



A CLINICAL STUDY ON RELATIONSHIP BETWEEN ELEVATED GAMMA GLUTAMYL TRANSPEPTIDASE (GGT) LEVELS AND CEREBROVASCULAR STROKE.

General Medicine

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ABSTRACT

Background: In this study we aimed to examine the association between Elevated Gamma Glutamyl Transpeptidase [GGT] levels and Cerebrovascular stroke. **Materials and Methods:** This study was conducted at ESIC Medical College, Sanathnagar, Hyderabad from December 2023- May 2024. The study population included 50 patients admitted in our Hospital with stroke history of 24-72 hrs. **Result:** The clinical and laboratory profile of 50 patients were evaluated. GGT is more strongly associated with ischemic stroke patients with a (P value: 0.0418 - Significant). Risk factor of Hypertension in stroke showed significantly elevated GGT levels. **Conclusion:** Elevated Serum GGT levels is an independent risk factor for stroke, even in the presence of other risk factors such as Diabetes, HTN, Dyslipidemia, and Age. It is a Novel Biomarker for predicting Stroke.

KEYWORDS

Gamma Glutamyl Transpeptidase (GGT), cerebrovascular Stroke, Ischemic stroke.

INTRODUCTION:

Stroke is a serious life-threatening medical condition that happens when blood supply to part of brain is cut off. Cerebro-vascular stroke is responsible for the largest proportion of neurological disorders causing a significant morbidity. According to the World Health Organization, Cerebrovascular stroke is the most common cause of death after heart disease [1]. It is responsible for the largest proportion of neurological disorders which are more often disabling than fatal and results in both physical and mental disability [2].

Brain Stroke is considered as one of the leading causes of death and disability worldwide [3,4]. Gamma Glutamyl Transpeptidase known as GGT is an enzyme found throughout the body, but it is mostly found in the liver. Increased concentration of serum gamma-glutamyl transferase (Transpeptidase) is also seen in Cerebrovascular stroke patients [5]. Stroke patients with diabetes, hypertension, dyslipidemia, obesity, and smoking will have higher level serum GGT level than those without these risk factors.

Gamma-glutamyl transferase (GGT) enzyme has an active involvement in atherosclerosis through its role in oxidative and inflammatory mechanisms. Recent evidence suggests that serum GGT is related to the risk and prognosis of cerebrovascular diseases mostly related to Anterior, Middle and Posterior Cerebral Arteries with Atheromatous plaques presenting as Brain Stroke.

γ -Glutamyl transpeptidase is an important enzyme in the maintenance of the steady-state concentration of glutathione both inside cells and in the extracellular fluids. Gamma-glutamyl transferase (GGT), a key enzyme in the metabolism of glutathione, performs important roles in antioxidant mechanism [6]. The enzyme activity is used diagnostically, but abnormal activity of higher levels of GGT is a significant contributor in the pathology of diseases in which an oxidative component is involved [7].

GGT accelerates the process of atherosclerosis through oxidative and inflammatory mechanisms [8,9,10]. As serum GGT is a widely and

easily available economical biochemical test, it is worth exploring in comparing the GGT activity in stroke patients for the diagnosis and follow-up treatment.

Oxidative stress predisposes to vascular injury, / endothelial dysfunction, leading to Atherosclerosis, cardio-vascular disease, and stroke. There is a good correlation between Serum Gamma Glutamyl Transpeptidase (GGT) with Cerebrovascular accidents, by its involvement in oxidative stress.

People with high serum GGT have higher mortality because it is an independent predictor of risk.

In a research study done by the American Heart Association published in the Journal of Circulation 2004 [11]; showed that human atherosclerotic plaques contain serum GGT activity. They found out that a triggering oxidative stress may be found within the atherosclerotic plaque.

AIM OF THE STUDY:

To evaluate the relationship between cerebrovascular stroke and serum gamma glutamyl transpeptidase (transferase) levels.

MATERIALS AND METHODS:

Inclusion Criteria:

- 1) Patients with acute cerebrovascular accident admitted to hospital were included in the study.
- 2) All patients irrespective of age and sex were included.
- 3) Patients who presented within 2nd to 3rd day of stroke were included in the study.

Exclusion Criteria:

- 1) Persons with chronic liver disease / diseases of biliary tract / pancreas/ Gall bladder / prostate cancer / other malignancies
- 2) Patients who are chronic alcoholics / alcohol dependents / binge alcoholics.

- 3) Patients who are on drugs like phenytoin, fibrates, barbiturates, rifampicin and OCP users.
- 4) Previous history of CVA stroke / TIA or CAHD / CCF.
- 5) Patients who did not give informed consent / were unable to give consent due to their critical state were excluded from the study.

Ethical Considerations:

This study was conducted after obtaining due permission from the Institutional Ethics Committee (IEC)

SAMPLE COLLECTION AND ANALYSIS:

Random venous blood sample of 5ml was collected

The serum was separated and analyzed for GGT (Gamma Glutamyl transpeptidase estimation) MEASUREMENT OF GGT - METHOD - SZASZ METHOD

Reagent kit for quantitative estimation of serum GGT activity in serum or plasma.

Study protocol: Totally 50 stroke patients who had first acute CVA (Cerebrovascular Accident) episode, who were admitted within first 24 - 72 hours were included in this study.

They were selected, irrespective of age groups Careful history was asked for screening for risk factors like systemic hypertension, diabetes mellitus, obesity, CKD and smoking.

CT- Scan Brain (plain) was done within 24- 72 hours of stroke/ admission and analyzed for:

1. Site of Lesion.
2. Nature of Lesion. (Infarct / Hemorrhage)
3. Infarct, whether single / multiple / massive
4. Hemorrhage whether (parenchymal / intra-ventricular extension)

The serum GGT values were compared among cases between various age groups, among sex (male vs female), among risk factors (systemic hypertension, diabetes mellitus, smoking) and between all forms of stroke namely, ischemic, hemorrhagic strokes, etc.

Statistical Tools:

Data was collected in Microsoft Excel V16.0. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2008) developed by Centre for Disease Control, Atlanta.

Using this software Range, frequencies, percentages, Mean, standard deviations, chi square and 'p' values were calculated. Kruskal Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi-square for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

ANALYSIS AND DISCUSSION:

The total number of patients selected for this study was 50 of which 30 were males and 20 were females irrespective of age- groups. All patients were thoroughly examined clinically CT- SCAN Brain Plain was taken within 24 - 72 hrs of stroke or admission.

AGE AND SEX INCIDENCE:

Of the 50 cases, 30 were male and 20 were female included in the study. In this study, stroke occurred commonly in the age group of 51-60 years in both male and female patients. In females stroke occurred commonly in the age group of 61-70 years. The patients with young stroke were 4 male and 1 female.

RISK FACTORS:

Out of 50 patients included in the study, 20 were found to be hypertensive (40%). The other risk factors present in this study were diabetes mellitus, and smoking.

Of the total cases, 20 were found to be hypertensive (40%); 10-diabetic (20%).

2 were patients of Chronic kidney disease (4%); and 14 cases were smokers. (28%)

7 cases were found to be both hypertensive and diabetic (14%);

5 cases collectively had all 3 risk factors, i.e., Systemic hypertension,

DM and obesity. (10%)

CT SCAN FINDINGS:

In this study, CT scan was able to detect Infarct in 40 cases of stroke (80%) Of those 2 cases were multi-infarct and 1 case was massive infarct. Remaining 10 were hemorrhagic stroke. (20%).

Of those 7 cases were of capsulo-ganglionic hemorrhage, 2 cases of thalamic hemorrhage and 1 case of cerebellar hemorrhage. The CT scan was taken after 2nd to 3rd day of acute stroke.

Table 1: Characteristics Of Study Population

Variable	Range	Study population
Gender	Male	30 (60%)
	Female	20 (40%)
Hypertension	YES	20 (40%)
	NO	30 (60%)
Diabetes	YES	10 (20%)
	NO	40 (80%)
CKD	YES	2 (4%)
	NO	48 (96%)
Dyslipidemia	YES	9 (18%)
	NO	41 (82%)
Smokers	YES	14 (28%)
	NO	36 (72%)

SERUM GGT Levels:

All the 50 stroke patients were estimated for serum GGT levels.

Normal range for Serum GGT is [4-40 IU / L.]

The aim of the study is to evaluate the relationship between serum GGT and various forms of stroke.

Of the total 50 cases, 32 were found to have significant elevation of GGT values (64%)

Of those 32 patients had drastically elevated values above 100 IU / L.

Of the total 50 cases, 19 male patients (63.3%) and 13 female patients (65%) had elevated GGT values.

Of the 19 male patients, who had elevated GGT values, the age-group affected was in the 51 - 60 years groups.

Of the 13 female patients, who had elevated GGT values, the age-group affected was in the 61 - 70 years group.

Of the total 50 cases, 20 were hypertensives (40%); of those 14 had elevated GGT values ($p=0.0253$ significant); 3 patients showed normal and 3 patients showed decreased values.

This shows that about 70% of hypertensives showed elevated GGT values and a good correlation exists between Hypertension and GGT. Often 50 cases, 10 were found to be Diabetic (20%).

Among them 5 had elevated GGT values (50%) ($p=0.1425$ - non-significant) were in the age group of 61- 70 years, 3 patients had normal and 2 patients had decreased values.

Of the 50 cases, 2pts, were CKD (4%); Among them 1 had elevated GGT values. (50%) ($p=0.7289$ - non-significant). in both.

Tab.2- Correlation Between Serum GGT Levels And Risk Factors

Serial NO:	Risk Factor	% patients with Elevated GGT	P Values <0.05(significant)
1	Hypertension	70%	0.0253(significant)
2	Diabetes	50%	0.1425(not significant)
3	CKD	50%	0.7289(not significant)

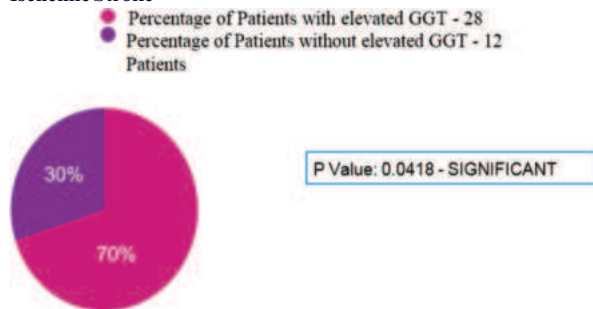
Of the 50 cases studied in our experimental study, Nine were dyslipidemic and they had elevated GGT values. Five patients have normal values. They have decreased values (p value = non-significant) This shows that in diabetes mellitus, CKD and obese / dyslipidemia patients there is no significant relationship among GGT values.

In all 50 cases of stroke patients, 40 Patients (80%) had Ischemic stroke-, (MICA / ACA / PCA (territories I and 10 had Hemorrhagic

stroke (CH (20 %). One has in Capsulo-ganglionic, Thalamic, cerebellar, etc., One patient had Intra-ventricular extension.

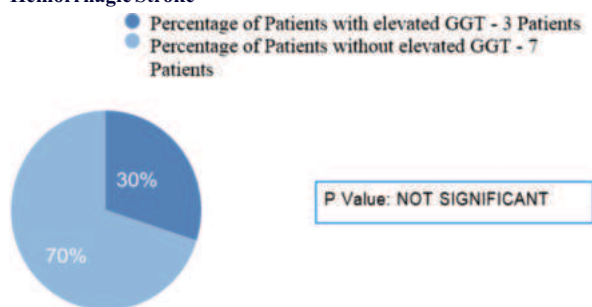
Of the 40 cases of Ischemic stroke, 28 had significant elevated values for GGT (70 %) ($p=0.0418$ – significant). This shows that the ischemic stroke patients have the significant raised levels of GGT.

Ischemic Stroke



Of those 28 had drastically elevated GGT values. (> 100 IU / L.) (Multi-infarct and massive infarct.) Of the 10 cases of hemorrhagic stroke, 3 patients had the elevated levels for GGT, which is non - significant. 1 patient of ICH had gross elevation of GGT values.

Hemorrhagic Stroke



A significant relationship exists in the age group of 61-70 years in female patients, and 51-60 years in male patients.

The activity of GGT is age-dependent value which is focused by this progressive increase in serum GGT with age in male and female age-groups.

6 cases (3 male and 3 female) above > 70 years had elevated GGT values.

The association between GGT and Age: ($P=0.0472$, which is found to be SIGNIFICANT)

This shows that older patients showed maximum elevations as age advances, GGT values tend to increase, showing a linear relationship.

In one experimental study in mice, Researchers produced occlusion of cerebral artery thereby producing hypoxia in brain leading to stroke in them and they showed significant elevations of serum GGT. They concluded that GGT is a dynamic indicator of endothelial response to stroke.

In another study done by American Heart Association / Circulation 2004; showed that human atherosclerotic plaques contain serum GGT activity [11].

Shengyang Jiang, MD PhD, Donglin Jiang, et al. [12] in their research, they found out that a triggering oxidative stress may be found within the atherosclerotic plaque.

All these studies showed the relationship between serum GGT and endothelial dysfunctional disorders, free radical injuries and their local expression in atherosclerotic plaques.

In the recent issue of stroke Jousilahti et al.[13], reported on the association of stroke with serum levels of GGT. The conclusion is that GGT is an independent risk factor for ischemic stroke irrespective of alcohol drinking.

Wookjin Yang, Dong-Wan Kang, and Seung-Hoon Lee et al. [14] reported that Oxidative stress, low-grade inflammation, and metabolic syndrome have been suggested as possible explanations for the association between Increased levels of GGT and stroke.

In the Research study done by Tao Yao, Jing Li, Qi Long, Gang Li Qin Cui, et al. in the Science Reports 2019 publication [15], they evaluated the relationship between raised serum Gamma-Glutamyl transferase and Intracranial Arterial Calcification in Acute Ischemic stroke.

In the Study done by Siqu Li, Anxin Wang, Xue Tian, Yingting Zuo, et al. [16], concluded that as a low measurable and accurate biomarker, GGT activity was positively associated with the risk of stroke adverse outcomes, namely, recurrence of ischemic stroke, and combined vascular events.

In the Study done by Doongar Singh and Sujata agarwal et al. [17], found that 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 data such as age and gender in their study. On the other hand, in the presence of factors like Diabetes, Hypertension, Dyslipidemia, 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.

In the Study done by Lagendra Singh and K.Pradhan et al. [18], observed that serum GGT level is significantly increased in stroke patients in elder age group. There is no significant difference of Serum GGT level in between male and female cases. Serum GGT level is significantly higher in patients suffering from Diabetes, Hypertension, Dyslipidemia, Smoking. Although mean serum GGT level is higher in Hemorrhagic stroke patients than ischemic stroke patients.

In our experimental research study of the total 50 patients, 40 patients were of ischemic stroke variety (80%); Of them 28 patients showed elevated GGT values (70 %) ($p=0.0418$ - significant). Hence, Serum GGT is found to be a significant indicator in patients of ischemic stroke.

CONCLUSION:

Serial studies of the association between GGT and stroke have also highlighted the potential of GGT as a novel biomarker for predicting stroke [10,11]. Nevertheless, it remains unclear why GGT is associated with stroke.

The Findings Of This Study Suggest The:

Of the total 50 cases, 64 % of patients showed elevated Serum Gamma – Glutamyl Transpeptidase values. Predominantly ischemic stroke patients (about 70%) had elevated GGT values. GGT is more strongly associated with Ischemic stroke patients, Of the Infarct cases, Massive and Multi-infarct cases showed drastically elevated GGT levels (i.e., > 100 IU/L). This may indicate the value of evaluating the GGT levels as an adjunctive biomarker for determining subtypes in stroke patients. Patients having increased serum GGT levels have high risk of stroke, Independent of alcohol consumption. In the elderly patient groups, (> 70 years) all of them showed elevated GGT values. There is no gender predilection for elevated GGT levels in CVA. Hypertensives (about 70 %) showed significantly elevated GGT levels. The study concludes that serum GGT levels is an independent risk factor for stroke, even in the presence of other risk factors such as diabetes mellitus, HTN, Dyslipidemias, age, sex. One of the finding of this study is to consider the increased levels of GGT, with no History of Alcohol consumption as a risk of Cerebrovascular Accident Stroke. We conclude People with high serum GGT have higher mortality because it is an independent predictor of risk.

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