VOLUME - 11, ISSUE - 04, APRIL - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Medicine

SERUM GAMMA GLUTAMYL TRANSFERASE AS A PLAUSIBLE FORTELLER OF ISCHAEMIC AND HAEMORRHAGIC STROKE AND ITS OUTCOME

Dr Abilesh Kumar* Associate Professor of Internal Medicine, JLNMCH, Bhagalpur. *Corresponding Author

Dr Surabhi SR, Internal Medicine JLNMCH, Bhagalpur.

ABSTRACT

BACKGROUND- Elevated serum GGT level may be a reflection of high degree of oxidative stress and oxidative stress is known to be associated with atherosclerosis. Moreover, here is link between increased GGT activity and occurrence or progression of atherosclerosis. The aim of our study is to see whether serum GGT level is an independent risk factor for stroke in young and elderly population without history of alcohol consumption.

METHOD- Total number of 100 cases including both male and female who presented with their first episode of stroke were taken and juxtaposed with 100 age and sex matched healthy control subjects from the department of general medicine without any obvious cerebro-vascular or cardiovascular disease and who visited for some other unrelated ailments. The patients and controls in both groups (A&B) were subjected to routine history taking, general survey, and systemic examination and biochemical tests.

RESULTS- This study reveals that the serum GGT level is significantly higher in cases (mean 55.34U/L+SD42.78) than controls (17.47U/L+SD4.31) with p value<0.0001.In logistic regression model it has been shown that the risk of stroke was 30.83 times for the patients with level of GGT>58 IU/L, 3.55 times more for patients with HTN, 2.88 times more for the females with waist circumference≥80cm and the risks were significant.

CONCLUSION- There is an elevated level of serum GGT in stroke patients then the non-stroke patients, the serum levels are independently allied with stroke in spite of the existence of other known threats for stroke

KEYWORDS : Stroke Gamma Glutamyl transferase

INTRODUCTION

Stroke, or a cerebrovascular accident, is the unexpected onset death of brain cells due to scarce blood flow. The WHO clinically defines stroke as a rapid onset of focal (or global as in subarachnoid hemorrhage) cerebral deficit, lasting more than 24 hours (unless interrupted by death or surgery) with no apparent cause other than a vascular one.

Gamma Glutamyl Transferase (GGT) also known as Gamma Glutamyl Trans peptidase is an enzyme found in the endothelial cell membranes of various organs in human body where it appears to mediate peptide transport. It was first discovered by Hanes in 1959.After its discovery the significance of increased level GGT in clinical practice has mainly been focused on ethanol toxicity and also some neoplasm and biliary tract obstruction. GGT has long been used as a marker of excessive alcohol consumption1.Several population based studies have found positive associations of GGT with incident of cerebrovascular events1. Yet the magnitude of associations differs between studies. However the proposed mechanism of increased serum GGT level with cerebrovascular disease and stroke is oxidative stress.2 Elevated serum GGT level may be a reflection of high degree of oxidative stress and oxidative stress is known to be associated with atherosclerosis.

Aims

Several epidemiological studies have shown that alcohol consumption is a risk factor for stroke.The relationship between alcohol consumption and stroke is believed to involve various mechanisms including alcohol induced hypertension, cardiomyopathy, coagulation disorder, atrial fibrillation and reduction in cerebral blood flow. GGT has long been used as a marker of excessive alcohol consumption[1]. These studies exposed the association between self-reported alcohol consumption and high GGT level with risk of stroke[2].As there may be error in measurement of alcohol consumption level by self report[3],as heavy drinkers may underreport their consumption[4], we have done our study in the non-alcoholic group. The aim of our study is to see whether serum GGT level is an independent risk factor for stroke in young and elderly population without history of alcohol consumption.

OBJECTIVES

1. Evaluation of GGT level in case of acute stroke in both and younger and older age group (40-80yrs) and comparing them with age and sex matched normal subjects(control group).
2. To see whether there is any differences in serum GGT level in acute stroke between the younger and older age group or men and women.
3. Correlation of serum GGT level in acute stroke with the other known risk factors (diabetes mellitus, hypertension, dyslipidemia) in these subjects.

MATERIAL AND METHODS

1. **Study area:** Post graduate Department of General Medicine JLN Medical College & Hospital, BHAGALPUR
2. **Study population:** Patients admitted in post graduate department of general medicine from Emergency and Medicine outdoor with CT SCAN reports showing acute stroke were selected non-randomly for the study.
3. **Study period:** The duration of study was between November 2019 to November 2021
4. **Sample size:** Total number of 100 cases including both male and female who presented with their first episode of stroke were taken and juxtaposed with 100 age and sex matched healthy control subjects
5. **Sample Design:** Patients and their relatives were fully explained in their mother language about the study. After getting proper informed consent from them, they were included in the study, if they fulfilled the following criteria:

Inclusion Criteria:

For case

- Age 40-80 yrs.
- Acute stroke(First episode) on CT scan showing
- Intracerebral hemorrhage
- Ischemic stroke
- Subarachnoid hemorrhage

For control

- Age 40-80 yrs.

- Admitted for respiratory distress like COPD, Asthma, gastroenteritis, fever like Malaria, Dengue, UTI, LRTI, URTI

Exclusion Criteria:

- Patients with past episode of stroke
- Patients without acute stroke
- Patients having diseases or factors in which serum GGT can rise, were excluded
  - oCongestive cardiac failure
  - oHistory of alcohol consumption
  - oHistory of Biliary tract disease
  - oHistory of drug use such as statins, NSAIDS, OCP, antihistaminic, antibiotics, clofibrate, antidepressants.

6. **Study design:** It is a observational cross sectional, comparative, hospital based study.
7. **Study tool:** Patient Performa, standard hematological, biochemical and radiological tests.

RESULTS AND ANALYSIS

Sampling Techniques:

Patients were assigned in the two arms of the study with the help of computer generated random numbers by the process of randomization.

Statistical Analysis:

Statistical Analyses were performed with help of Epi Info (TM) 3.5.3. EPI INFO is a trademark of the Centres for Disease Control and Prevention (CDC).

Both univariate and multivariate analysis were performed to find the Odds Ratio with 95% confidence interval and corresponding p-values. Under univariate analysis frequency tables were prepared to find the Odds Ratio with their confidence interval being 95% and under multivariate analysis Multiple Logistic Regression had been used to find the Odds Ratio with their confidence interval being 95% after adjusting the confounding factors.

Overall Findings Of The Subjects (cases& Controls) Under Study:

Table-1: Age distribution

Age Group (in years)	Number	%
40 - 49	36	18.0%
50 - 59	53	26.5%
60 - 69	65	32.5%
70 - 79	46	23.0%
Total	200	100.0%

The mean age (mean ± s.d.) of the subjects was 59.92±10.12 years, with range of 40 - 79 years and the median age was 62.0 years. Most of the subjects were with ≥60 years (55.5%) which was significantly higher (Z=4.16; p=0.0001).

Table-2: Level of GGT and subjects of the two groups

Level of GGT (in IU/L)	Cases (n=100)	Control (n=100)	TOTAL
>58	30	0	30
Row %	100.0	0.0	100.0
Col %	30.0	0.0	15.0
≤58	70	100	170
Row %	41.2	58.8	100.0
Col %	70.0	100.0	85.0
TOTAL	100	100	200
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0

Since two of the cell frequencies were zero Chi-square test was not applicable and odds ratio could not be calculated. But Fisher exact test showed that proportion of subjects with acute stroke were having significantly higher level of GGT (i.e. >58 IU/L) (p= 0.000001).

The mean level of GGT (mean ± s.d.) of the cases was 55.34±42.78IU/L with range 16–290 IU/L and the median was 45.0IU/L.

The mean level of GGT (mean ± s.d.) of the controls was 17.47±4.31IU/L with range 9–28 IU/L and the median was 17.0IU/L.

t-test showed that the mean GGT level of the cases was significantly higher than that of the controls (t198= 8.80;p=0.0001),

Table-3: Comparison of level of GGT on admission of the cases under study

Parameters	Level of GGT (IU/L)	t_{98}	p-value
Age (in years)			
>60 (n=51)	46.21±15.98	2.21	0.02*
≤60 (n=49)	64.84±57.69		
Gender			
Male (n=53)	67.09±54.80	3.03	0.003*
Female (n=47)	42.09±14.38		
DM			
Present (n=44)	48.30±43.58	0.47	0.63
Absent (n=56)	45.21±18.83		
HTN			
Present (n=87)	56.75±45.09	0.85	0.39
Absent (n=13)	45.91±20.54		
TG (mg/dl)			
≥150 (n=50)	59.58±52.13	0.99	0.32
<150 (n=50)	51.10±30.73		
Cholesterol (mg/dl)			
≥200 (n=47)	58.51±50.99	0.80	0.42
<200 (n=53)	51.76±31.23		
HDL (mg/dl)-Male			
<40 (n=15)	70.78±62.23	1.05	0.29
≥40 (n=38)	57.73±28.09		
HDL (mg/dl)-Female			
<50 (n=19)	43.16±14.03	0.60	0.54
≥50 (n=28)	40.51±15.11		
WC (cm)-Male			
<90 (n=15)	58.83±35.91	1.45	0.15
≥90 (n=38)	88.00±84.22		
WC (cm)-Female			
<80 (n=22)	38.88±11.22	1.46	0.14
≥80 (n=25)	44.92±16.38		
Type of stroke			
Ischemic (n=33)	59.01±51.90	Ischemic Vs Non-ischemic-0.40	0.69
		Ischemic Vs SAH -1.09	0.27
Non-Ischemic (n=59)	55.53±31.02	Non-Ischemic Vs SAH 1.51	0.13
SAH (n=8)	38.75±4.49		

* Statistically significant

Mean GGT was significantly higher for the patients with age≤60 years (p=0.02) and males (p=0.003). No significant was found for all other parameters (p>0.05).

DISCUSSION

The stroke population in our study comprised of of 54% Hemorrhage, 33% ischemia, 5% of hemorrhagic infarction and 8% subarachnoid hemorrhage. The proportion of type of stroke differs from the study done by Das et al.The difference crops up probably due to more admission of intra cerebral hemorrhage patients which are being referred from the district care hospitals for better management.

As discussed earlier alcohol consumption can cause stroke and alcohol can increase serum GGT level, this study did not

take any alcoholic into account, in both the case and control groups. So the results of this study in reference to serum GGT levels is not prejudiced by alcohol consumption.

This study reveals that the serum GGT level is significantly higher in cases (mean 55.34U/L+SD42.78) than controls (17.47U/L+SD4.31) with p value<0.0001.In logistic regression model it has been shown that the risk of stroke was 30.83 times for the patients with level of GGT>58 IU/L, 3.55 times more for patients with HTN, 2.88 times more for the females with waist circumference≥80cm and the risks were significant. However, the risk of stroke was 4.21 times more for the patients with level of cholesterol >200 mg/dl, 2.51 times more for DM, 1.45 times more for males with HDLC>40 mg/dl, 1.09 times more for females with HDLC>50 mg/dl, 2.48 times more for smokers and 2.28 times more for males with WC>90 cm but the risks were not significant. No risk of stroke was found for age and level of TG. But risk was not significant for level of cholesterol, DM, level of HDL, smoker, and waist circumference for male>90cm. The risk was significant for GGT>58, HTN and WC for female >80cm and highest for GGT level. This implies that GGT can independently cause stroke even in the presence of other stroke risk factors such as diabetes mellitus, hypertension, and dyslipidemia.

Serum GGT is higher in age group 40-60 yrs,(24 hr. GGT mean 64.84U/L+SD 57.69) than age group 60-80 yrs.(24 hr. GGT 46.21U/L+SD15.98) with p value 0.029.This implies that serum GGT level is significantly higher in 40-60 yrs. of age group with p value <0.05.

Serum GGT level is significantly higher in male than female (p value<0.05). 24 hr GGT in male patients is higher (mean 67.09U/L+SD 54.80) than female (mean 42.09U/L+SD 14.38) with p value 0.003. This study support the observation that GGT level is higher in male than female. Probably this may be due to increased incidence of smoking in male than female as it can increase oxidative stress and so can increase serum GGT level.

This study observes that Serum GGT is higher in diabetics (24 hr. GGT mean 48.30U/L+SD43.58) as compared to nondiabetics (24 hr. GGT mean 45.91U/L+SD 18.83) with p value 0.63.

In this study there is no significant correlation found between hypertension and non-hypertension with serum GGT level. The 24 hr. serum GGT level in hypertensive is mean 56.75U/L+ SD45.09 compared to mean 45.91U/L+ SD 20.54 in non-hypertensive with p value 0.39.

This study does not show statistically significant observation between serum GGT level and TG>150.The 24 hr. serum GGT level in TG>150 patients is mean 59.58U/L+SD 52.13 compared to 51.10U/L +SD 30.73 in TG<150 patients with p value 0.32.

There is no correlation between metabolically significant waist circumference (in male >90 cm and in female >80 cm) with serum GGT level. The 24 hr. serum GGT level in waist circumference of male >90 cm is 88.00U/L+SD 84.22 with male<90cm is 58.83U/L+SD35.91with p valve 0.15and that of female>80cm is 44.92U/L+SD16.38 with female <80cm is 38.88U/L +SD11.22 with p value of 0.15.Most of the studies done to show relation between BMI and serum GGT.As it is very difficult to take weight and height in stroke patients BMI is not taken into account in this study.

This study does not show any statistically significant correlation between stroke type and serum GGT. In ischemic stroke mean serum GGT level in 24 hr. is 59.01 U/L+SD 51.90. Similarly in non-ischemic stroke containing intracerebral hemorrhage mean GGT level in 24 hour is 55.53U/L+SD 31.02and subarachnoid hemorrhage the mean serum GGT level in 24 hr. is 38.75 U/L+ SD4.49. The finding that the serum GGT levels are slightly more in our study, may be due to small population of ischemic stroke patients(n=33).The explanation for higher serum GGT level in ischemic stroke may be due to the role of GGT activity in the evolution and instability in different vascular zones.

Regarding the association between serum GGT level and outcome of stroke (death or survival) no studies are done till now. Thus this study concludes that serum GGT level is an independent risk factor of stroke even in the absence of alcohol consumption.

Limitation Of Study

- **Study Design:** This study is an observational cross sectional case control study. Most of the studies done to show that serum GGT is a risk factor of stroke are prospective studies. They have followed a group of cohort for a number of years and have observed incidence of stroke in the population.
- **Sample Size:** The sample size in our study is small (100 cases and 100 controls). This can influence the study result.
- The diabetics and hypertensives in our study might be under OHA or Insulin and anti hypertensives, this may influence the results.
- Stroke patients were followed only for 10 days. This may under report the incidence of mortality in this study.
- Alcoholic patients were not included in the study from the very beginning. Patients were taken into this study solely depending on their history. Some patients may underreport the alcohol consumption. This may influence the result of the study.
- There is a referral bias for hemorrhagic stroke patients. This may influence the study results.

CONCLUSION

There is an elevated level of serum GGT in stroke patients then the non-stroke patients, the serum levels are independently allied with stroke in spite of the existence of other known threats for stroke. Serum GGT is appreciably elevated in age group of 40-60 yrs more so amongst the males hypertensives who have an altered lipid profile. The serum GGT level is found to be significantly higher amongst the patients with ischemic stroke rather than the non-ischemic ones. Further it was brought into being that the serum GGT level couldn't predict the outcomes (survival or death) in stroke patients. Higher the level of GGT, higher is the risk of stroke this was not confounded by the alcohol consumption. Finally, it appears that more number of large scale prospective study needs to appraise and institute the prognostic value of GGT in predicting a stroke and further foretelling the course of the disease.

REFERENCES

1. WannametheG ,Ebrahim S ,Shaper AG .GGT :determinants and association with mortality from ischaemic heart disease and all causes. Am J Epidemol.1955 ;142:699-708.
2. Emdin ,Pompella A.GGT ,atherosclerosis and cardiovascular disease : triggering oxidative stress within the plaque . Circulation 2005;112:2078-2080
3. Lee DH, Blomhoff R, Jacobs DR. Is serum GGT a marker of oxidative stress? Free Radic Res 2004; 38 : 535-539.
4. DemirkranB ,GurayY.The relationship between saphenous coronary bypassgraft occlusion and serum GGT activity. Turk KariyolDermArs2010 ;38(5):321-6
5. StrangesS ,Trevisan M, Dorn JM .Body fat distribution ,liver enzymes and risk for hypertension. Hypertension 2005;46:1186-93
6. Camargo CA .Moderate alcohol drinking and stroke: The epidemiological evidence .Stroke 1989 ;20:1611-1626