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A CROSS SECTIONAL STUDY ON CLINICAL PROGNOSTIC SIGNIFICANCE OF GAMMA- GLUTAMYL TRANSFERASE IN PATIENTS DIAGNOSED WITH ACUTE STROKE IN A TERTIARY CARE HOSPITAL

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ABSTRACT:

INTRODUCTION: There are over 12.2 million new strokes each year worldwide. Stroke is the third leading cause of death and the sixth leading cause of disability in India. Hypertension and diabetes are significant risk factors, with hypertension present in 75% of stroke cases in some regions.Initial diagnosis is often based on a rapid clinical assessment of symptoms and signs but Imaging tests like CT and MRI scans are crucial for confirming the diagnosis, determining the type of stroke, and guiding treatment decisions.[4]Atherogenesis is the development of atherosclerotic plaques in the arteries, which can lead to heart attacks and strokes. The association between GGT levels and atherosclerosis supports the potential use of GGT as a predictive biomarker for atherosclerotic events like stroke.

MATERIALS AND METHODS:

Patients who are fulfilling the inclusion and exclusion criteria will be included in the study. History taking and physical examination will be done in all the patients according to the prefixed proforma. All the patients will be evaluated for the Radiological investigations like CT/ MRI to confirm Acute Stroke, Gamma glutamyl transferase levels, Complete Blood Picture, Random blood glucose levels, Liver function test , Renal function tests , Serum electrolytes and Electrocardiogram. The National Institute of Health Stroke Scale(NIHSS) is used to assess stroke severity and Modified Rankin Scale(MRS) is used to assess the functional neurological deficit.

RESULTS: shows that the average age of the patients is 60 years, with a standard deviation of 11 years, suggesting a moderate variation in age among the patients. The gender distribution shows that 58.3% of the patients are male and 41.7% are female. higher GGT levels are significantly associated with more severe disability outcomes on the MRS, particularly noted in the most severe categories: Severe disability (MRS 5) and Death (MRS 6) are highly prevalent with high GGT levels (86.7% and

94.4%, respectively). majority of the Ishaemic stroke patients had higher GGT levels than hemorrhagic stroke patients.

CONCLUSION: In conclusion, the current study found that elevated GGT levels are prevalent among older stroke patients and males, with a significant association between high GGT levels and more SSsevere strokes. Elevated GGT levels were also more common in ischemic and severe hemorrhagic stroke cases. Additionally, higher GGT levels correlated with greater disability and mortality highlighting GGT as a potential biomarker for predicting stroke severity and outcomes. These findings underscore the importance of GGT in assessing stroke risk and tailoring patient management strategies.

Key Words: Acute Stroke, Gamma- Glutamyl Transferase, Functional Neurological Deficit

INTRODUCTION:

The World Health Organization (WHO) defines stroke as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than vascular origin".[1] ICD-11 definition of stroke requires the presence of acute neurological dysfunction and encompasses cerebral ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, and stroke not known to be ischemic or hemorrhagic.[2] There are over 12.2 million new strokes each year worldwide. Stroke is the third leading cause of death and the sixth leading cause of disability in India. Hypertension and diabetes are significant risk factors, with hypertension present in 75% of stroke cases in some regions.[3] Initial diagnosis is often based on a rapid clinical assessment of symptoms and signs but Imaging tests like CT and MRI scans are crucial for confirming the diagnosis, determining the type of stroke, and guiding treatment decisions.[4]Atherogenesis is the development of atherosclerotic plaques in the arteries, which can lead to heart attacks and strokes. GGT is implicated in the pathogenesis of atherosclerosis due to its role in oxidative stress and inflammation. It is believed that GGT may contribute to the oxidation of low density lipoprotein (LDL), a critical step in plaque formation.[5] The association between GGT levels and atherosclerosis supports the potential use of GGT as a predictive biomarker for atherosclerotic CVD [6]. Further research is needed to fully understand the mechanisms by which GGT contributes to cardiovascular pathology and to establish its utility in clinical practice.

MATERIALS AND METHODS:

AIM AND OBJECTIVES

Aim: This study aimed to assess the relation between stroke and GGT.

Objectives

- To study the levels of GGT in patients diagnosed with acute stroke.
- To identity the potential differences in GGT levels in different types of strokes.

SAMPLE SIZE:

N= 96 The prevalence of acute ischemic stroke is 0.268. With a level of significance of 5% and an allowable error of 9%, using the formula below, the sample size is estimated as 96. Sample size = 4pq/l2 p = prevalence q = 1-p 1 = allowable error

INCLUSION CRITERIA: • Adult patients who had a stroke attended the casualty. • Patients are willing to participate in the study and give written informed consent for the study

EXCLUSION CRITERIA: Patients with renal failure, hepatic failure Transient ischemic stroke, Pregnant females, Patients who have active infections, patients with history of neoplasia and alcoholic patients were excluded.

Patients who are fulfilling the inclusion and exclusion criteria will be included in the study. History taking and physical examination will be done in all the patients according to the prefixed proforma.

All the patients will be evaluated for the Radiological investigations like CT/ MRI to confirm Acute Stroke, Gamma glutamyl transferase levels, Complete Blood Picture, Random blood glucose levels, Liver function test , Renal function tests , Serum electrolytes and Electrocardiogram. The National Institute of Health Stroke Scale(NIHSS) is used to assess stroke severity and Modified Rankin Scale(MRS) is used to assess the functional neurological deficit.

The NIHSS is composed of 11 items, each of which scores a specific ability between a 0 and 4. For each item, a score of 0 typically indicates normal function in that specific ability, while a higher score is indicative of some level of impairment. [7]The individual scores from each item are summed in order to calculate a patient's total NIHSS score. The maximum possible score is 42, with the minimum score being a 0.[8,9] The Modified Rankin Score (mRS) measures the degree of functional neurological disability after a stroke. This scale can be assessed in person or by telephone with the patient or caregiver. Minimum: 0, Maximum: 6 (lower is better).

RESULTS:

TABLE-1 shows that the average age of the patients is 60 years, with a standard deviation of 11 years, suggesting a moderate variation in age among the patients. The gender distribution shows that 58.3% of the patients are male and 41.7% are female. Fig -1 shows that the data reveal significant variability in blood pressure measurements with an average systolic blood pressure of 151 mmHg and diastolic blood pressure of 89 mmHg. Biochemical parameters show that the average levels of Gamma-Glutamyl Transferase and Total Cholesterol are 64 U/L and 212 mg/dL, respectively, with considerable variability indicated by the standard deviations. Random Blood Sugar levels also show a high degree of variation, averaging 146 mg/dL. In terms of disease prevalence, 47.9% of the patients have diabetes, and 57.3% have hypertension.

Table 2 shows that 5.2% of patients have minor strokes (NIHSS score 1-4), 56.3% moderate strokes (NIHSS score 5-15), 24.0% moderate to severe strokes (NIHSS score 16-20), and 14.6% severe strokes (NIHSS score 21-42).Table 3 shows that It shows that higher GGT levels (>40 U/L) are more common in older age groups, particularly notable in the 61-70 (80%) and 71-80 (75%) age ranges but there was no statistically significant association. Table 4 shows that Males exhibit a higher prevalence of elevated GGT levels (75%) compared to females and the association was statistically significant.

Table 5 shows that Minor Stroke patients predominantly had lower GGT levels while Moderate to Severe and Severe Stroke categories demonstrate a higher prevalence of elevated GGT levels, with 73.9% and 92.9% respectively having GGT >40 U/L. The chi-square test (11.329, df = 3, p = .010) confirms a significant association between higher GGT levels and more severe stroke outcomes, suggesting that elevated GGT might be linked to greater neurological damage or poor recovery in stroke patients. Table 6 infers that among Improved patients 45.8% had high GGT and 54.2% had low GGT, among Improving patients More patients with high GGT levels (59.1%) are improving compared to those with low GGT levels (40.9%). Among patients who were Unchanged, a significant majority with high GGT levels (72.7%) remained unchanged in their condition and among expired patients very high percentage (87.5%) had high GGT levels, suggesting a potential correlation between high GGT levels and poorer outcomes. The overall chi-square test statistic (p-value = 0.012) across these outcomes highlights significant differences in recovery and mortality rates associated with GGT levels, suggesting that high GGT levels could be indicative of more severe stroke impacts or poorer prognostic outcomes.

Table 7 interprets that the data indicates, Patients with high cholesterol (>240 mg/dL) predominantly have higher GGT levels (68.4%). The trend continues with borderline high cholesterol (200-239 mg/dL) where 80% have high GGT levels even with normal cholesterol levels. Table 8 shows that higher GGT levels are significantly associated with more severe disability outcomes on the MRS, particularly noted in the most severe categories: Severe disability (MRS 5) and Death (MRS 6) are highly prevalent with high GGT levels (86.7% and 94.4%, respectively). majority of the Ishaemic stroke patients had higher GGT levels than hemorrhagic stroke patients.

DISCUSSION:

Stroke is a major cause of morbidity and mortality globally, significantly affecting patients' quality of life and healthcare systems. Understanding the factors influencing stroke outcomes is essential for enhancing patient management and prognostication. Gamma-glutamyl transferase (GGT), an enzyme involved in glutathione metabolism and oxidative stress, has emerged as a potential biomarker for cardiovascular and cerebrovascular conditions. This study examines the clinical and prognostic significance of GGT levels in acute stroke patients in a tertiary care hospital, focusing on its association with demographics and comorbidities, types of cerebral stroke, and outcomes in terms of disability and mortality.

The demographic profile of acute stroke patients in this study shows an average age of 60 years (SD = 11 years). The majority of patients (38.5%) fall within the 51–60 year age group, while the age groups under 40 and over 80 are the least represented. The gender distribution being 58.3% male and 41.7% female. The above results were similar with the study done by Kumar et al., which is an Indian study with a mean age of 58.3 years and majority being male, 67.2%. The results were contradictory with the study done in London, with the mean age being 68.9 years, with 48% female patients. This changing trend can be explained by demographic profile and specific population studies.

In this study, higher GGT levels (>40 U/L) were more common in older age groups. Specifically, the 61-70 age range had 80% of patients with elevated GGT levels, and the 71-80 age range had 75%. Previous studies have also explored the relationship between age and GGT levels in various contexts. Some studies have reported similar trends, where GGT tends to increase with age.[10] However, the significance of this association can vary based on the study population, sample size, and specific patient characteristics. Elevated GGT levels are often associated with oxidative stress and inflammation. While the statistical significance may not be strong in this study, the trend suggests that age-related factors could influence GGT levels. It's essential to consider other factors that may affect GGT levels, such as liver function, lifestyle, and comorbidities. Future research could explore the underlying mechanisms linking age, GGT, and stroke risk. This study is similar to the Indian study where majority of males with acute stroke were found to have increased GGT rather than females.[11]

Patients with moderate to severe strokes demonstrate a higher prevalence of elevated GGT levels. 73.9% of patients in this category have GGT >40 U/L. Among patients with severe strokes, the association with elevated GGT levels is even more pronounced. 92.9% of severe stroke patients have GGT >40 U/L. The chi-square test ($p = .010$) confirms a significant association between higher GGT levels and more severe stroke outcomes. This suggests that elevated GGT might be linked to greater neurological damage or poor recovery in stroke patients. Previous study done by Tao Yao et al have reported similar associations between GGT levels and stroke severity. Elevated GGT has been linked to worse outcomes, including increased disability and mortality rates. The exact mechanisms underlying this association are not fully understood. Elevated GGT could reflect oxidative stress, inflammation, or liver dysfunction, all of which may contribute to stroke severity. Monitoring GGT levels in acute stroke patients could provide additional information for risk stratification and treatment planning.[10] Further research is needed to explore the causal relationship and potential interventions.

This study's findings indicate a significant association between elevated GGT levels and the occurrence of ischemic strokes, with 58% of cases having elevated GGT levels (>40 U/L). The odds ratio suggests that individuals with lower GGT levels are less likely to experience an ischemic stroke, highlighting higher GGT levels as a potential risk factor. The findings are consistent with those of previous studies by Li et al., Tu et al., Gurbuzer et al., Yao et al., Farooq Dar et al., Kumari et al., and Kim et al., all of which demonstrate that elevated gamma-glutamyl transferase (GGT) levels are associated with an increased risk of ischemic stroke.[10-16] Furthermore, Li et al. highlighted the role of elevated GGT levels in the recurrence of stroke events, suggesting that GGT is not only a significant risk factor for initial stroke occurrence but also plays a crucial role in predicting the likelihood of subsequent strokes. This emphasizes the importance of ongoing monitoring and management of GGT levels in patients with a history of stroke to support better long-term outcomes. Joushilahti et al. in

another study, found a significant association between serum GGT concentration and the risk of total and ischemic stroke, as well as intracerebral haemorrhage in men and subarachnoid haemorrhage.[17] This study found that among 96 stroke patients, severe disability was noted in 15 cases, moderately severe disability in 13 cases, and moderate disability in 25 cases. Elevated gamma-glutamyl transferase (GGT) levels were observed in 86.7% of patients with severe disability, 53.8% of patients with moderately severe disability, and 60% of patients with moderate disability. This indicates a clear correlation between higher GGT levels and poorer stroke outcomes. Li et al. explored the association between GGT levels and post-stroke cognitive impairment in a multicenter cohort study. Their findings indicated that elevated GGT levels were linked to a higher risk of cognitive impairment following a stroke.[18] the high percentage of patients with elevated GGT levels who either remained unchanged or expired indicates a potential link between higher GGT levels and poorer stroke recovery or prognosis. The statistical significance of these results, as noted in the chi-square test, underscores the importance of GGT as a potential biomarker for stroke outcomes. Chung et al. (2019) conducted a comprehensive population-based cohort study that investigated the variability of gamma-glutamyl transferase (GGT) and its associations with mortality, myocardial infarction, and stroke.[19]

SUMMARY OF THE STUDY

In this study of acute stroke patients, the average age was 60 years, with 58.3% being male and 41.7% female. The largest age group was 51-60 years (38.5%). Diabetes was prevalent in 47.9% of patients, higher than in previous studies, and hypertension was present in 57.3% of patients. Higher GGT levels (>40 U/L) were more common in older age groups, particularly 61 70 years (80%) and 71-80 years (75%). Males had a higher prevalence of elevated GGT levels (75%) than females (50%), with a statistically significant difference. Minor strokes mainly were associated with lower GGT levels, while moderate to severe strokes had a higher prevalence of elevated GGT levels (73.9%), and severe strokes showed an even stronger association (92.9%). Elevated GGT levels were found in 58% of ischemic stroke cases and 81.5% of severe hemorrhagic stroke cases. In terms of disability, severe disability was noted in 15 cases, moderately severe in 13, and moderate in 25 out of 96 patients, with elevated GGT levels observed in 86.7% of patients with severe disability, 53.8% with moderately severe, and 60% with moderate disability. These findings highlight GGT as a potential biomarker for predicting stroke severity and outcomes.

CONCLUSION

In conclusion, the current study found that elevated GGT levels are prevalent among older stroke patients and males, with a significant association between high GGT levels and more severe strokes. Elevated GGT levels were also more common in ischemic and severe hemorrhagic stroke cases. Additionally, higher GGT levels correlated with greater disability and mortality highlighting GGT as a potential biomarker for predicting stroke severity and outcomes. These findings underscore the importance of GGT in assessing stroke risk and tailoring patient management strategies.

LIMITATIONS:

As the study was conducted in tertiary care hospital, results cannot be generalised to the community

CONFLICT OF INTEREST: Nil

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TABLE-1: Distribution of demographic profile of the patients

Category	Parameter	Mean/Count	Standard Deviation/Percentage
General	Mean	60	11
Gender			
	Sex - F	40	41.7%
	Sex - M	56	58.3%
Age (years)			
	30-40	3	3.1%
	41-50	15	15.6%
	51-60	37	38.5%
	61-70	20	20.8%
	71-80	20	20.8%
	>80	1	1.0%

FIG-1: Baseline Characteristics of disease status and biochemical parameters

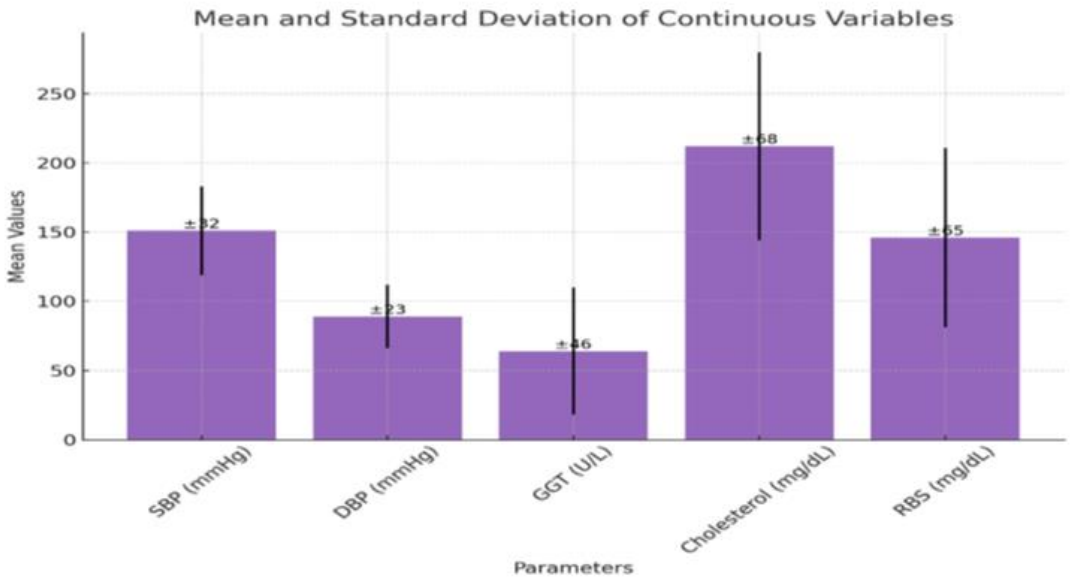

TABLE-2: Assessment and Statistical Analysis of Stroke Severity Based on NIHSS Score

Category	Parameter	Score Interpretation	Mean	Standard Deviation	Median	Percentile 25	Percentile 75	Count	Percentage
NIHSS Total Score Interpretation	Total score		13	7	13	8	17		
	1-4	Minor Stroke						5	5.2%
	5-15	Moderate Stroke						54	56.3%
	16-20	Moderate to Severe Stroke						23	24.0%
	21-42	Severe Stroke						14	14.6%

Table 3: Association of Age and GGT levels

Age Category	GGT <40 (1.00)	GGT >40 (2.00)	Total
30-40	1 (33.3%)	2 (66.7%)	3 (100%)
41-50	7 (46.7%)	8 (53.3%)	15 (100%)
51-60	16 (43.2%)	21 (56.8%)	37 (100%)
61-70	4 (20.0%)	16 (80.0%)	20 (100%)
71-80	5 (25.0%)	15 (75.0%)	20 (100%)
>80	1 (100.0%)	0 (0.0%)	1 (100%)
Total	34 (35.4%)	62 (64.6%)	96 (100%)

- Pearson Chi-Square: **6.677, df = 5, p = .246**

TABLE-4: Association of Gender and GGT Category

Sex	GGT <40 (1.00)	GGT >40 (2.00)	Total	Odds Ratio	Chi-Square
Male	14 (25.0%)	42 (75.0%)	56 (100%)	0.333, CI: [0.140, 0.792]	6.376, df = 1, p = .012
Female	20 (50.0%)	20 (50.0%)	40 (100%)		
Total	34 (35.4%)	62 (64.6%)	96 (100%)		

TABLE-5: Assessment of Stroke Severity Based on NIHSS Scores and GGT Category

Total score	GGT <40 (1.00)	GGT >40 (2.00)	Total	Chi square test
Minor Stroke	4 (80.0%)	1 (20.0%)	5 (100%)	11.329, df = 3, p = .010
Moderate Stroke	23 (42.6%)	31 (57.4%)	54 (100%)	
Moderate to Severe stroke	6 (26.1%)	17 (73.9%)	23 (100%)	
Severe stroke	1 (7.1%)	13 (92.9%)	14 (100%)	
Total	34 (35.4%)	62 (64.6%)	96 (100%)	

TABLE-6:Analysis of Outcomes by GGT Categories

Outcome	GGT>40	GGT<40	Total	P-value
Improved	11 (45.8%)	13 (54.2%)	24 (100%)	chio square 12.867 df 4, p value 0.012
Improving	13 (59.1%)	9 (40.9%)	22 (100%)	
LAMA (Left Against Medical Advice)	1 (25.0%)	3 (75.0%)	4 (100%)	
Unchanged	16 (72.7%)	6 (27.3%)	22 (100%)	
Expired	21 (87.5%)	3 (12.5%)	24 (100%)	
Total	62 (64.6%)	34 (35.4%)	96 (100%)	

TABLE-7:Analysis of total cholesterol Categories by GGT Categories

Total cholesterol	GGT>40	GGT<40	Total	P-value
>240	13 (68.4%)	6 (31.6%)	19 (100%)	0.191
200-239	16 (80.0%)	4 (20.0%)	20 (100%)	
<200	33 (57.9%)	24 (42.1%)	57 (100%)	
Total	62 (64.6%)	34 (35.4%)	96 (100%)	

TABLE-8: Analysis of MRS by GGT Categories

MRS	GGT >40(Count, %)	GGT<40 (Count, %)	Total (Count, %)
0: No symptoms.	1 (16.7%)	5 (83.3%)	6 (100%)
1: No significant disability	3 (33.3%)	6 (66.7%)	9 (100%)
2: Slight disability.	6 (60.0%)	4 (40.0%)	10 (100%)
3: Moderate disability.	15 (60.0%)	10 (40.0%)	25 (100%)
4: Moderately severe disability	7 (53.8%)	6 (46.2%)	13 (100%)
5: Severe disability.	13 (86.7%)	2 (13.3%)	15 (100%)
6: Death.	17 (94.4%)	1 (5.6%)	18 (100%)
Total	62 (64.6%)	34 (35.4%)	96 (100%)