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ORIGINAL RESEARCH PAPER

Internal Medicine

A STUDY OF SERUM GAMMA GLUTAMYL TRANSFERASE(GGT) LEVELS IN PATIENTS WITH ACUTE ISCHEMIC STROKE(AIS) IN A TERTIARY CARE CENTRE, MANDYA.

KEY WORDS: Gamma-Glutamyl Transferase (GGT), Acute Ischemic Stroke (AIS), National Institute of Health Stroke Scale (NIHSS), Diabetes Mellitus, Hypertension.

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ABSTRACT

Background: Gamma-glutamyl transferase (GGT) is an enzyme involved in oxidative stress and atherosclerosis, both of which play a key role in the pathogenesis of ischemic stroke. Elevated GGT levels may reflect the extent of oxidative damage in acute ischemic stroke (AIS) patients. **Objective:** This study aims to evaluate the association between serum GGT levels and AIS, its severity based on the National Institute of Health Stroke Scale (NIHSS), and its relation to stroke risk factors such as diabetes, hypertension, and stroke location. **Methods:** A cross-sectional study was conducted at a tertiary care hospital between December 2023 and May 2024. A total of 120 participants were recruited, comprising 60 AIS patients and 60 age- and sex-matched healthy controls. Serum GGT levels were measured, and stroke severity was classified using the NIHSS. **Results:** AIS patients had significantly higher serum GGT levels compared to controls (46.20 ± 29.50 IU/L vs. 25.75 ± 6.10 IU/L, $p < 0.001$). GGT levels positively correlated with stroke severity, with the highest levels observed in patients with severe strokes (NIHSS > 21: 85.60 ± 38.50 IU/L, $p < 0.001$). No significant differences in GGT levels were found based on stroke location, age, or comorbidities such as diabetes or hypertension. **Conclusion:** Elevated serum GGT levels are associated with acute ischemic stroke and its severity. GGT could serve as a potential biomarker for assessing stroke severity and guiding early intervention.

INTRODUCTION

Gamma-glutamyl transferase (GGT) is an enzyme from the transferase family that facilitates the transfer of gamma-glutamyl groups from peptides like glutathione to other peptides or amino acids. Glutathione, produced during normal metabolic processes, plays a key role in reducing oxidative stress, protecting cells from damage [1]. GGT assists in the cellular uptake of extracellular glutathione, a crucial antioxidant defence mechanism [2]. By doing so, GGT helps combat oxidative stress but also contributes to the development of atherosclerosis through oxidative and inflammatory processes [3].

In addition to its antioxidant role, serum GGT levels are commonly used to assess liver dysfunction and alcohol consumption [4]. Elevated GGT has also been linked to several factors including older age, male gender, higher body mass index (BMI), smoking, sedentary lifestyle, hypertension, and various metabolic conditions such as hyperglycaemia, dyslipidaemia, and menopause.[5]

Stroke, the second most common cause of death worldwide [6], led to 6.1 million deaths in 2019[7]. The condition imposes a heavy burden not only on patients but also on their families and healthcare systems. In India, stroke prevalence has ranged between 44.29 and 559 per 100,000 people over the last decade [8].

Ischemic stroke results in brain damage due to oxygen deprivation, which triggers the production of free radicals and increases serum GGT levels [9]. The rise in GGT is thought to be driven by oxidative stress, which is also associated with the progression of atherosclerosis [10]. Some studies have suggested a direct link between high GGT levels and the advancement of atherosclerosis [11].

Given the limited research in India on the relationship between serum GGT levels and stroke, this study aims to compare GGT levels in acute ischemic stroke (AIS) patients with healthy controls, and to investigate the correlation between GGT levels and stroke severity as measured by the National Institute of Health Stroke Scale (NIHSS) [12].

Objectives

- To evaluate the association between S.GGT level and risk factors of stroke like diabetes mellitus, hypertension and dyslipidaemia.
- To evaluate the association between S.GGT levels and severity of stroke by using NIHSS score.
- To evaluate the association between S.GGT levels and location of stroke in patients with acute ischemic stroke.

MATERIALS AND METHODS

This cross-sectional study was conducted between December 2023 and May 2024 at a tertiary care hospital in Mandya. A total of 120 participants were recruited, comprising 60 patients with acute ischemic stroke (AIS) and 60 age- and sex-matched healthy controls. AIS was confirmed by neuroimaging (CT or MRI), and stroke severity was assessed using the National Institute of Health Stroke Scale (NIHSS).

Inclusion Criteria

- **AIS patients:** Individuals diagnosed with acute ischemic stroke within 72 hours of symptom onset, confirmed by neuroimaging.
- **Controls:** Age- and sex-matched individuals with no history of cerebrovascular disease, cardiovascular disease, or other major illnesses.

Exclusion Criteria

Participants with the following conditions were excluded:

- Chronic liver disease, known to affect serum Gamma-Glutamyl Transferase (GGT) levels.
- Renal disease (chronic kidney disease, on dialysis).
- Alcohol abuse (due to its known effect on GGT levels).
- Active infections or malignancies.

Sample Size Calculation

From a review of the literature, the mean GGT level in cases was found to be 23.3 ± 11.8 IU/L and that of the controls was 15.0 ± 5.7 IU/L ($p < 0.001$) [1]. In the present study, expecting similar results with 80% power and 95% confidence level, and considering the minimal detectable difference of GGT level between the two groups as 5 IU/L, our study required a minimum of 60 cases of acute ischemic stroke and 60 controls.

Data Collection

Data were collected through detailed medical history, clinical examination, and laboratory investigations. Demographic information such as age, sex, comorbidities (type 2 diabetes mellitus and hypertension), and stroke characteristics (stroke type and location) were recorded.

Measurement of Serum Gamma-Glutamyl Transferase (GGT) Levels Blood samples were collected from each participant upon admission (for AIS patients) or during routine health checkups (for controls). Serum GGT levels were measured using an automated enzymatic method at the hospital's biochemistry laboratory. The normal reference range for serum GGT in healthy individuals was considered 5–50 IU/L.

Categorization of Stroke Severity

Stroke severity was assessed using the National Institute of Health Stroke Scale (NIHSS):

- **Mild Stroke:** NIHSS score 0-4
- **Moderate Stroke:** NIHSS score 5-15
- **Moderate-Severe Stroke:** NIHSS score 16-20
- **Severe Stroke:** NIHSS score > 21

Area of Infarction Classification

The stroke location was classified based on neuroimaging findings as:

- Anterior Circulation Stroke
- Posterior Circulation Stroke
- Lacunar Stroke

Statistical Analysis

All data were analysed using SPSS Version 26.0. Continuous variables, including serum GGT levels, were presented as mean ± standard deviation (SD). Categorical variables, such as sex and presence of comorbidities, were expressed as percentages.

- Independent t-tests were used to compare serum GGT levels between AIS patients and controls.
- Analysis of variance (ANOVA) was used to assess the variation in GGT levels among stroke severity groups (based on NIHSS scores), areas of infarction, and age categories.
- Pearson's correlation was used to evaluate the relationship between serum GGT levels and NIHSS scores.
- A p-value of <0.001 was considered statistically significant.

RESULTS

Table 1: Baseline Characteristics of Study Participants

Characteristic	AIS Patients (n = 60)	Controls (n = 60)	p-Value
Age (years)	58.50 ± 14.75	55.30 ± 15.10	0.32
Male (%)	45 (75%)	42 (70%)	0.56
Type 2 Diabetes Mellitus	36 (60%)	33 (55%)	0.44
Hypertension (%)	39 (65%)	36 (60%)	0.50
Smoking (%)	22 (37%)	18 (30%)	0.48
Body Mass Index (kg/m²)	26.8 ± 3.4	24.9 ± 2.9	0.12

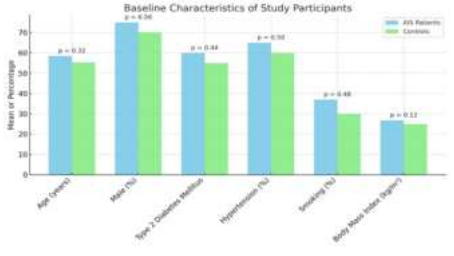

Table 2: Comparison of Cases and Controls

Parameter	Cases (n = 60)	Controls (n = 60)	p-Value
Mean age (years)	58.50 ± 14.75	55.30 ± 15.10	0.32
Males (%)	75% (45)	70% (42)	0.56
Type 2 Diabetes Mellitus	60% (36)	55% (33)	0.44
Hypertension (%)	65% (39)	60% (36)	0.50

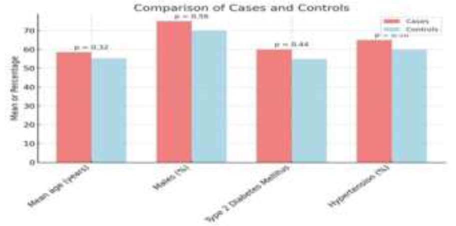

Table 3: Serum GGT in Acute Ischemic Stroke Patients and Controls

Parameter	Number (n)	Mean ± SD	p-Value
AIS Patients (n = 60)	60	46.20 ± 29.50 IU/L	< 0.001
Controls (n = 60)	60	25.75 ± 6.10 IU/L	< 0.001

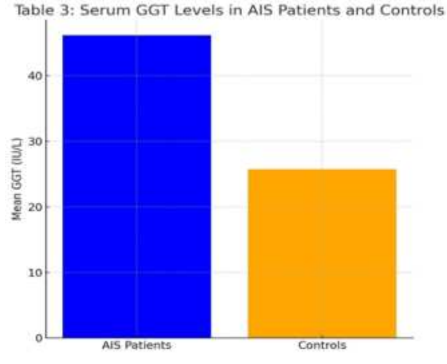

Table 4: Variation in Serum GGT with NIHSS Scores

Severity of Stroke	Number (n)	Mean ± SD (GGT) IU/L	p-Value
Moderate (NIHSS 5-15)	40	36.10 ± 19.50	< 0.001
Moderate-Severe (NIHSS 16-20)	12	49.20 ± 23.15	< 0.001
Severe (NIHSS > 21)	8	85.60 ± 38.50	< 0.001

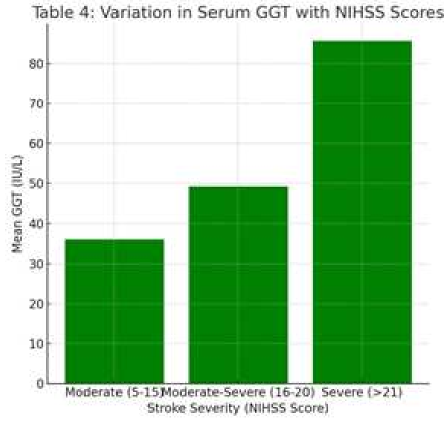

Table 5: Variation in Serum GGT With Respect to Area of Infarction and Age of the Patient

Parameter	Number (n)	Mean ± SD (GGT) IU/L	p-Value
Anterior Circulation Stroke	45	48.50 ± 32.00	0.52
Posterior Circulation Stroke	8	42.15 ± 15.80	0.52
Lacunar Stroke	7	35.80 ± 8.10	0.52
Age 18-39	10	32.20 ± 17.40	0.34
Age 40-59	25	48.80 ± 26.75	0.34
Age 60 and above	25	45.00 ± 31.20	0.34

Table 6: Variation in Serum GGT Levels with Type 2 Diabetes Mellitus, Hypertension, and Sex of the Patient

Parameter	Number (n)	Mean ± SD (GGT) IU/L	p-Value
Type 2 Diabetes Mellitus	36	46.80 ± 29.00	0.28

No Diabetes	24	38.00 ± 22.10	0.28
Hypertension	39	43.75 ± 27.10	0.71
No Hypertension	21	40.20 ± 26.40	0.71
Male	45	46.30 ± 29.20	0.07
Female	15	32.50 ± 17.30	0.07

DISCUSSION

In this study, we evaluated the relationship between serum Gamma-Glutamyl Transferase (GGT) levels and acute ischemic stroke (AIS) to explore GGT's role as a biomarker for stroke severity. Our findings reveal a statistically significant elevation in GGT levels in AIS patients compared to healthy controls ($p < 0.001$), reinforcing the hypothesis that oxidative stress, as reflected by elevated GGT, plays a pivotal role in ischemic stroke pathophysiology.[13]

Serum GGT Levels in AIS Patients vs. Controls

AIS patients exhibited significantly higher serum GGT levels (46.20 ± 29.50 IU/L) compared to controls (25.75 ± 6.10 IU/L, $p < 0.001$). This observation is consistent with earlier studies linking GGT to oxidative stress and atherosclerosis, both contributing to ischemic stroke development [14]. The elevated GGT levels in AIS patients reflect increased oxidative stress caused by ischemia, emphasizing the enzyme's potential as a biomarker for cerebrovascular events.

GGT and Stroke Severity

Our study shows a positive correlation between serum GGT levels and stroke severity, as measured by NIHSS scores. Patients with severe strokes (NIHSS > 21) had substantially higher GGT levels (85.60 ± 38.50 IU/L) compared to those with moderate strokes (36.10 ± 19.50 IU/L, $p < 0.001$). This finding suggests that GGT may serve as a surrogate marker for stroke severity. Elevated GGT in severe cases could provide clinicians with a useful biochemical marker for prognosis, aiding in the early identification of patients who may require intensive monitoring and intervention.

GGT Variation with Stroke Location and Age

No significant differences in GGT levels were observed based on stroke location (anterior, posterior, or lacunar strokes) or age categories. This indicates that GGT elevation is more closely related to the overall ischemic process and oxidative stress rather than the specific anatomical site of infarction or the patient's age. The lack of variation across age groups further supports GGT's role as a marker of ischemia, unaffected by aging.

GGT And Comorbidities (Diabetes, Hypertension)

Interestingly, GGT levels did not significantly differ between patients with and without type 2 diabetes mellitus or hypertension. These results align with previous studies that reported varying associations between GGT and cardiovascular risk factors. In the setting of AIS, the acute ischemic event appears to be the dominant factor driving GGT elevation, rather than the presence of underlying comorbidities such as diabetes or hypertension.

GGT and Gender Differences

Although male patients had higher GGT levels compared to females, the difference did not reach statistical significance ($p = 0.07$). While males are generally known to have higher baseline GGT levels, the trend observed in our study suggests that ischemia-related oxidative stress is the primary factor influencing GGT in AIS patients, rather than gender-specific differences. Further studies with larger cohorts could explore these gender-related differences in more detail.

Clinical Implications

The results of our study suggest that serum GGT could be a valuable biomarker for the early diagnosis and management of acute ischemic stroke. The significant correlation between GGT and stroke severity indicates that GGT could help stratify patients based on the severity of their neurological deficits. Since GGT is an inexpensive and widely available test, its use in stroke protocols could enhance early identification and management of high-risk patients, potentially improving clinical outcomes.

Study Strengths and Limitations

One of the key strengths of this study is the relatively large sample size, which provided sufficient power to detect significant associations between serum GGT levels and stroke outcomes. Additionally, the use of the NIHSS as a standardized tool to assess stroke severity ensures the clinical relevance of our findings.

However, the study has several limitations. Being cross-sectional in nature, it cannot establish causality between GGT levels and stroke severity. We also did not account for other potential confounders, such as alcohol consumption and genetic predispositions, which may influence GGT levels. Future longitudinal studies are needed to explore the predictive value of GGT in post-stroke recovery and recurrence.

CONCLUSION

In conclusion, serum GGT levels are significantly elevated in patients with acute ischemic stroke, particularly in those with more severe strokes. GGT shows promise as a potential biomarker for assessing stroke severity. However, further research is needed to confirm its prognostic value [15] and explore whether interventions targeting oxidative stress could modify GGT levels and improve clinical outcomes in stroke patients.

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