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Research Article

GAMMA GLUTAMYL TRANSFERASE LEVELS IN PATIENTS WITH ACUTE STROKE: AN ANALYTICAL STUDY

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ABSTRACT

Objectives: Stroke is a significant global health issue with a major socioeconomic burden, ranking as the second leading cause of death worldwide. While stroke rates have declined in high-income countries, they have increased in low- to middle-income countries, including India. The World Health Organization defines stroke as a disturbance of cerebral function caused by vascular factors, classified as ischemic or hemorrhagic.

Methods: Ischemic stroke is primarily caused by atherosclerosis in the brain's arteries, including the proximal aorta, leading to embolus formation. Other factors contributing to stroke include arterial stenosis, coexisting thrombosis, artery-to-artery embolism, micro atheroma, lipohyalinosis, and occlusive diseases of small brain arteries. Cardiogenic embolism, often associated with atrial fibrillation, contributes to a significant proportion of ischemic strokes. Gamma-glutamyl transferase (GGT), commonly used as a marker for alcohol consumption and liver diseases, is also linked to oxidative stress, inflammation, and atherosclerosis. Elevated GGT levels are associated with various stroke risk factors.

Results: GGT plays a crucial role in cellular intake of glutathione, an important antioxidant. Paradoxically, it can generate reactive oxygen species in the presence of certain metals. Studies have found a correlation between high serum GGT levels and stroke risk, potentially due to oxidative stress and atherosclerosis progression.

Conclusion: Despite its primary use as an alcohol consumption marker, GGT has emerged as a potential independent biomarker for vascular diseases, including stroke. However, limited research exists on the association between GGT and acute stroke. This study aims to evaluate GGT levels in patients with acute stroke, exploring potential differences among stroke types to better understand the impact of GGT on acute stroke.

Keywords: Stroke, global health, socioeconomic burden, ischemic stroke.

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INTRODUCTION

Stroke is a major global health issue that contributes significantly to morbidity and mortality, imposing a substantial socioeconomic burden. It is the second leading cause of death worldwide, responsible for 6.2 million deaths in 2011. Over the past four decades, stroke incidence has decreased by 42% in high-income countries but has increased by over 100% in low- to middle-income countries. In India, the cumulative incidence of stroke ranged from 105 to 152/100,000 persons/year in different regions [1,2].

Stroke is defined by the World Health Organization as the rapid development of focal or global disturbance of cerebral function that lasts for more than 24 h or leads to death, with no apparent cause other than vascular origin. It is classified into two broad categories: Ischemic stroke, caused by cerebral thrombosis or embolism, and hemorrhagic stroke, caused by intra-cerebral, or subarachnoid hemorrhage [3].

The most common cause of ischemic stroke is atherosclerosis in the arteries supplying the brain, both large and small. Atherosclerosis in the proximal aorta can also lead to the formation of emboli that cause ischemic stroke. Other causes include severe arterial stenosis or occlusion due to atherosclerosis, coexisting thrombosis, artery-to-artery embolism, micro atheroma, lipohyalinosis, and occlusive diseases of the small penetrating brain arteries. Cardiogenic embolism, often resulting from atrial fibrillation, accounts for about 20% of ischemic strokes. Various other occlusive disorders can also contribute to stroke pathogenesis [4,5].

Gamma-glutamyl transferase (GGT) is an enzyme involved in the transfer of a gamma-glutamyl group from one molecule to another. It is primarily used as a marker for alcohol consumption and hepatobiliary diseases. However, recent studies have shown that GGT may have a role in oxidative and inflammatory mechanisms, as well as atherosclerotic pathogenesis, making it a potential biomarker for assessing the risk of cardiovascular diseases. Higher GGT levels have been associated with advanced age, male gender, increased body mass index, smoking, sedentary lifestyle, hypertension (HTN), tachycardia, hyperglycemia, abnormal lipid levels, hypertriglyceridemia, menopause, and oral contraceptive use [6,7].

GGT plays a crucial role in intracellular intake of extracellular glutathione, an important antioxidant. Paradoxically, cellular GGT may also generate reactive oxygen species in the presence of iron or other transition metals. Several studies have found an association between elevated serum GGT levels and the risk of stroke, potentially linked to oxidative stress and the progression of atherosclerosis [8].

Despite GGT being primarily studied as a biomarker for alcohol consumption, its independent role in vascular diseases, including stroke, has recently emerged. However, there is limited research on the correlation between GGT and acute stroke. This study aims to evaluate GGT levels in patients diagnosed with acute stroke and identify potential differences in GGT levels among different types of strokes, with the goal of understanding the impact of GGT on acute stroke [9,10].

METHODS

Study design

This was hospital-based observational study.

Study type
This was as analytical study.

Study place
This study was conducted at the Medicine Department of SMS Hospital, Jaipur.

Study duration
The study duration was from April 2021 to December 2022

Sample size
A sample of 60 CVA patients (30 with ischemic stroke and 30 with hemorrhagic stroke) with 30 controls are adequate at 95% confidence interval and power of 80% to verify the expected difference of 22.81 in mean and S.D.

20.54 for serum GGT level in between two study group (as per seed article: serum GGT level in acute stroke)

Inclusion criteria
The following criteria were included in the study:
- Adult patients who have stroke who attended the emergency department within 24 h of attack.
- Willing to give consent

Exclusion criteria
The following criteria were excluded from the study:
- Chronic liver or kidney diseases
- Active infections
- History of neoplasia
- Alcoholic patients
- Enrolled in other study

Statistical analysis
- Data were entered in excel sheet. Quantitative data were expressed as mean ±standard deviation (SD).
- Qualitative data were expressed as frequency and percentage.
- Independent sample t test of significance would be used when comparing between two means (quantitative data).
- Chi-square (χ^2) test of significance was used to compare proportions between qualitative parameters.
- The confidence interval was set to 95%, and the margin of error accepted at 5%. The p≤0.05 was considered significant, p≤0.001 was considered as highly significant, and p>0.05 was considered insignificant.

RESULTS

Among cases, the mean GGT level in smokers was 69.85 (SD=11.00), while in controls it was 35.33 (SD=4.61). For non-smokers, the mean GGT level among cases was 60.94 (SD=11.55), and among controls, it was 31.71 (SD=5.16). The p-value was 0.004, indicating a significant difference in GGT levels between smokers and non-smokers in both groups.

Among cases, the mean GGT level in patients with HTN was 76.17 (SD=9.50), while in controls it was 32.85 (SD=5.13). For those without HTN, the mean GGT level among cases was 57.22 (SD=6.43), and among controls, it was 32.76 (SD=5.41). The calculated p<0.001 indicating a highly significant difference in GGT levels between patients with HTN and those without HTN in both the case and control groups.

The correlation analysis showed significant associations between serum GGT levels and age (r=0.1, p=0.428 in cases; r=0.26, p=0.159 in controls), HBA1C (r=0.79, p<0.001 in cases; r=0.21, p=0.27 in controls), DM (r=−0.7, p<0.001 in cases; r=−0.2, p=0.409 in controls), smoking (r=−0.4, p=0.004 in cases; r=−0.3, p=0.08 in controls), HTN (r=−0.8, p<0.001 in cases; r=−0, p=0.967 in controls), dyslipidemia (r=−0.5, p<0.001 in cases; r=−0.1, p=0.759 in controls), Vitamin B12 (r=−0.7, p<0.001 in cases; r=0.19, p=0.329 in controls), and gender (r=−0.1, p=0.453 in cases; r=−0.4, p=0.034 in controls).

Table 1: Smoking wise GGT classification

Smoking	Case		Control	
	Mean	SD	Mean	SD
Yes	69.85	11.00	35.33	4.61
No	60.94	11.55	31.71	5.16
	p value			0.004

GGT: Gamma-glutamyl transferase

Table 2: HTN wise classification of GGT

HTN	Case		Control	
	Mean	SD	Mean	SD
Yes	76.17	9.50	32.85	5.13
No	57.22	6.43	32.76	5.41
	p value			<0.001

Table 3: Correlation of various parameters with GGT

Parameters	Correlation* with GGT			
	Case		Control	
	r	p value	r	p value
Age	0.1	0.428	0.26	0.159
mRS score	0.25	0.058	-	-
HBA1C	0.79	<0.001	0.21	0.27
DM	−0.7	<0.001	−0.2	0.409
Smoking	−0.4	0.004	−0.3	0.08
HTN	−0.8	<0.001	−0	0.967
Dyslipidemia	−0.5	<0.001	−0.1	0.759
Vitamin B12	−0.7	<0.001	0.19	0.329
Gender	−0.1	0.453	−0.4	0.034

*Pearson correlation for continuous variable and biserial point correlation for dichotomous variables, DM: Diabetes mellitus, HTN: Hypertension

DISCUSSION

This study aimed to assess the usefulness of GGT levels in cerebrovascular accident (CVA) patients and evaluate the association between serum GGT levels and stroke risk factors. The study included 60 CVA patients (30 with ischemic stroke and 30 with hemorrhagic stroke) and 30 controls from Jaipur, India [11].

The mean age of CVA cases was 58.4, while controls had a mean age of 55.37. Gender distribution was comparable between cases and controls. Serum GGT levels were significantly higher in CVA cases compared to controls (p<0.0001) [12].

Similar findings were reported by other studies. Singh *et al.* and Jousilahti *et al.* observed elevated serum GGT levels in CVA cases compared to controls. The Eurostroke Project by Bots *et al.* also found an increased risk of stroke associated with higher serum GGT levels [13].

Regarding the type of stroke, serum GGT levels did not significantly differ between ischemic and hemorrhagic stroke patients. This finding was consistent with Singh *et al.* study. However, the Eurostroke Project reported an association between higher serum GGT levels and increased risk of hemorrhagic stroke [14].

In terms of age groups, serum GGT levels were highest in the ≥66 years age group for both cases and controls. Singh *et al.* also observed higher serum GGT levels in the same age group. Gender did not significantly affect serum GGT levels in this study, which aligns with the findings of Gurbuzer *et al.* However, a study by Mijovic *et al.* reported higher GGT levels in males compared to females [15,16].

Among the stroke risk factors analyzed, diabetes mellitus (DM), smoking, HTN, dyslipidemia, and Vitamin B-12 deficiency were significantly associated with elevated GGT levels in CVA patients [17].

In conclusion, this study found that serum GGT levels were significantly increased in CVA patients compared to controls. There was no significant difference in GGT levels between ischemic and hemorrhagic stroke patients. Serum GGT levels were higher in older age groups and showed associations with DM, smoking, HTN, dyslipidemia, and Vitamin B-12 deficiency. These findings contribute to the understanding of GGT's potential as a biomarker for assessing stroke risk and its associated factors [18].

CONCLUSION

Serum GGT levels were found to be significantly elevated in patients with cerebrovascular accidents (CVA) compared to control subjects. However, no significant correlation was observed between serum GGT levels and demographic factors such as age and gender in this study. On the other hand, in the presence of risk factors like DM, HTN, dyslipidemia, and smoking, serum GGT levels were significantly higher. These findings highlight the potential of GGT as a valuable biomarker for assessing the presence of these risk factors in CVA patients. Further research investigating serum GGT levels in CVA patients is warranted to determine whether GGT plays a causal role or merely serves as a marker of critical illness. Such studies would provide crucial insights into the underlying mechanisms and clinical significance of GGT in relation to CVA.

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