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Serum Gamma Glutamyl Transferase Levels in Association with Lipids and Lipoproteins in Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Serum gamma glutamyl transferase is widely used as a marker for alcohol induced liver disease. Recently it has gained importance due to its role in type2 diabetes mellitus. A raised serum gamma glutamyl transferase level indicates hepatic steatosis and visceral fat deposition, leading to insulin resistance and diabetes. In the present study we examined the association between serum gamma glutamyl transferase levels with lipids and lipoproteins in diabetes mellitus.

Methodology: The study was carried out on 50 subjects with type2 diabetes mellitus and compared with 50 ages and sex matched healthy controls attending outpatient department of General Medicine, Narayana medical college, Nellore. Serum gamma glutamyl transferase was measured by calorimetric kinetic assay. Fasting blood sugar was measured by glucose oxidase method using automated analyzer. Serum triglycerides, total cholesterol and high density lipoprotein are measured by standard enzymatic procedures and low density lipoprotein by friedwald equation.

Results: Serum gamma glutamyl transferase levels in diabetic cases were significantly elevated compared to normal healthy controls [$p < 0.001$]. There was a positive correlation between gamma glutamyl transferase, lipids and low density lipoprotein and inverse correlation with high density lipoprotein ($r = -0.298$).

Conclusion: Our results suggest a possible role of gamma glutamyl transferase in the pathophysiology and progression of type2 diabetes mellitus.

INTRODUCTION

There is a growing body of evidence that serum gamma glutamyl transferase (GGT) is a predictor of type2 diabetes mellitus (T2DM) independent of factors associated with excess alcohol consumption and liver disease.¹ Serum GGT is a cell surface protein

and plays a key role in glutathione metabolism. Glutathione is the main intracellular thiol antioxidant agent in mammalian cells². Serum GGT activity is affected by both genetic and environmental factors³. Various tissues produce GGT which differ in their sugar moieties. Most of the serum GGT is derived from liver tissue and binds to carriers like lipopro-

teins and albumin.^{4,5} A numbers of recent studies have suggested that abnormal hepatocellular function is associated with obesity, insulin resistance, and type 2 diabetes^{6,7}. The loss of a direct effect of insulin to suppress hepatic glucose production and glycogenolysis in the liver causes an increase in hepatic glucose production.⁸ Raised liver enzymes reflect chronic ectopic fat deposition⁹. Serum GGT may be a simple and reliable marker of visceral and hepatic fat deposition and hepatic steatosis which can lead to hepatic insulin resistance and long term hepatic insulin resistance may lead to T2DM¹⁰. In this contest the study was under taken to study the serum GGT levels and its possible associations with triglycerides, total cholesterol ,low density lipoprotein(LDL) and high density lipoprotein (HDL) in T2DM.

MATERIALS AND METHODS

The study was carried out on 50 subjects with T2DM and 50 age and sex matched healthy controls recruited from General Medicine outpatient department, of Narayana medical college and hospital , Nellore, A.P.All the subjects underwent a complete medical evaluation by a physician. Informed and written consent was obtained from all subjects. Both male and female subjects between 18-65 years of age were included in the study. Pregnant, lactating women, alcoholics, patients with liver disease and

patients on insulin and other drugs which might influence lipid and glucose levels and liver enzymes were excluded from the study.

Biochemical parameters: Fasting blood sugar is measured by glucose oxidase method using automated chemistry (Humaster-300, GMBH, Germany) analyzer using Human kits. Serum triglycerides, total cholesterol and HDL cholesterol are analyzed by standard enzymatic procedures and LDL cholesterol by friedwald equation. Serum GGT is measured by calorimetric kinetic assay.

Statistical analysis is performed using SPSS software (16.0). *P-value* < 0.05 is considered as statistically significant.

RESULTS

All subjects are grouped into normal and diabetic cases. Table 1: Demonstrates the mean \pm SD values of the main characteristics of diabetic cases and controls. Serum GGT was significantly elevated in diabetic cases [mean \pm SD 67.20 \pm 22.97] compared to normal healthy controls [mean \pm SD 24.71 \pm 7.91] p-value <0.001. Subjects with diabetes had significantly elevated levels of fasting blood sugar, total cholesterol, triglycerides and LDL cholesterol but HDL cholesterol is significantly decreased in diabetics compared to healthy controls.

Table 1: Main characteristics of diabetic cases and controls

Biochemical parameters	Cases (n=50)	Controls (n=50)	p-value
GGT (IU/L)	67.20 \pm 22.97	24.71 \pm 7.91	<0.001
Fasting blood sugar (mg/dl)	160.9 \pm 33.23	88.88 \pm 6.27	<0.001
Cholesterol (mg/dl)	408.68 \pm 84.53	157.02 \pm 27.18	<0.001
Triacyl glycerol (mg/dl)	247.76 \pm 127.25	85.78 \pm 31.23	<0.001
HDL(mg/dl)	30.42 \pm 5.24	79.94 \pm 15.35	<0.001
LDL(mg/dl)	156 \pm 12.52	93.72 \pm 19.99	<0.001

Data are expressed as mean+ standard deviation. P <0.05 were significant.

Correlation between serum GGT and biochemical characteristics in subjects with and without diabetes: The analysis for correlation of serum GGT with biochemical characteristics of the subjects indicated a positive correlation between GGT and lipids and LDL lipoprotein but inverse correlation to HDL lipoprotein($r = -0.298$).

Fig 1. Demonstrates the correlation between serum GGT and fasting blood sugar. There is a significant positive correlation between serum GGT and fasting blood sugar in subjects with diabetes ($r=0.35$) Fig 2. Shows a strong positive correlation between serum GGT and triglycerides in subjects with T2DM ($r=0.112$).

Figure 3. shows a strong negative association between serum GGT and HDL in subjects with T2DM ($r=-0.298$).

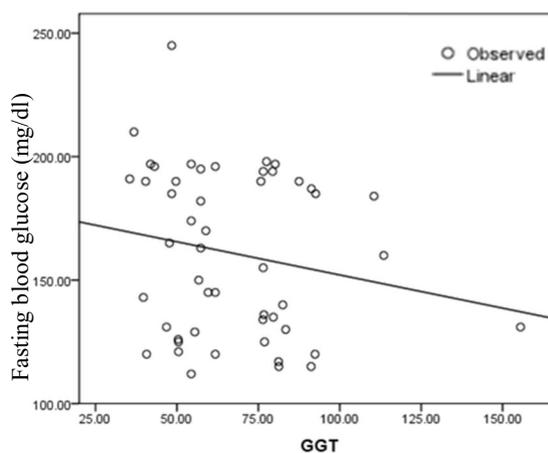


Figure 1: Association between serum GGT and fasting blood glucose in subjects with T2DM

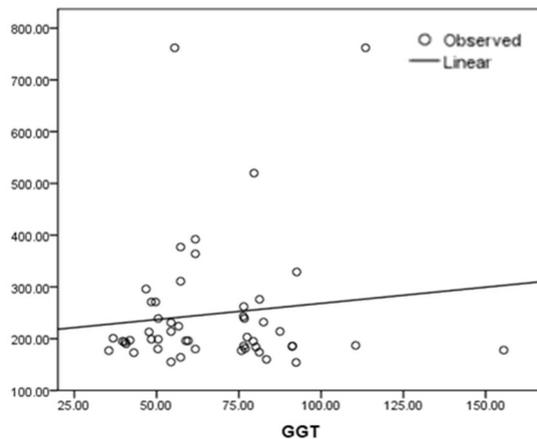


Figure 2: Association between serum GGT and triglycerides in subjects with T2DM

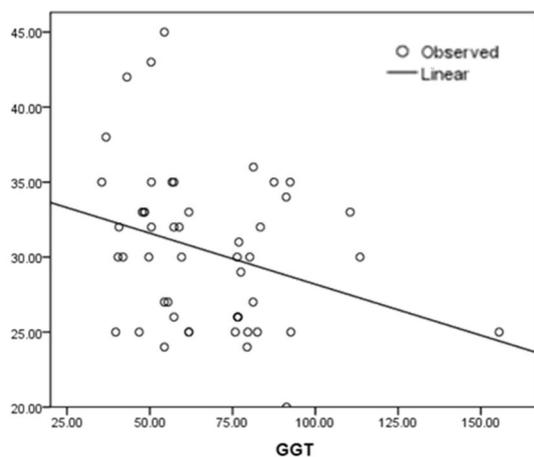


Figure 3: Association between serum GGT and HDL lipoprotein in subjects with diabetes

DISCUSSION

GGT has been known mainly as a marker of alcohol consumption and liver diseases.¹¹ Serum GGT within normal ranges has been reported to be associated with risk factors of cardiovascular diseases and components of metabolic syndrome.¹² many studies hypothesized to link GGT and diabetes¹³. This study was done to estimate serum GGT levels and analyze its association with blood glucose, lipids and lipoproteins in subjects with diabetes and compared with age and sex matched healthy controls. Studies in humans and animal models have indicated that serum GGT levels were significantly elevated in diabetes¹⁴. In our study we observed that serum GGT levels were significantly elevated in subjects with diabetes compared to normal controls [$p < 0.0001$]. Similar studies on the relationship between liver enzymes and diabetes in both sexes in general population have found higher levels of serum GGT in diabetes. Our results demonstrated that increased serum GGT lev-

els were associated with increased levels of glucose in diabetes. Recent studies on diabetic middle aged men and women have shown increased levels of GGT when compared with liver enzymes, alcohol consumption, and body mass index. Serum GGT was also correlated with insulin resistance-markers, waist-circumference, triglycerides, fasting plasma glucose, HbA1c, systolic and diastolic blood pressure. In parallel to this our study also observed association of serum GGT with blood glucose, lipids and lipoproteins; however in our study we have excluded subjects with a history of alcoholism. Our results are consistent with those of previous studies and indicate that elevated serum GGT is associated with an increased risk of diabetes. One explanation for our findings is that the elevation of serum GGT could be an expression of excess fat deposited in liver, which is regarded as a feature of the insulin resistance syndrome. We observed a significant correlation between GGT, lipids, lipoproteins and blood sugar levels. In our study slightly positive association between serum GGT and fasting blood sugar ($r=0.08$) was observed. Previous study on patients with diabetes after a three year follow-up period had showed that raised GGT was correlated with central obesity, increased fasting glucose, triglycerides, and blood pressure in both sexes. In subjects with T2DM a strong positive association between serum GGT and triglycerides ($r=0.112$), serum GGT and LDL lipoprotein ($r=0.05$), serum GGT and cholesterol ($r=0.027$) was observed. We also observed a strong negative association between serum GGT and HDL lipoprotein ($r=-0.298$). Association of GGT with lipids and lipoproteins could be explained by the antioxidant property of GGT.^{15, 16} Elevated GGT could reflect subclinical inflammation, which represents the underlying oxidative stress. GGT levels are closely related to oxidative stress because cellular GGT has a central role in glutathione homeostasis by initiating the breakdown of extracellular glutathione, a critical antioxidant defense for the cell.^{17, 18}

CONCLUSION

Our study shows that serum GGT levels are significantly associated with T2DM, serum triglycerides, total cholesterol and LDL lipoprotein and inversely correlated to HDL lipoprotein accelerating the progression of T2DM related cardiovascular risk. Our study high lightens the role of serum GGT in developing T2DM and can be used as a marker to diagnose T2DM.

Conflicts of interest: none

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