

Correlation between Lipid parameters and gamma glutamyl transferase in type 2 diabetes mellitus

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Abstract

Background: Serum gamma glutamyl transferase (GGT) which is a simple and reliable marker of liver fat deposition leads to hepatic insulin resistance and long term hepatic insulin resistance may lead to type 2 diabetes mellitus (DM). In this context, the present study was under taken to study the serum GGT levels and its possible associations with serum triglyceride (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C) and high density lipoprotein cholesterol (HDL-D) in type 2 DM.

Material and methods: The study was conducted at HSK hospital, Bagalkot from Jan 2016 to Jun 2016. The diagnosis of DM was based on WHO criteria. Sixty subjects participated in each group (DM and Controls). Fasting sample was collected and fasting blood sugar (FBS), HbA1c, urea, creatinine, GGT, and lipid parameters were estimated. Data was analysed using SPSS software. Student's t test and Pearson correlation was applied for quantitative data.

Results: The serum levels of FBS, PPBS, HbA1c, creatinine, urea, TG and VLDL were raised significantly in cases compared to controls, whereas serum HDL was significantly decreased in cases compared to controls (p=0.000). There was statistically significant (p=0.001) positive correlation between the TGL and GGT. HDL-C was significantly, negatively correlated with GGT.

Conclusion: There was positive correlation between GGT and TG, TC, LDL-C and VLDL-C, only TGL was significant, and there was significant negative correlation between HDL and GGT. Hence serum GGT can be used as marker of cardiovascular diseases in type 2 DM patients.

Key words: Diabetes mellitus, Gamma Glutamyl transferase, Lipid profile

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Introduction

Diabetes mellitus (DM) is a major metabolic and non-communicable disease, its prevalence is increasing exponentially. World-wide, type 2 DM constitutes for about 90% of all the cases and is more in men than women^[1,2]. The prevalence of DM worldwide was 2.8% in 2000 and is estimated to rise to 4.4% in 2030. The total number of DM is projected to 592 million by 2035. India presently has more than 50 million diabetic patients, making India “the diabetes capital of the world”^[1,3,4].

Dyslipidemia is a one of the major risk factor for coronary heart disease^[5]. The variations of serum lipid profile from their normal levels can predict the coronary artery disease^[6,7]. Hyperglycaemia and atherosclerosis are related in type-2 DM^[8]. Patients with type-2 DM have increased risk of cardiovascular disease associated with atherogenic dyslipidaemia^[9].

Persistent hyperglycaemia causes glycosylation of proteins, mainly collagen cross linking and matrix proteins of arterial wall. This eventually leads to endothelial cell dysfunction and further to atherosclerosis^[10]. The cardiovascular disease is a cause of morbidity and mortality, commonly presents as an abnormally high level of triglycerides (TG), a high proportion of small dense low density lipoprotein cholesterol (LDL-C), low high density lipoprotein cholesterol (HDL-C), and postprandial lipemia^[11,12,13]. This pattern of lipid profile in DM type 2 is termed diabetic dyslipidemia^[14].

Gamma glutamyltransferase (GGT) catabolises extracellular glutathione^[15]. It is present, in the liver, bile duct, lungs, pancreas, brain, gall bladder, kidneys and the heart muscles. In the diseases of all these organs, there will be significant increase in serum GGT levels^[16,17]. The GGT levels can also be raised in patients who are for a long duration on drugs like phenytoin, barbiturates, amiodarone, tomoxifen and steroids and also who have undergone biliopancreatic surgeries^[18]. Although GGT is produced in all tissues, differences in the sugar moieties allow that only the liver GGT is detectable in serum^[19]. The studies have demonstrated that abnormal hepatocellular function is associated with obesity, insulin resistance, and type 2 diabetes^[20,21,22]. 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^[20,23].

Raised liver enzymes reflect chronic ectopic fat deposition^[24]. Serum GGT may be a simple and reliable marker of hepatic fat deposition and hepatic steatosis which can lead to hepatic insulin resistance and long term hepatic insulin resistance may lead to type 2 DM^[25]. Only few studies have compared the serum GGT with lipid profile, hence, in this context, the present study was under taken to study the serum GGT levels and its possible associations with TG, TC, LDL-C, and HDL-C in type 2 DM.

Material and Methods

The study was conducted at HSK hospital, Bagalkot from Jan 2016 to Jun 2016. The study was approved by institutional ethics committee. Informed consent was obtained from all the participants. The diagnosis of DM was based on WHO criteria. Sixty subjects participated in each group (DM and controls). Alcoholics, smokers, patients with diabetic complications, chronic liver diseases, HIV, severe anemia, CRF, other systemic conditions and patients on iron preparations, lipid lowering drugs were excluded. Pregnant women were also excluded from the study. Under aseptic precautions 5 ml of fasting sample was collected and following biochemical parameters were estimated. FBS and PPBS were estimated by GOD-POD method, serum urea by DAM method, creatinine by Jaffe's method. TG was measured by GOP-PAP method^[25,26]. TC and HDL-C were measured by

CHOD-PAP method^[25-29]. Kits were supplied by Biosystems Pvt Ltd, GGT estimated by IFCC method kit supplied by Transasia (Normal 7-50 IU/L), Biosystems A 25 fully automated instrument was used for estimation of above mentioned parameters. LDL-C and VLDL-C were calculated using Fried Wald's formula^[30,31]. HbA1c was measured by using Nycocard reader. Post prandial blood sugar (PPBS) was also estimated.

Statistical analysis

Data was tabulated in excel, analysed using SPSS window version; SPSS, 11.5 Inc, Chicago IL. Student's t test and Pearson correlation was applied for quantitative data. All the values were expressed in mean±SD.

Results

In the present study, the mean age of cases and controls was 46.3±10.0 and 49.4±12.7 years respectively, there was no statistically difference between two groups (p=0.429).

The serum levels of FBS, PPBS, HbA1c, creatinine, urea, TG and VLDL-C were raised significantly in cases compared to controls, whereas serum HDL-C was significantly decreased in cases compared to controls (p=0.000). The serum concentration of TC and LDL-C was increased in cases compared to controls, but it was not statistically significant (p value was 0.386 and 0.294 respectively) (Table 1).

Table 1: Comparison of biochemical parameters between cases and control

Parameter	Controls	Cases	p value
FBS mg/dl	86.1±10.3	171.7±38.2	0.000
PPBS mg/dl	115.0±17.6	274.7±78.4	0.000
GGT mg/dl	19.0±5.1	42.1±15.4	0.000
HbA1c %	5.1±0.7	8.0±1.2	0.000
Urea mg/dl	18.8±5.7	32.7±9.3	0.000
Creatinine mg/dl	0.9±0.1	1.2±0.2	0.000
TG mg/dl	116.3±31.7	153.1±33.3	0.002
TC mg/dl	183.8±36.0	194.5±37.5	0.386
HDL-C mg/dl	49.7±4.7	33.4±3.7	0.000
VLDL-C mg/dl	23.2±6.3	30.2±6.5	0.002
LDL-C mg/dl	110.8±32.6	122.4±33.6	0.294

FBS: Fasting blood sugar

PPBS: Post prandial blood sugar

GGT: Gamma glutamy transferase

TG: Triglyceride

TC: Total cholesterol

HDL-C High density lipoprotein cholesterol

VLDL-C Very low density lipoprotein cholesterol

LDL-C: Low density lipoprotein cholesterol

Table 2: Correlation of GGT with lipid parameters in type 2 DM

Parameters	GGT (r value)	p
TG	0.56	0.001
TC	0.34	0.15
HDL-C	-0.45	0.04
VLDL-C	0.24	0.34
LDL-C	0.29	0.22

GGT: Gamma glutamy transferase

TG: Triglyceride

TC: Total cholesterol

HDL-C High density lipoprotein cholesterol

VLDL-C Very low density lipoprotein cholesterol

LDL-C: Low density lipoprotein cholesterol

There was statistically significant ($p=0.001$) positive correlation between TG and GGT the correlation coefficient was 0.56. There was positive correlation between TC, VLDL-C and LDL-C, but it was not statistically significant. HDL-C was significantly, negatively correlated with GGT.

Discussion

In the present study, serum GGT was significantly higher in DM patients compared to age and sex matched healthy control group, this finding is in accordance with previous studies^[32]. Studies in humans and animal models have showed that serum GGT levels were significantly elevated in diabetes^[33].

As we searched the literature, we could find only one original research article on DM that compared lipoproteins and GGT. But studies in other conditions like coronary artery disease, metabolic syndrome and obesity are available.

Study by Emirogulu MY et al,^[34] on acute coronary syndrome found no correlation between GGT and Lipid profiles ($r=0.166$ $p=0.03$ for GGT and TC, $r=0.12$ $p=0.043$ for GGT and LDL-C) but Desai G M et al^[6] showed TG, TC and LDL were positively correlated with GGT and only TG showed significant correlation($r=0.58$, $p=0.04$). HDL was negatively correlated with GGT ($r=-0.44$, $p=-0.30$). The current study also showed similar results in type 2 DM.

The study by Khan S N et al^[35] on metabolic syndrome subjects showed TG was significantly correlated with GGT ($r=0.91$, $p=0.02$) and HDL showed significant negative correlation with GGT($r=-0.192$, $p=0.018$), but study on cardiac syndrome X in Turkey by Demir B et al^[36] showed that TC and LDL were negatively correlated with GGT and were not statistically significant, HDL and TG were positively correlated with GGT but only TGL was statistically significant correlation($r=0.293$, $p=0.039$). P. Josephine Latha et al^[37] in their study on obese individuals showed that there was positive correlation between GGT and TC ($r=0.72$), TGL ($r=0.662$), LDL ($r=0.669$), VLDL ($r=0.662$) which were highly significant positively. HDL was negatively correlated($r=-0.773$) with GGT and was found to be highly significant.

Rajarajeswari D et al^[20] observed a significant correlation between GGT and lipoprotein levels. Positive association between serum GGT and triglycerides ($r = 0.112$), serum GGT and LDL lipoprotein ($r = 0.05$), serum GGT and cholesterol($r=0.027$) were observed. In the current study, it was found that TGL was positively correlated with GGT, but other lipoproteins were not significantly correlated with GGT. We also observed a significant negative correlation between serum GGT and HDL lipoprotein ($r = -0.298$), which was similar to the results of the study by Rajarajeswari D et al.

Lipid triad^[38] in DM comprises of hypertriglyceridemia, low levels of HDL-C and the appearance of small, dense, LDL (sdLDL)^[39,40]. The present study also revealed similar results. Many studies demonstrated that in type 2 DM, there is increased reactive oxygen species production and induce higher oxidative damage in the circulation and also have reduced antioxidant defenses mechanisms^[41].

Association of GGT with lipids and lipoproteins could be explained by the antioxidant property of GGT^[21,42]. 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 defence for the cell^[43,44].

The limitations of the present study were small sample size and diet history was not considered in detail. Hence further large sample size with detailed diet history is required.

In conclusion in the current study there was a positive correlation between GGT and TG, TC, LDL and VLDL, however only the correlation between GGT and TG was significant, and there was significant negative correlation between HDL and GGT. Hence, serum GGT can be used as a marker of cardiovascular disease in type 2 DM patients.

References

1. Nagaraj S, Kiran SS, Gandham R, Silvia WDCR, Nagaraja MR, Nasar AS, et al. Study of prevalence of

- non-alcoholic fatty liver disease in type 2 diabetes mellitus patients and variations in liver function tests, lipid profile and mean platelet volume in patients with fatty liver in comparison with patients without fatty liver. *Int J Res Med Sci* 2016;4:871-6.
- Agarwal J. Prevalence of elevated hepatic enzymes among north Indian patients with type 2 diabetes mellitus. *Santosh University Journal of Health Sciences* 2015;1(1):3-6.
 - King GL. The role of inflammatory cytokines in the diabetes and its complications. *J Periodontol* 2008;(1):1527-34.
 - Kumar KPS, Bhowmik D, Srivastava S, Paswan S, Dutta AS. Diabetes epidemic in India-A comprehensive review of clinical features, management and remedies. *The pharma innovation* 2012;2:17-33.
 - American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2005;28:37-42.
 - Desai GM, Raghunandana R, Akka KK, Bandi BC. A Cross Sectional Study of Serum Gamma-glutamyl Transferase Activity with reference to Atherogenic Lipid Indices in Patients with Ischemic Heart Disease. *J of Evolution of Med and Dent Sci* 2014;3(10):2655-62.
 - Sharma R, Mahajan M, Ravikant. Comparative account of serum lipids, lipoproteins and apolipoprotein-B in patients of coronary heart disease. *IJCB* 2004;19(1):10-13.
 - Devrajani BR., Shah SZ, Soomro AA, Devrajani T. Type 2 diabetes mellitus: A risk factor for Helicobacter pylori infection: A hospital based case-control study. *Int J Diabetes Dev Ctries* 2010;30(1):22-6.
 - Roberto T, Dodesini AR, Lepore G. Lipid and Renal disease. *J Am Soc Nephrol* 2006;17:S145-7.
 - Krishna P, Roopakala, Prasanna KM. Dyslipidemia in type 1 diabetes mellitus in the young. *Int J Diab Dev Ctries*, 2005;25(4):110-12.
 - Haffner SM. Lipoprotein disorders associated with type 2 diabetes mellitus and insulin resistance. *Am J Cardiol* 2002;90:55-61.
 - Goldberg IJ. Clinical review 124: Diabetic dyslipidemia: causes and consequences. *J Clin Endocrinol Metab* 2001;86:965-71.
 - Ginsberg HN. REVIEW: Efficacy and mechanisms of action of statins in the treatment of diabetic dyslipidemia. *J Clin Endocrinol Metab* 2006;91:383-92.
 - Rosalki SB, Tarlow D, Rau D. Plasma gamma-glutamyltransferase elevation in patients receiving enzyme-inducing drugs. *Lancet* 1971 August;2(7720):376-77.
 - Whitfield JB. Gamma-glutamyl transferase. *Crit Rev Clin Lab Sci* 2001;38:263-355.
 - Doi Y, Kubo M, Yonemoto K, Ninomiya T, Iwase M, Tanizaki Y, et al. Liver enzymes as a predictor for incident diabetes in a Japanese population: the Hisayama study. *Obesity (Silver Spring)* 2007;15:1841-50.
 - Balogun WO, Adeleye JO, Akinlade KS, Adedapo KS, Kutu M. Frequent occurrence of high gamma-glutamyl transferase and alanine amino transferase among Nigerian patients with type 2 diabetes. *Afr J Med Med Sci* 2008;37:177-83.
 - Kang YH, Min HK, Son SM, Kim IJ, Kim YK. The association of serum gamma glutamyltransferase with components of the metabolic syndrome in the Korean adults. *Diabetes Res Clin Pract* 2007;77:306-13.
 - Huseby NE. Multiple forms of serum gamma-glutamyltransferase. Association of the enzyme with lipoproteins. *Clin Chim Acta* 1982;124:103-12.
 - Rajarajeswari D, Sharmila Krishna T, Prasad Naidu M, Naidu JN. Serum gamma glutamyl transferase levels in association with lipids and lipoproteins in type2 diabetes mellitus. *Int J Res Med Sci* 2014;2:838-41.
 - Sabanayagam C, Shankar A, Li J, Pollard, Ducatman A. Serum gamma-glutamyl transferase level and diabetes mellitus among US adults. *Eur J Epidemiol.* 2009;24(7):369-73.
 - Lim JS, Lee DH, Park JY, Jin, Jacobs. A strong interaction between serum-g-glutamyl transferase and obesity on the risk of prevalent type 2 diabetes: results from the third national health and nutrition examination survey. *Clin Chem* 2007;53(6):1092-8.
 - Duckworth, William C, Hamel FG, Peavy DE. Hepatic metabolism of insulin. *Am J Med* 1988;85.5:71-6.
 - Kasapoglu B, Turkay C, Bayram Y, Koca C. Role of GGT in diagnosis of metabolic syndrome: a clinic-based cross-sectional survey. *Indian J Med Res* 2010;132(1):56-61.
 - Lippi G, Targher G, Montagnana M, Salvagno GL, Guidi GC. Relationship between gamma-glutamyl transferase, lipids and lipoprotein(a) in the general population. *Clin Chim Acta* 2007;384:163-6.
 - Buccolo G, David H. Quantitative determination of serum triglycerides by the use of enzymes. *Clinical Chemistry* 1973;19:476-82.
 - Werner M, Gabrieison DG, Eastman J. Ultramicro Determination of Serum Triglycerides by Bioluminescent Assay. *Clinical Chemistry* 1981;27(2):268- 71.
 - Allen JK, Hensley WJ, Nicholls AV, Whitfield JB. An enzymic and centrifugal method for estimating high-density lipoprotein cholesterol. *Clin Chem* 1979 Feb;25(2):325-7.
 - Lopes-Virella MF, Stone P, Ellis S, Colwell JA. Cholesterol determination in high-density lipoproteins separated by three different methods. *Clin Chem* 1977 May;23(5):882-4.
 - Miller NE, Thelle DS, Forde OH, Mjos OD. The Tromsø heart-study. High-density lipoprotein and coronary heart-disease: a prospective case-control study. *Lancet* 1977 May 7;1(8019):965-8.
 - Friedwald WT, Levy RI, Fredrickson DS. Estimation of the Concentration of Low-Density Lipoprotein Cholesterol in Plasma, Without Use of the Preparative Ultracentrifuge. *Clin Chem* 1972;18:499-502.
 - Koro CE, Bowlin SJ, Bourgeois N, Fedder DO. Glycemic control from 1988 to 2000 among US adults diagnosed with type 2 diabetes a preliminary report. *Diabetes Care* 2004;27(1):17-20.
 - Duk-Hee L, Gross MD, Jacobs DR. Association of serum carotenoids and tocopherols with γ -glutamyltransferase: the cardiovascular risk development in young adults (CARDIA) Study. *Clin Chem* 2004;50.3:582-8.
 - Emiroglu MY, Esen OB, Bulut M, Karapinar H, Kaya Z, Akcakoyun M, et al. Gamma glutamyltransferase levels and its association with high sensitive C-reactive protein in patients with acute coronary syndromes. *N Am J Med Sci* 2010 Jul;2(7):306-310.
 - Khan SN, Kodliwadmath MV. GGT as A Marker for Assessment of Metabolic Syndrome. *RJPBCS Jan-Feb* 2015;6(1):840-5.
 - Demir B, Temizhan A, Keskin G, Baser K, Turak O, Cay S. Comparison of serum gamma-glutamyltransferase levels between patients with cardiac syndrome X and healthy asymptomatic individuals. *Kardiologia Polska* 2012;70(1):31-7.
 - Latha PJ, Ganesan S. Correlation of Serum Gamma Glutamyl Transferase with Atherogenic Dyslipidemia in

- Obese Individuals. *Sch J App Med. Sci* 2015;3(1F):387-391.
38. Grundy SM. Hypertriglyceridemia, atherogenic dyslipidemia, and the metabolic syndrome. *Am J Cardiol* 1998;81:18B-25B.
 39. Taskinen MR. Diabetic dyslipidaemia: from basic research to clinical practice. *Diabetologia* 2003;46:733-49.
 40. Ginsberg HN, Zhang YL, Hernandez-Ono A. Metabolic syndrome: focus on dyslipidemia. *Obesity (Silver Spring)* 2006; 14 Suppl 1:41S-9S.
 41. Tangvarasittichai S. Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus. *World J Diabetes* 2015;6(3):456-80.
 42. Lee DH, Blomhoff R, Jacobs Jr DR. Is serum gamma glutamyl transferase a marker of oxidative stress? *Free Radic Res* 2004;38(6):535-9.
 43. Azhar I, Iftikhar U, Ali FA, Memon S, Zuberi N. Comparison of gamma glutamyl transferase in normal and in type 2 diabetics. *J Pak Med Assoc* 2010;60(11):945-8.
 44. Targher G, Bertolini L, Poli F, Rodella S, Scala L, Tessari R, et al. Non-alcoholic fatty liver disease and risk of future cardiovascular events among type 2 diabetic patients. *Diabetes* 2005;54(12):3541-6.