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SERUM GAMMA GLUTAMYL TRANSFERASE ACTIVITY IN PATIENTS WITH CARDIOVASCULAR DISEASES ASSOCIATED WITH DIABETIC MELLITUS

Ravoori Saideswar Rao* and Vanita Lal**

*Tutor, Department of Biochemistry, Government Institute of Medical Sciences.
**Chief Medical Superintendent Professor, Department of Biochemistry, Government Institute of Medical Sciences.

***Corresponding Author: Ravoori Saideswar Rao**

Tutor, Department of Biochemistry, Government Institute of Medical Sciences.

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ABSTRACT

Back ground: Gamma glutamyl tranaferase(GGT) is a widely used marker for liver function and is correlated with alcohol intake. An increase GGT activity is linked with influx of GGT–carrying Lipoproteins into plaque. **Materials and Methods:** The study design is a cross sectional study with 280 participants consisting of a 3 groups. Group-1 Cardiovascular disease (CVD) without diabetes,Group-2 CVD with diabetes,Group-3 Healthy individuals. The analysis of GGT, RBS, lipid profile ,SGOT and SGPT were done in central hospital laboratory of SRMC&RI by using standard kits in Dimension RxL autoanalyser. The results were expressed as mean ±SD.The data analysis was done by using ANOVA and Pearson's correlation. **Result:** We observed a statistically significant increase ($p < 0.001$) in serum GGT levels in group 1& 2 compared to group 3. There is no statistically significant in serum GGT levels in cardiovascular disease with diabetes and without diabetes. There is good significant correlation between the GGT with total cholesterol($r = 1$). A week correlation was obtained between GGT and triglycerides, LDL and negatively correlated with HDL. **Conclusion:** Higher Gamma glutamyl transferase levels are associated to cardiovascular disease in people with and without diabetes.There is increased concentration of GGT in serum compared to healthy individuals.

KEYWORDS: Gamma Glutamyl Transferase, Oxidative Stress, Atherosclerosis, Cardiovascular Disease.

INTRODUCTION

Gamma glutamyl transferase (γ GT-EC: 2.3.2.2) is an enzyme that facilitates amino acid transport across the cell membranes and play a key role in the glutathione (GSH) metabolism meister cycle.[1] Glutathione is predominately intracellular whereas a major fraction of the cellular γ GT is on the external surface of cell membranes [2]. Hanes et al. were the first to describe γ GT in human tissue, and the diagnostic usefulness of γ GT was first reported by Szczeklik et al.[3]

Gamma glutamyl transferase is found mainly in membranes of cells that show high secretory or absorptive capacity such as the epithelial cells lining the biliary tract, hepatic canaliculi, proximal renal tubules, pancreatic acinar tissue, pancreatic ductules and intestional brush border cells. Measurable γ GT activity has not been found in skeletal muscle or myocardium.[3] The role of Gamma glutamyl transferase in Gamma glutamyl cycle is to transport of amino acids. The enzyme present in serum appears to originate primarily from the hepatobiliary system. Gamma glutamyl transferase is a sensitive indicator of the presence of hepatobiliary disease[4,5], being elevated in most subjects with liver disease, also alcoholic hepatitis, acute myocardial infarction.[12]

The primary role of γ-Glutamyl transferase ectoactivity is to recycling of intracellular GSH synthasis. A gamma glutamyl transferase - mediated oxidative stress has been repeatedly reported, capable of inducing oxidation of lipids and oxidation of protein thiols.[11]

Oxidative damage of proteins and lipids caused by free radicals is involved in pathogenesis of different diseases like cancer, atherosclerosis, inflammation.[7] Glutathione, the major intracellular non protein thiol, is mainly known as an important protector against free radical damage by providing reducing equivalents for several key antioxidant enzymes and also by scavenging hydroxyl radicals and singlet oxygen. However, it has been reported that the GSH metabolism by γ GT in the presence of iron leads to reactive oxygen species (ROS) generation.[9] The oxidation of LDL through GSH/ γ GT-dependent iron reduction takes place within the atheromatous plaque. Hence, there are two possible explanations for the association between serum γ GT and cardiovascular risk: either γ GT derives in part from

atheromatous plaques, which would be more common and diffuse in patients with adverse cardiovascular risk profiles, or γ GT is associated with the risk factors even before the plaques are fully developed. Oxidative stress is closely related to atherosclerosis.[9]

Increase in circulating γ GT complexes with low density lipoprotein and helps in it's oxidation which promotes the formation of plaques.[14] The reactive thiol of cysteinyl-glycine originated during γ GT- mediated cleavage of GSH may cause the reduction of ferric Fe(III) to ferrous iron Fe (II), thus starting a redox – cycling process resulting in the production of the reactive oxygen species superoxide anion and hydrogen peroxide, both capable of stimulating prooxidant reactions shown in Fig.1. Gamma glutamyl transferase pro-oxidant effects are likely within atherosclerotic coronary, carotid, and cerebral plaques, where catalytically active enzyme has been histochemically identified.[8]

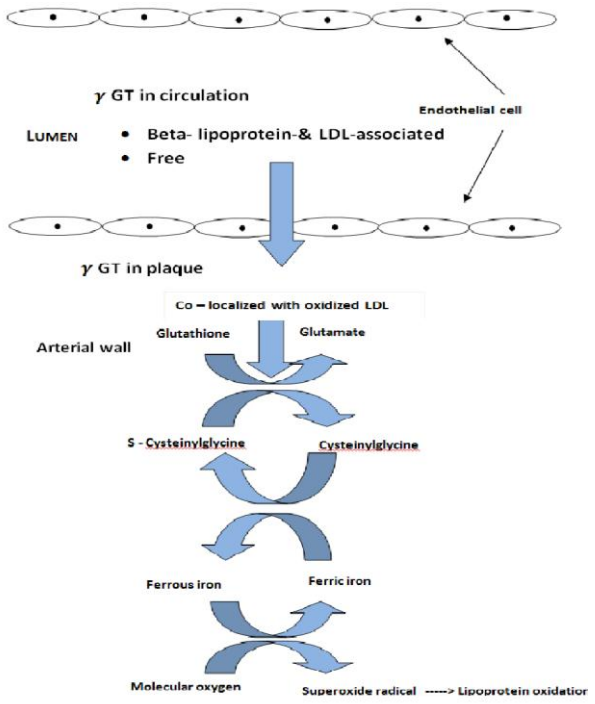

Figure. 2. Role of γ GT in the formation of atheromatous plaque γ GT (gamma glutamyl transferase) LDL (low density lipoprotein).

Gamma glutamyl transferase and Cardiovascular Diseases: In clinical practice, gamma glutamyl transferase is a commonly used diagnostic test. Although γ GT is mainly seen as an indicator for liver function and alcohol consumption, several studies showed that it is associated with morbidity and mortality from causes other than liver disease, including cardiovascular disease(CVD), there are now indications of γ GT having a direct involvement in atherosclerotic plaque formation and it's have role in cardiovascular diseases [13]. In western countries, two- to three fold increases in the rick of atherosclerotic diseases have been reported among individuals with diabetes. In these populations, cardiovascular disease is the leading cause of death among those with diabetes.[15]

MATERIALS AND METHODS

This was a cross sectional study done in a Sri Ramachandra Medical college & Hospital, Chennai. CVD with diabetes, CVD without diabetes patients were recruited from Cardiology Intensive care unit. Informed consent was obtained from participants and approved by institutional ethical committee (REF: CSP/13/MAR/27/50).

The total number of participant were 280. Study participant were categorized into 3 groups. **Group I:** 90 cardiovascular disease patients age 30 – 60 years of both sexes were selected for this group. Exclusion criteria for this group were diabetes, liver disease and alcoholics. **Group II:** 90 cardiovascular disease with diabetes patients age 30 – 60 years of both sexes were selected for this group. Exclusion criterias for this group were liver disease and alcoholics. **Group III:** 100 healthy individuals age 30 - 60 years without any disease and both sexes were selected for this group. Exclusion criterias for this group were diabetes mellitus, cardiovascular disease, liver disease and alcoholics. The blood sample from 280 individuals was collected in random state using vacutainers with (Li-heparin) & without anticoagulants sterile gel tubes. These tubes were centrifuged at 3500rpm for 10 minutes & serum was separated.

Methodology

Gamma glutamyl transferase, Lipid profile (total cholesterol, triglycerdies, HDL and LDL) ,Liver function test (alanine transaminase, aspartate transaminase) and Plasma Glucose Estimation are measured using standard kits by ADIVA 1800 and RxL Dimension fully automated analyzers.

Statistical Analysis

The results of all the parameters was expressed as mean $\pm$ SD. Statistical analysis were done by using ANOVA and Pearson's correlation.

RESULT

The results of our study are shown below.

Table. 1: Demographic Data & Biochemical Parameters in the Study Groups.

Parameters	Group- I(n=90)	Group- II(n=90)	Group- III (n=100)	F value	Sig.
γ GT(U/L)	**44.71±42**	**42.73±37.25**	**19.73±9.964**	**17.729**	**0.000**
Total Cholesterol (mg/dl)	159.26±46.460	152.27±40.669	163.56±32.293	1.912	0.150
Triglycerides (mg/dl)	149.89±117.935	144.53±88.243	102.85±40.904	8.443	0.000
HDL (mg/dl)	36.77±14.361	36.96±15.527	42.83±11.167	6.086	0.003
LDL (mg/dl)	112.21±37.047	103.02±39.583	114.77±29.551	2.821	0.001
Age (in years)	51.99±8.266	54.23±7.642	44.44±9.482	35.004	0.000

In our present study, a significant ($p<0.001$) increase in serum gamma glutamyl transferase levels was observed between cases (group-I & group-II) and control (group-III). No significant increase in the enzyme levels was observed between cases (cardiovascular disease with and without diabetes).

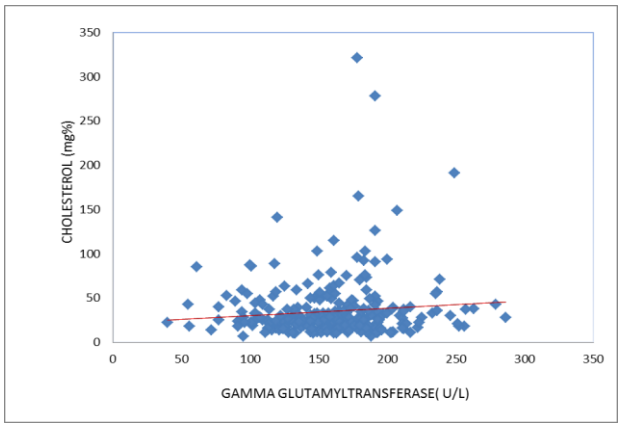

Figure. 3: Correlation between serum Gamma glutamyl transferase & Cholesterol.

A weak correlation between serum Gamma glutamyl transferase & Cholesterol.

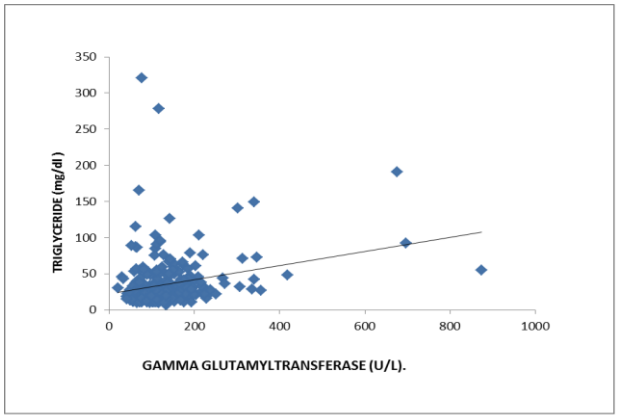

Figure. 4: Correlation between serum Gamma glutamyl transferase & Triglycerides.

A weak correlation between serum Gamma glutamyl transferase & Triglyceride

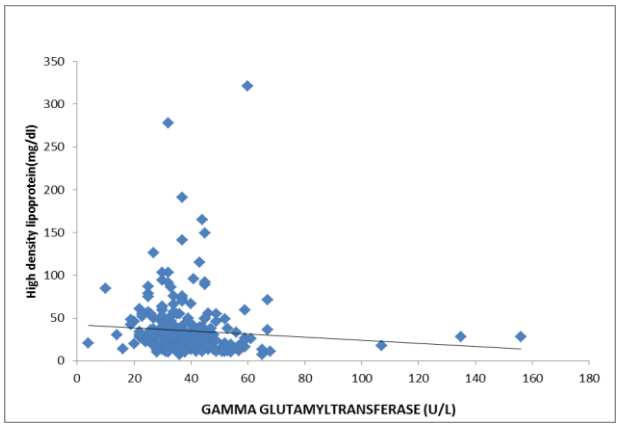

Figure. 5: Correlation between serum Gamma glutamyl transferase & High density lipoprotein.

A negative correlation between serum Gamma glutamyl transferase & High density lipoprotein.

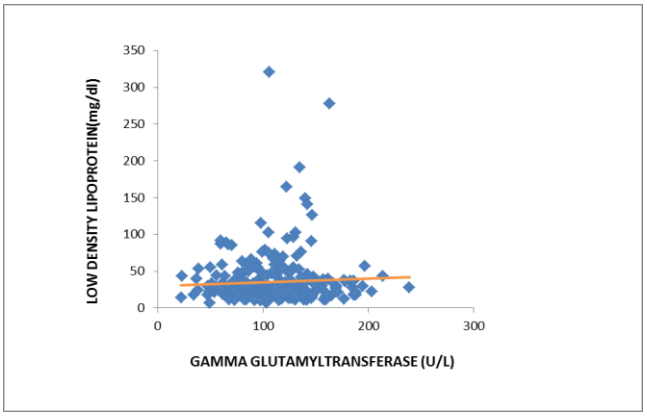

Figure. 6: Correlation between serum Gamma glutamyl transferase & Low density lipoprotein.

A weak correlation between serum Gamma glutamyl transferase & Low density lipoproteins.

DISCUSSION

In our present study, a significant ($p<0.001$) increase in serum gamma glutamyl transferase levels was observed between cases and control. No significant increase in the enzyme levels was observed between cases (cardiovascular disease with diabetes and without diabetes).

The possible link between γ GT and cardiovascular diseases is association between γ GT and (both classical and novel) cardiovascular risk factors (oxidative stress and direct involument of γ GT in atheromatous plaque formation).[18] Gamma glutamyl transferase is present in blood and on the surface of most cell types, where it catalyzes the cleavage of extracellular, glutathione to a -glutamyl moiety and cysteinyl-glycine (Cys-Gly). The latter triggers iron-dependent oxidation of low-density lipoprotein (LDL). In human atherosclerotic plaques, catalytically active γ GT co localizes with oxidized LDLs (oxLDLs) and CD68_ foam cells, suggesting that the pro-oxidative action of Cys-Gly may causally link γ GT activity with CVD risk.[10,17]

Current epidemiological and experimental studies shown that elevated serum γ GT is a sensitive marker for oxidative stress.[11]

A number of previous studies have confirmed that traditional cardiovascular risk factors were similar determines of the risk of cardiovascular disease in people with diabetes and without diabetes.[16] In a Finnish study of 28,838 men and women (3.9% with diabetes), effects sizes for the association between γ GT and coronary heart disease risk across percentiles of γ GT were apparently higher in participants with diabetes than in the general population.[18]

In our present study we found a good significant correlation between the γ GT with total cholesterol. A weak correlation was obtained between γ GT and triglycerides, low density lipoprotens and negatively correlated with high density lipoprotens.

Ruttmann et al showed that γ glutamyl transferse was significantly associated with established risk factors such as cholesterol, triglycerides and negatively correlated with high density lipoproteins.[13]

CONCLUSION

Higher Gamma glutamyl transferase levels are associated to cardiovascular disease in people with and without diabetes. There is increased concentration of γ GT in serum of people with CVD compared to healthy individuals.

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REFERENCES

1. Massimo bellini, Emanuele tumino et al. Serum γ – Glutamyl-Transpeptidase Isoforms in Alcoholic Liver Disease. Alcohol & Alcoholism, 1997; 32(3): 259-266.
2. Owen w. griffith, Richard j. bridges et al. Transport of γ- Glutamyl Amino Acids: Role of Glutathione and γ -Glutamyl Transpeptidase. Proc. Natl.Acad.Sci. USA, 1979; 76(12): 6319-6322.
3. Elemer Nemesanszky and John A.Lott et al. Gamma glutamyl Transferase & Its Isoenzyme: Progresses and Problems. CLIN.CHEM, 1985; 31(6): 797-803.
4. Lucla Sacchetti , Gluseppe Castaldo et al. The Gamma Glutamyl Transferase Isoenzyme Pattern in serum as a single discriminating between hepatobiliary diseases, including neoplasias. CLIN.CHEM, 1988; 34(2): 352-355.
5. Jeslie M. shaw, jack w. London et al. Isolation of gamma glutamyl transferase from human liver , and comparision with enzyme from human kidney. CLIN.CHEM, 1978; 24(6): 905-915.
6. Phlllp R.Wenham, David B. Horn et al. Muliple forms of gamma glutamyl transferase – A clinical study. CLIN.CHEM, 1985; 31(4): 569-573.
7. Yves Artur, Maria Wellman-Bednawska et al. Associations between serum Gamma glutamyl transferase and Apo lipoproteins –Relationships with hepatobiliary diseases. CLIN.CHEM, 1984; 30(8): 1318-1321.
8. Michele Emdin, Claudio Passiono et al. Gamma – glutamyltransferase as a cardiovascular risk factor. European Heart Journal, 2006; 27: 2145-2146.
9. Dr Enouiu at al. Study of the pro-oxidant and antioxidant properties of glutathione on proteins and lipids oxidative damage: the relevance to atherogenesis, 1998.
10. Michele Emdin, Alfonso Pomplla et al. Gamma glutamyl transferase, Atherosclerosis, and Cardiovascular disease: Triggering oxidative stress within the plaque. J. Am. Heart. Assoc, 2005; 112: 2078-2080.
11. Duk-hee lee, Rune blomhoff et al. Is Serrum Gamma Glutamyltransferase a Marker of oxidative Stress? Free Radical Reasearch, 2004; 38(6): 535-539.
12. Textbook of clinical biochemistry by TIETZ Fourth Edition, 612-613.
13. Elfriede Ruttmann, Larry J. Brant et al. Gamma glutamyltransfersae as a Risk Factor for Cardiovascular Disease Mortality. J. Am. Heart Assoc, 2005; 112(14): 2130-2137.
14. Okan Turgut, lzzet Tandogan at al. Gamma glutamyltransferase to determine cardiovascular Risk: Shifting the Paradigam Forward.J Atherosclerosis, 2011; 18(3): 177-181.
15. Asia Pacific Cohort Studies Collaboration. The effects of diabetes on the risks of major cardiovascular diseases and death in the asia pacific region. Diabetes care, 2003; 26: 360-366.
16. Duk Hee Lee, Karri Silventoinen et al. serum gamma glutamyl transferase predicts non-fatal myocatdial infarction and coronary heart disease among 28 838 middle aged men and women. European Heart Journal, 2006; 27: 2170-2176.

17. Dagmar Drogam, Cornelia Weikert et al. Plasma gamma glutamyl transferase, Cysteinyl-Glycine, and oxidized low-density lipoprotein: A pathway Associated with Myocardial infarction risk ?. J. Am. Heart Assoc, 2010; 30: 2053-2058.
18. Andre Pascal kengne, Sebastien Czernichow et al. Gamma glutamyl transferase and risk of cardiovascular disease mortality in people with and without diabetes: pooling of three british health surveys. J. Hepatology, 2012; 30: 30-30.