



Serum Gamma-Glutamyl Transferase in Coronary Artery Disease Patients

Roopa A K, Rama Devi K

Institute of Biochemistry Madras Medical College, Chennai

Abstract

Gamma-glutamyl transferase is an enzyme located in the external surface of cellular membrane. It is helpful in replenishing intracellular antioxidant glutathione by cleaving extracellular glutathione contributing to antioxidant inadequacy. Increased levels of GGT has been found to be associated with coronary heart disease, stroke, systemic hypertension, cardiac arrhythmias and heart failure. Studies show the presence of catalytic GGT in the atherosclerotic plaques. This study was carried out to explore the relationship between GGT and coronary artery disease (CAD). Twenty five angiographically proven CAD patients attending cardiology OPD for follow up and twenty five age and sex matched healthy controls were studied. GGT and lipid profile were analysed.

Results

Serum GGT was found to be higher in cases than in control subjects. GGT levels correlated positively with total cholesterol and LDL cholesterol. There was also a positive correlation between GGT levels and coronary complexity.

Conclusion

GGT, an indicator of antioxidant inadequacy can be used as a predictive biomarker for coronary artery disease.

Key Words: Coronary Artery Disease (CAD), Gamma-glutamyl transferase (GGT), glutathione.

Introduction

Coronary artery disease (CAD) is the principal cause of mortality and morbidity and it is a worldwide public health problem. Atherosclerosis plays a significant role in the pathogenesis of the development of cardiovascular events, where oxidative stress is a significant mechanism underlying it. Gamma-glutamyl transferase (GGT) which is a marker of liver dysfunction especially used for the diagnosis of alcohol abuse, is now found to be associated positively with cardiovascular events, stroke, Diabetes and even cancer (1). In this study, we aimed to investigate the role of GGT on

oxidative stress in the development of CAD and to find out whether it can be used diagnostically as one of the cardiovascular risk factors in our population.

Materials and Methods

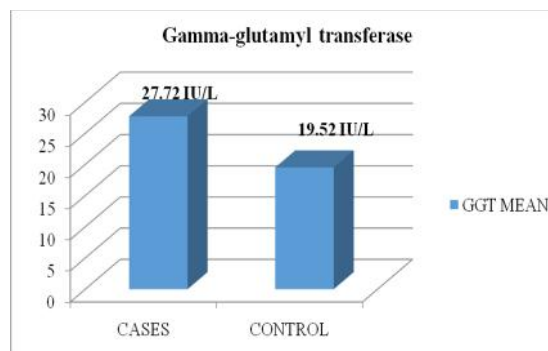
Twenty five angiographically proven CAD patients who came to the outpatient department during follow up were investigated. Twenty five age and sex matched healthy controls were also included. Alcoholic patients, patients with abnormal kidney function were excluded from the study. Serum GGT, Fasting plasma glucose and lipid profile (Cholesterol, TGL and HDL) were analysed by spectrophotometric method using Roche cobas 6000 analyser. LDL was calculated from Friedwald's formula.

Statistical analysis was done using SPSS software version 24.0

Results

Mean values of GGT were obtained in both groups and were correlated with fasting plasma glucose and lipid profile.

Fig(1) showing mean GGT levels in cases Vs control group



FPG- Fasting plasma glucose

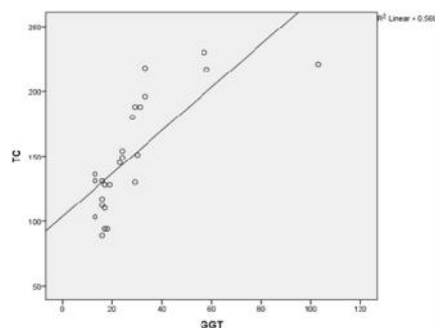
CASES	MEAN (mg/dL)	SD	PEARSON CORRELATION COEFFICIENT	P VALUE
FPG	108.44	35.12	-0.037	0.861
TC	149.60	43.35	0.754	0.000**
HDL	40.64	10.52	0.443	0.027*
TGL	148.12	66.67	0.057	0.788
LDL	79.53	36.5	0.754	0.000**

** correlation significant at 0.01 level

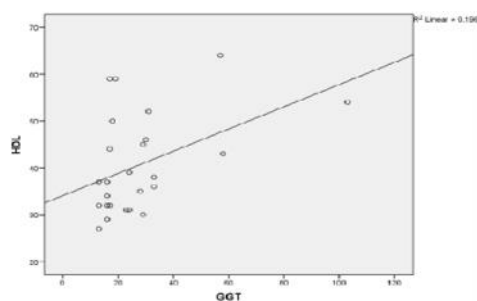
* correlation significant at 0.05 level

Fig(2-5) showing correlation between GGT and lipid profile

Fig (2)



Fig(3)



Fig(4)

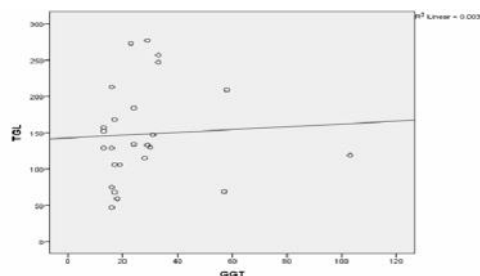
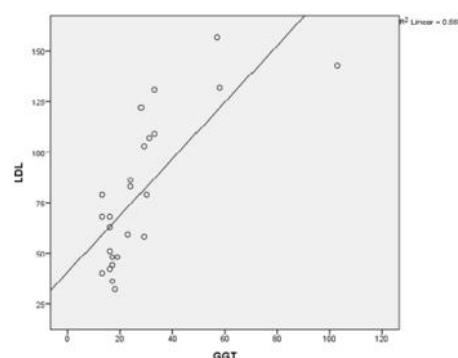
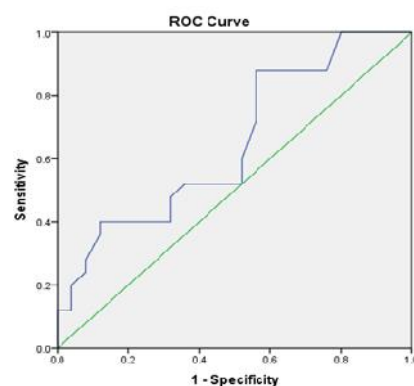


Fig (5)



Fig(6) Receiver Operating Characteristics curve showing the sensitivity and specificity of GGT value observed in the study



Area under the curve	0.650
Std error	0.078
Cut off value	15.5 IU/L
Sensitivity (true positive)	88%
1-Specificity (false positive)	56%

Mean value of GGT obtained in cases(27.7 IU/L) were comparatively higher than in controls (19.5 IU/L). Significant positive correlation was obtained between GGT and total cholesterol, HDL-C and LDL-C values and negative correlation was observed with fasting plasma glucose values. Receiver operating characteristics(ROC) curve was obtained to determine the cut off value above which GGT values contribute to the disease.

A cut off value of 15.5 IU /L with 88% sensitivity and 44% specificity can be used to segregate the cases from controls.

Discussion

Gamma -glutamyltransferase,an enzyme located in the membranes of various cells with secretory and absorptive capacity -(i.e) intestine, pancreas, biliary ducts, proximal convoluted tubule (2). Kidney is found to have highest GGT concentration but maximum contribution for serum GGT is from hepato biliary system (3,4). GGT has two subunits- larger and smaller with the latter facing cell exterior and having catalytic activity(5). One of the functions of GGT is to catabolise glutathione, a thiol containing antioxidant.

Glutathione is synthesised and transported out of the cell and it is cleaved by GGT into glutamyl andcysteinyl-glycine dipeptide .Thecysteinyl glycine dipeptide is a strong reducing agent which reduces Fe^{3+} to Fe^{2+} which in turn is responsible for the production of superoxides and hydrogen peroxide. The superoxides promote the peroxidation of LDL to oxidised LDL, which is preferentially taken up by monocyte macrophage system in the atherosclerotic plaques.

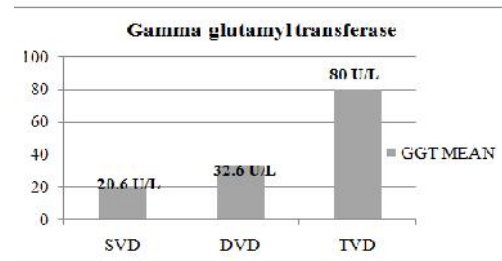
Catalytically active GGT is found to be in the atherosclerotic plaques(6,7) and it correlated positively with the serum GGT activity indicating that GGT has a direct role in the development of atherosclerosis, plaque instability ,rupture and consequent coronary ischemic events.

In the Framingham offspring study (8),GGT conferred 13% increase in the risk for CVD and 26% increase in the risk for mortality for each standard deviation higher log GGT.In the British regional heart study(9),increase in GGT (> 24 U/L) was associated with 22% and 44% increase in the relative risk for all cause and CHD related mortality. In our study, we have observed an increase in $\text{GGT} > 15.5$ U/L is related to the incidence of CAD.

In the study done by Wannamethee SG et al, a strong association of GGT and CVD mortality was found in younger men (10).Similarly in our study out of 25 patients, 16 patients developed CAD in young age (<55 years) and their mean GGT level was 26.3 IU/L.

In the study done by Yu Mao et al(11), GGT levels showed statistically significant difference between triple vessel disease and other groups. In our study, patients were grouped according to coronary severity and GGT levels correlated positively with the number of vessels blocked as shown by coronary angiography. The mean GGT level in the patient group comprising single vessel disease(SVD) is 20.6 IU/L, in double vessel disease (DVD) it was found to be 32.6 IU/L and in triple vessel disease(TVD) highest concentration of about 80 IU/L was observed.Fig(7) showing mean GGT levels in patients categorised in three groups.

SVD,DVD,TVD



It has been hypothesized that GGT elevation seen in cardiovascular events may be due to the co-morbidities that are associated with coronary artery disease, eg.fatty liver can cause elevations in GGT(12) . Whether GGT is directly involved in the pathophysiology of CAD or it is an epiphenomenon associated with co-morbidities need to be elucidated.

Conclusion

There is an association between GGT levels and coronary artery disease. The levels also correlated with the severity of blocks observed in coronary angiography. This concludes that gamma glutamyltransferase ,with the level of more than 15.5 U/L is a potential pro-oxidant contributing to the oxidative stress and therefore can be considered as a biomarker of CAD in our population.

Limitations

The sample size of the study is small. Secondary increase in GGT due to fatty liver was not ruled out. Patients were not followed up for future coronary ischemic events and mortality.

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