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Original Research Article

A Study on Serum Gamma Glutamyl Transferase Level in Metabolic Syndrome Patients in Tertiary Care Hospital

Sonya R.[1], Sobana D.[2], Niranjini R.[3]

[1]Assistant Professor, Department of Biochemistry, Govt. Kanyakumari Medical College, Tamil Nadu, India

[2]Assistant Professor, Department of Biochemistry, Govt. Thoothukudi Medical College, Tamil Nadu, India

[3]Assistant Professor, Department of Biochemistry, Govt. Thoothukudi Medical College, Tamil Nadu, India

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Corresponding Author: Dr. Sonya R.

Conflict of interest: Nil

Abstract:

Background: Metabolic Syndrome is a cluster of cardiovascular risk factors such as obesity, insulin resistance, dyslipidemia, impaired glucose tolerance and hypertension, leading to increased cardiovascular morbidity and mortality. Gamma-glutamyl transferase or gamma-glutamyl transpeptidase (GGT) is a cell surface enzyme expressed in the liver, kidney, cerebrovascular endothelium and extracellular catabolism of antioxidant glutathione. Elevated GGT levels is the reflection of high degree of oxidative stress, seen in central obesity. Also epidemiological studies have shown increased GGT with increased risk for cardiovascular morbidity and mortality. Hence GGT is found to be good predictor of susceptibility to cardiovascular risk factors like type II DM and hypertension.

Aims and Objectives: To estimate the level of serum GGT and its association with metabolic syndrome.

Materials and Methods: This is a case control study done in 50 cases of metabolic syndrome patients and 50 apparently healthy normal subjects in the age group between 18 – 60 years, attending Sree Mookambika Institute of Medical Sciences were included. Anthropometric measurements such as height, weight, waist circumference and BMI were measured for both the study and control groups and serum levels of fasting blood glucose, total cholesterol, triglycerides, HDL, GGT were measured using enzymatic methods. Patients with alcoholic liver disease, cholestasis, cardiac disease, known alcoholics, severely ill and on anti-epileptics were excluded.

Results: The serum levels of fasting blood glucose, total cholesterol, triglycerides and HDL and GGT showed statistically significant levels in metabolic syndrome patients when compared to controls with a p value < 0.05.

Conclusion: Metabolic syndrome is a significant public health problem even in low socio-economic states of India that needs to be tackled with proven strategies. Patients with metabolic syndrome have significantly elevated levels of GGT showing a significant association with metabolic syndrome, probably due to the presence of insulin resistance, oxidative stress. Thus serum GGT levels serves as a marker for assessing metabolic syndrome.

Keywords: Metabolic Syndrome, GGT, Insulin Resistance, Inflammation, Oxidative Stress.

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Introduction

Increased food intake, decreased physical activity with decreasing demands has led to the increased prevalence of obesity, increased blood pressure, diabetes and abnormal lipid profile. [1] The cluster of all the above features is called metabolic syndrome. Metabolic syndrome (MetS) is a cluster of cardiovascular risk factors such as obesity, insulin resistance, dyslipidemia, hypertension and abnormal glucose tolerance. [2]

Due to rapid transition in lifestyle and nutrition in urban areas, there is increased prevalence of metabolic syndrome in various countries of south Asia. [3] There is high prevalence of metabolic syndrome and associated risk factors in low socioeconomic population groups in urban slum areas. Metabolic syndrome is associated with a twofold risk of cardio vascular disease and fivefold risk of diabetes. Individuals with metabolic syndrome have 30%-40% probability of developing diabetes and cardio vascular disease within 20 years, depending on the number of components

present. [4] World Health Organization (WHO), National Cholesterol Education Program – Adult Treatment Panel III (NCEP-ATP III) and International Diabetes Federation (IDF) have proposed various guidelines for identifying metabolic syndrome clinically. [5]

It is associated with increased risk for diabetes mellitus and cardiovascular abnormalities. [6] According to International Diabetes Federation (IDF) criteria, metabolic syndrome is defined as increased waist circumference (>90cm in men and >80cm in women), raised triglycerides, low HDL, raised fasting plasma glucose and raised blood pressure (SBP>130mmHg and DBP>85mmHg). [7] Chronic inflammation plays a key role in the pathogenesis of insulin resistance and metabolic syndrome.

Gamma-glutamyl transferase or gamma-glutamyl transpeptidase (GGT) is a cell surface enzyme expressed in the liver, kidney, cerebrovascular endothelium and extracellular catabolism of antioxidant glutathione. [8] Various studies have shown that oxidative stress and chronic inflammation are involved in the pathogenesis of metabolic syndrome. Elevated GGT levels is the reflection of high degree of oxidative stress, seen in central obesity. [9] Also epidemiological studies have shown increased GGT with increased risk for cardiovascular morbidity and mortality. Hence GGT is found to be good predictor of susceptibility to cardiovascular risk factors like type II DM and hypertension. [10] It is hypothesized in various studies that elevation of liver enzymes, particularly GGT levels have predictive value in the diagnosis of metabolic syndrome. With increasing association of GGT with Metabolic Syndrome, we proposed this study especially in South Indian population, where there is a paucity of published reports.

Aims and Objectives: To estimate the level of Gamma Glutamyl Transferase level and its association with metabolic syndrome.

Material and Methods

A case control study was carried out between May 2017 and April 2018 in Sree Mookambika Institute of Medical Sciences, Kulasekharam. The study was conducted in the patients who attended outpatient clinic in the Department of Medicine. Fifty subjects of MetS were selected as cases based on modified ATP III criteria. Fifty healthy age and sex matched subjects were selected as controls.

Patients with cardiac diseases, severe renal diseases, cirrhosis, and acute liver disease due to viral cause, malignancy, pregnancy and alcohol consumption were excluded. After getting clearance from the Institutional Ethical Committee (SMIMS/IHEC No: 1/Protocol no: 14/2016), study population was selected and examined after informed consent. The height and weight of all the subjects in the study were recorded. The waist circumference (WC) was measured between the inferior margin of the ribs and the superior border of the iliac crest. [11] Body mass index (BMI), expressed as kg/m2 and was calculated by dividing weight (in kilograms) by the square of height (in meters) [12]. Blood pressure was recorded in sitting position in the left arm using mercury sphygmomanometer. Two readings were taken 5 minutes apart and the mean of the two were taken as blood pressure. [13]

Blood samples of 5 ml were collected after 8-12 hours of overnight fasting, after getting informed consent. Fasting plasma glucose (FPG), serum total cholesterol, serum triglycerides, high density lipoprotein and gamma glutamyl transferase levels were recorded. Plasma glucose was measured using glucose oxidase peroxidase method. Serum total cholesterol (TC), triglycerides (TGL) by standard enzymatic procedures, high density lipoprotein (HDL) by direct assay method. Gamma glutamyl transferase (GGT) measured using enzymatic kits by IFCC method. All the parameters were measured using Beckman Coulter AU480 clinical chemistry autoanalyser.

Statistical Analysis: Data collected were entered in the Microsoft excel sheet. Analysis was done using SPSS version 20. Percentage, mean and standard deviation were calculated. Independent sample "t" tests were done for comparison of variables in two groups. The p values of < 0.05 were considered as statistically significant.

Results

The present study was undertaken to analyze the level of serum GGT in metabolic syndrome patients with that of apparently healthy age matched controls. The study population was 100, of which 50 are metabolic syndrome patients and 50 are healthy age matched controls.

The age group of the study population was between 18 years to 60 years. The mean age for males in the control group is 50.23 + 6.70. The mean age for females in the control group is 51.36 + 7.58. The mean age for males in the study group is 53.12 + 6.52. The mean age for females in the study group is 50.80 + 6.23. Among the 50 persons in control group, 28 are males and 22 are females. Among the 50 subjects in the study group, males and females are equally distributed.

Table 1:

Group	Gender		Total
	Male	Female	
Control	28	22	50
Case	25	25	50
Total	53	47	100

The mean and SD of anthropometric measurements and lipid parameters among MetS and controls are compared in Table 2. It is shown that BMI, waist circumference, fasting blood glucose, serum triglycerides, total cholesterol and serum GGT have statistically significant elevation among the Mets patients when compared to healthy controls.

The serum HDL value shown significant decrease in the study group, when compared to control group.

Table 2:

Group		N	Mean	Std. Deviation	P value
Age	Control	50	50.78	7.05	0.384
	Case	50	51.96	6.42	
Weight	Control	50	61.62	4.35	<0.0001
	Case	50	85.30	5.13	
Waist Circumference	Control	50	87.96	5.21	<0.0001
	Case	50	105.96	8.00	
BMI	Control	50	24.31	2.04	<0.0001
	Case	50	31.73	1.62	
Systolic BP	Control	50	118.48	6.19	<0.0001
	Case	50	144.68	13.31	
Diastolic BP	Control	50	77.94	6.20	<0.0001
	Case	50	95.60	6.72	
FPG	Control	50	86.16	7.01	<0.0001
	Case	50	130.02	17.82	
TC	Control	50	168.20	17.83	<0.0001
	Case	50	234.02	34.10	
TGL	Control	50	127.74	11.30	<0.0001
	Case	50	163.82	16.94	
HDL	Control	50	50.36	6.64	<0.0001
	Case	50	38.54	6.17	
GGT	Control	50	37.84	8.68	<0.0001
	Case	50	66.52	8.19	
	Case	50	2.21	1.17	

The mean GGT level in the control group is 37.84+8.68 U/L.

The mean serum GGT level in the study subjects is 66.52+8.19 U/L. Thus the mean GGT level in study group is higher than the control group with a p value of < 0.001.

Comparison of serum GGT level between control group and study group:

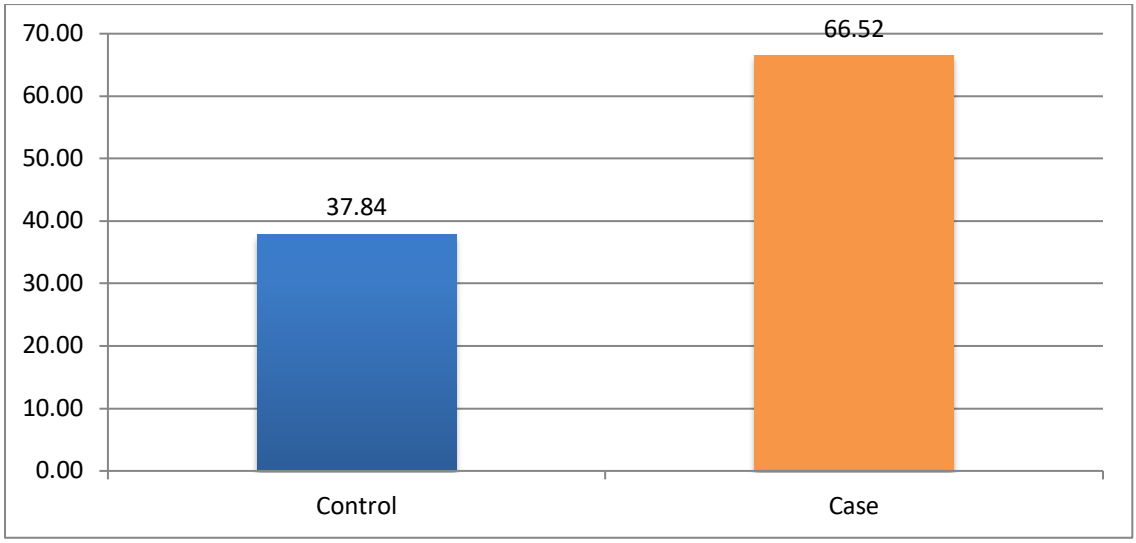

Figure 1:

Table shows mean Serum GGT levels between control and study group.

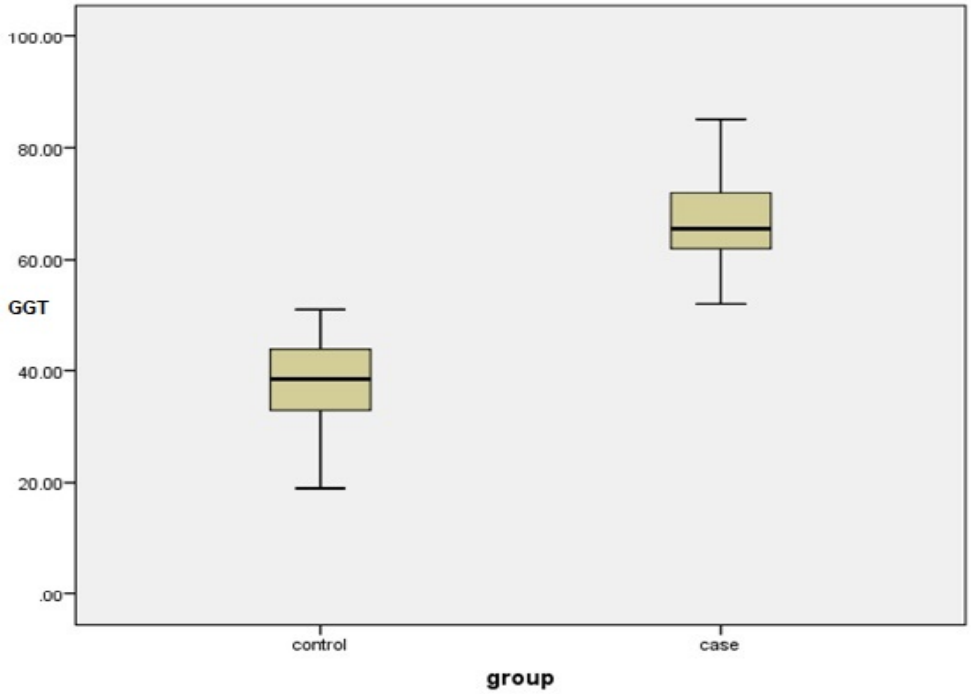

Figure 2:

Table shows the box plot of the GGT between the study and the control group.

Discussion

The present study was conducted to find out the level of GGT among metabolic syndrome patients. The associated biochemical parameters like fasting plasma glucose, serum total cholesterol, serum triglycerides and serum high density lipoproteins were also estimated. The mean waist circumference among cases in our study population was 105.96+8 cm as compared to controls (87.96+5.21), which is statistically significant.

This shows that there was a statistically significant association between the study and control group. Abdominal obesity is the major component of metabolic syndrome. Racette SB et al also concluded that increased waist circumference is found to be responsible for insulin resistance. It decreases the level of HDL fraction of cholesterol and increases the triglyceride levels leading to hypertension. [14]

In our study, the mean BMI among the cases was found to be 31.73+1.62 and that of the controls was 24.31+2.04, which is statistically significant. Recent studies have shown that both overweight and obese middle aged persons were at an increased

risk for cardiovascular morbidity and mortality. [15] So both these anthropometric indices are essential for determining the individuals at risk for CHD. Similar study by Niranjan et al [16] has shown that obesity is associated with metabolic syndrome patients and elevated serum levels of GGT due to higher degree of lipid peroxidation in individuals with central obesity. In our study, the mean fasting plasma glucose level in cases was found to be 130+17.82 and is statistically significant compared to that of the control group (86.16+7.01). In an observational study conducted by Sangsu et al, they have also found out that elevated GGT level is a predictor of type 2 diabetes mellitus, due to their close association with metabolic syndrome. [17]

In the current study, the mean serum total cholesterol in cases was 234.02+34.10 and in control group was 168.20 +17.83. The mean serum triglycerides in cases was 163.82+16.94 and in control group was 127.74+11.30. The mean serum HDL in cases was found to be 38.54+6.17 and in control group was 50.36+6.64. This statistically significant differences in TC, Triglycerides and HDL values between case and control groups are similar to the findings observed in studies done by Masilamani V et al, Ramachandran et al, Bansal S. [18]

The mean serum GGT level was found to be 37.64+8.19 U/L, which is significantly higher than that of the control group (44.44+6.26 U/L). Similar statistical significance was noted by studies conducted by Masilamani V [19] et al and Rantala et al [20] A number of studies have shown the direct association of serum GGT levels with Metabolic syndrome components even after adjusting for age, sex, BMI and alcohol consumption. Elevation of GGT level could be due to the excess deposition of fat in the liver (non-alcoholic fatty liver disease), which causes hepatic insulin resistance and hence systemic insulin resistance, which contributes to Metabolic Syndrome. The development of dyslipidemia in MetS is explained by the presence of insulin resistance, which leads to increased lipolysis. [21]

Recent studies shows GGT is not only the marker of fatty liver, but also the marker for oxidative stress. Experimental studies have found that GGT plays a major role in maintaining intracellular antioxidant defence through its role in the intracellular transport of glutathione into the cells. [22] GGT is an ectoenzyme, which is found in the outer side of cell membrane, helps in maintaining intracellular concentrations of glutathione (GSH).

Thus increased serum concentration of GGT correlates with increased oxidative stress in patients with MetS.

Conclusion:

The main finding in the present study was a significant high level of serum gamma glutamyl transferase in patients with metabolic syndrome. GGT is the predictive marker for obesity, hypertension, diabetes, insulin resistance, dyslipidemia and metabolic syndrome. Increasing awareness and early identification of these clusters of risk factors by measuring serum GGT level may help in early intervention and prevention of coronary heart disease.

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