnectedness of metabolic dysregulation leading to Acute ischemic stroke and reinforces the notion that insulin resistance, as indicated by the TyG index, is a risk factor for AIS.

Table 1: Relationship of TGI with severity of Acute Ischemic Stroke

Severity of AIS	Number	Mean TGI	P value
Mild	**9 (22.6%)**	1.58±0.82	**0.05**
Moderate	**20 (50%)**	1.07±0.45	
Severe	**11 (27.6%)**	1.68±0.96	

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 3, 2025

Table 2 details the laboratory findings, including serum calcium levels, TyG index, and other metabolic parameters. TyG index is elevated in cases as compared to controls, and is stastically significant. This reinforces the potential role of triglyceride glycemic index in predicting stroke risk.

Serum calcium did not show any significant difference between both the groups .

Table 2: Comparison of mean lab investigations among study groups

Mean	**Cases**	**Controls**	**P value**
Calcium	8.68±0.67	8.84±0.59	0.274
FBS	116.8±40.7	102.4±35.3	0.094
Triglyceride	148.3±73.5	120.6±33.3	**0.033**
TGI	1.36±0.75	1.25±0.41	0.430

Table 3 explore the correlation between laboratory findings (such as TyG index and calcium levels) and the severity of AIS . A positive relationship would suggest that these metabolic markers are relevant to stroke risk . In this study , calcium, triglycerides and FBS individually did not corelate to the severity of stroke, as the p values are not significant.

Table 3: Relationship of mean inverstigations with severity of Acute Ischemic Stroke

Severity of AIS	**Volume**	**Calcium**	**Triglyceride**	**FBS**
Mild	1.18±1.5	8.8±0.67	153.2±67.4	102.1±22.2
Moderate	11.15±18.8	8.59±0.57	135.4±79.6	125.7±48.4
Severe	13.3±15.2	8.76±0.905	167.6±67.8	112.6±35.1
P value	0.195	0.675	0.334	0.504

Figure 1: Bar graph showing mean TGI levels among NIHSS severity groups

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 3, 2025

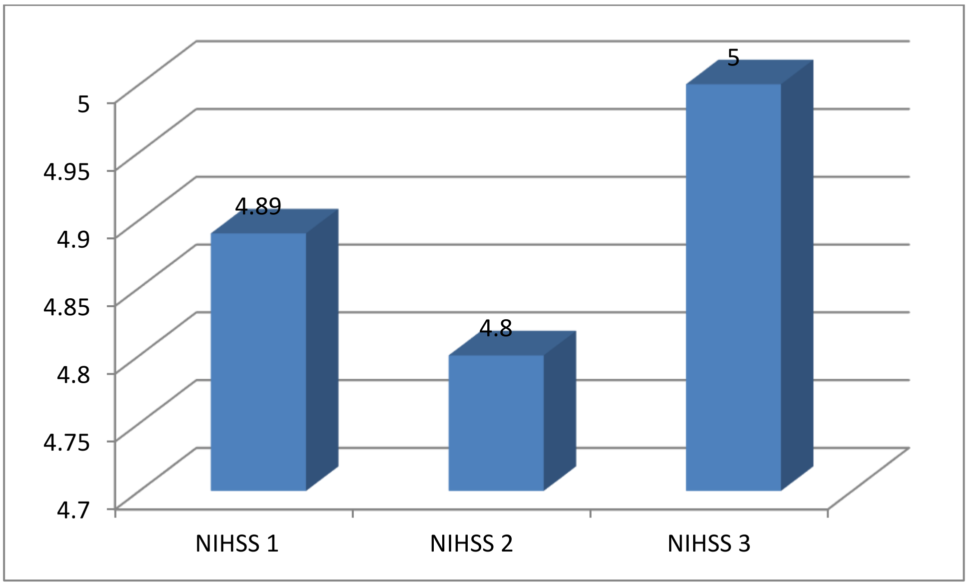
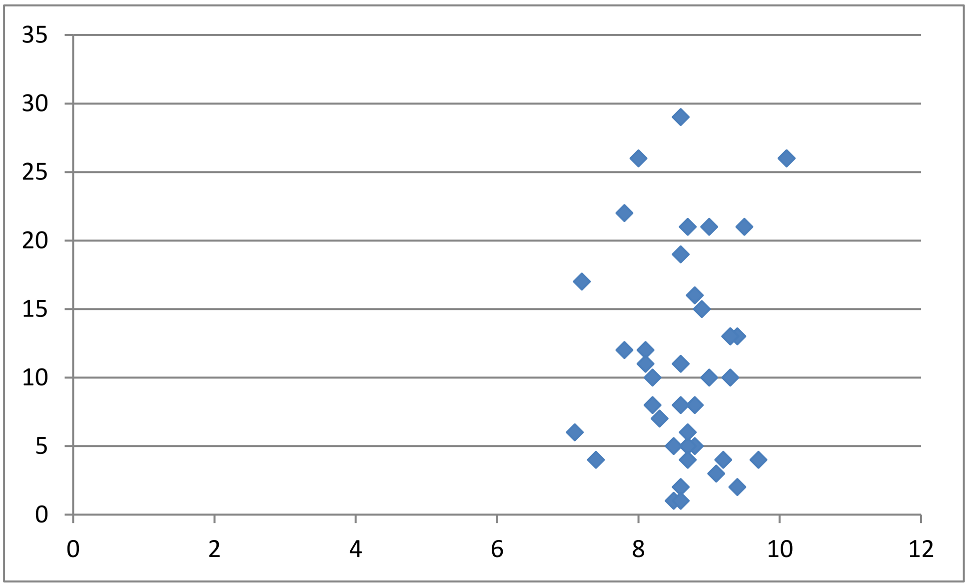
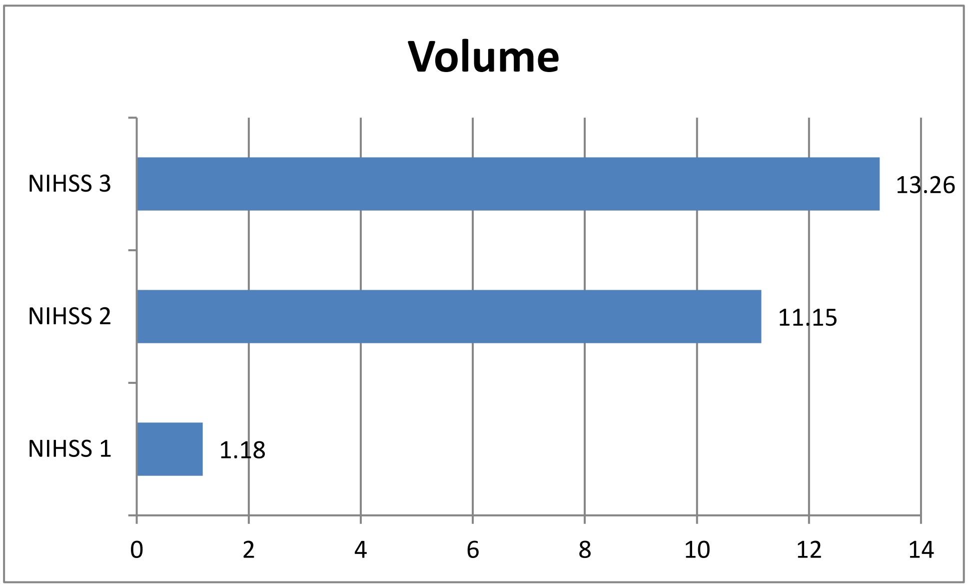


Figure 2: Scatter plot showing calcium levels according to NIHSS total score



ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 3, 2025

Figure 3: Bar graph showing mean volume of infarct among NIHSS severity groups



DISCUSSION:

The present study aimed to investigate the role of calcium and triglyceride glycemic index (TyG index) as potential biomarkers in acute ischemic stroke. The findings demonstrate a significant association between elevated TyG index with an increased risk of acute ischemic stroke.

Our findings are in line with other research that found a positive correlation between t he TyG index and the incidence of ischaemic stroke. Yang et al.'s systematic review and meta -
analysis revealed that a higher TyG index was linked to a significantly higher risk of ischaem ic stroke (OR: 1.56, 95% CI: 1.41-
1.72).2 Zhou et al. also found that patients with ischaemic stroke had a higher TyG index tha n controls, and that an elevated TyG index was an independent predictor of poor functional o utcomes.[(1)]

These results imply that the pathophysiology of ischaemic stroke may be significantly influen ced by the TyG index, a proxy for insulin resistance.Our investigation found that acute ischae mic stroke patients had lower serum calcium levels than controls, however this difference wa s not statistically significant.

Serum calcium levels and infarct size in acute ischaemic stroke were found to be negatively c orrelated in an Indian study by Borah M. et al.[(3)]

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 3, 2025

However, after an acute ischaemic stroke, higher blood calcium levels were linked to a worse short-term result and a higher risk of long-term death, according to a study by Chung JW et al. (9)
According to the authors' hypothesis, the severity of the stroke may be increased by neuronal damage and death resulting from disruption of calcium homeostasis during ischaemic episodes.
Hsu et al. went into more detail about the several ways that calcium could affect the course of a stroke, including its involvement in inflammation, oxidative stress, and excitotoxicity.(10)

Our study discovered a good association between the TyG index and calcium levels in predicting the risk of acute ischaemic stroke, taking into account the interaction between the two.
This connection emphasises how intricately insulin resistance and metabolic imbalance interact to cause ischaemic stroke.
Insulin resistance has been linked to oxidative stress, inflammation, and endothelial dysfunction, all of which can support the onset and advancement of atherosclerosis.(11).
In addition to affecting calcium signalling and homeostasis, these mechanisms may raise the likelihood of ischaemic episodes.Age- and sex-matched controls, a case-control design, and a thorough evaluation of numerous clinical and laboratory indicators are some of our study's strong points.

Limitations

The study's singlecenter design and small sample size may restrict how far the results may be applied.
Furthermore, a causal association between the biomarkers and stroke outcomes cannot be established due to the cross-sectional methodology.To better understand the function of calcium and the TyG index in predicting the risk and prognosis of acute ischaemic stroke, larger sample numbers and longitudinal designs are needed in future research.

ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 3, 2025

Examining the fundamental processes that connect these biomarkers to the pathophysiology o f stroke could yield important information for the creation of focused treatment approaches.

Conclusion:

In conclusion, our study demonstrates that elevated TyG index is associated with an increased risk of acute ischemic stroke. Whereas, serum calcium was not significantly associated with cases of acute ischemic stroke This biomarker may serve as useful tools in risk stratification for ischemic stroke patients. Incorporating these markers into clinical practice, along with other established risk factors, could aid in the early identification of individuals at high risk for ischemic stroke and guide secondary preventive strategies.

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ISSN: 0975-3583, 0976-2833 VOL16, ISSUE 3, 2025

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