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ORIGINAL ARTICLE

The Impact of Increased Serum GGT Levels and NAFLD on the Components of Metabolic Syndrome

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ABSTRACT

Prevalence of metabolic syndrome is increasing worldwide and researchers have found the importance of serum GGT levels in metabolic syndrome patients. Serum GGT levels are related to the components of metabolic syndrome. Aim: To evaluate the serum GGT levels in metabolic syndrome patients and its association with metabolic syndrome components. Materials and The study consists of 60 patients with metabolic syndrome and 60 age matched healthy individuals. Fasting blood glucose, lipid profile, liver function test were analyzed using standard kits and non alcoholic fatty liver disease (NAFLD) was also detected by ultra sound using Voluson E6 machine. Anthropometric measurements and blood pressure was also taken from the participants with their consent. A significant increased serum GGT levels was found in the study group compared to control group ($p<0.001$). Metabolic syndrome patients showed increased serum GGT levels and USG findings also conformed NAFLD. We reported a significant positive correlation between waist circumference and serum GGT ($r = 0.376$, $p < 0.001$), fasting blood glucose and serum GGT ($r = 0.400$, $p <0.001$), serum triglycerides and serum GGT ($r = 0.242$, $p <0.01$), systolic blood pressure and serum GGT ($r = 0.282$, $p < 0.01$), diastolic blood pressure and serum GGT ($r = 0.305$, $p < 0.01$). Conclusion: Elevated serum GGT may be an early biomarker for the development of metabolic syndrome.

KEY WORDS : Metabolic syndrome, GGT, Insulin resistance, NAFLD

Introduction

Gamma-glutamyl transferase (GGT) is a cell surface protein contributing to the extracellular catabolism of glutathione (GSH). The enzyme is produced in many tissues but mostly derived from the liver[1]. GGT hydrolyses glutathione into glutamate and a cysteinyl glycine dipeptide, and inside the cell the amino acids are subsequently reduced producing additional reduced glutathione[2]. Serum GGT is independently associated with several pathological conditions including cardiovascular disease, diabetes and metabolic syndrome[3] and metabolic syndrome being fore run of CVD and diabetes.

Metabolic syndrome is a cluster of risk factors characterized by hypertension, atherogenic dyslipidemia, hyperglycemia, abdominal

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obesity, increased low density lipoprotein and decreased high density lipoprotein [4]. It is considered that hepatic manifestation of metabolic syndrome is non alcoholic fatty liver disease (NAFLD)(5). Metabolic syndrome is very frequent condition globally affecting 20 – 25% of the world's adult population [6].People with metabolic syndrome are at an increased risk of atherosclerotic cardiovascular diseases and type 2 diabetes mellitus[7].

Many previous studies reported that levels of serum GGT could be an early biomarker for the development of Metabolic syndrome[8-11]. As patients with elevated serum GGT have higher risk of developing Metabolic syndrome and elevated GGT is associated with individual Metabolic syndrome components. Therefore we decided to determine the serum GGT levels in Metabolic syndrome patients and its association with Metabolic syndrome components[12-13].

Materials and methods

In the present study, 60 Metabolic syndrome subjects and 60 age matched healthy individuals of 20 years and above were included in the study. The study was conducted at sri muthukumaran medical college hospital and research institute from august 2014 to December 2014. International Diabetes Federation (IDF) criteria were used to select the metabolic syndrome patients. The main criteria for diagnosing metabolic syndrome is central obesity (waist circumference > 90 cm for men and >80 cm for women) plus any 2 abnormalities of the following list. Fasting blood sugar level greater than 100 mg/dl (Hyperglycemia), Serum triglycerides levels more than 150mg/dl (Hypertriglyceridemia), Low HDL cholesterol levels (Men - < 40 mg/dl and Women - < 50 mg/dl) and the last criteria is hypertension (Systolic blood pressure - > 130mmHg and Diastolic blood pressure- > 85mmHg)[14]. Cases with history of renal disease, cardiac disease, active infection, any malignancy, known alcoholic patients, pregnant and lactating women were excluded from the study. Fasting blood samples were collected. The samples were centrifuged and analyzed using Konelab 20 auto analyzer on the same day of collection.

Biochemical parameters including fasting blood glucose, lipid profile, liver function test were analyzed using standard methods with thermo scientific reagents. VOLUSON E6 machine with convex probe was used to detect non alcoholic fatty liver disease in the participants.

Anthropometic measurements of waist and hip circumference were measured using inch tap. Blood pressure was measured in an appropriate mercury sphygmomanometer.

Statistical analyses were performed using IBM SPSS statistics version 20. Student's't' test, chi square test were used for comparison of qualitative data. Correlation coefficient were used to analyze the association between the parameters in the case group. 'p' value <0.05 is considered significant. Data were defined as mean ± SD.

Results

Serum GGT levels and Metabolic syndrome:

The present study confirms the serum GGT levels in Metabolic syndrome patients is higher than non Metabolic syndrome control groups. Serum levels of TGL, HDL and fasting plasma glucose levels are significantly different in two groups. Systolic blood pressure, BMI and waist circumference was also found to be higher in among the Metabolic syndrome groups which stood statistically significant (Table.No.1).

Table.No. – 1: Clinical and biochemical characteristics of the study and control population.

VARIABLES	STUDY GROUP (n = 60) MEAN ± S.D	CONTROL GROUP (n = 60) MEAN ± S.D	P VALUE
AGE	48.11 ± 11.4	48.5 ± 11.0	NS
BMI	28.3 ± 3.7	22.1 ± 3.4	<0.001
SBP	121.2 ± 15.8	111.4 ± 13.3	<0.001
DBP	77.9 ± 9.3	73.1 ± 8.0	<0.01
WAIST CIRCUMFERENCE	96.0 ± 7.8	77.0 ± 8.9	<0.001
FBS	138.6 ± 52.4	87.8 ± 9.7	<0.001
HDL	39.8 ± 8.5	45.8 ± 9.1	<0.001
TGL	173.4 ± 69.4	88.0 ± 25.3	<0.001
GGT	36.9 ± 19.9	24.4 ± 9.4	<0.001
AST	27.2 ± 17.3	21.7 ± 6.5	<0.01
ALT	20.6 ± 13.8	14.2 ± 7.4	<0.01

P value <0.05 is considered significant.
NS – Not significant.

NAFLD and Metabolic Syndrome

Among 60 Metabolic syndrome patients 18 are having grade I fatty liver and 5 are having grade II fatty liver and the remaining 37 patients are normal Which stood statistically significant.

P value was obtained by using Chi square statistical analysis(Table.No.2).

Table.No. 2: Analysis of NAFL in the study and control population

FATTY LIVER	STUDY GROUP	CONTROL GROUP	TOTAL	P VALUE
GRADE-I	18	0	18	
GRADE – II	5	0	5	
NORMAL	37	60	97	
TOTAL	60	60	120	<0.001

Table.No. 3: Correlation between serum GGT and components of metabolic syndrome

VARIABLES	r VALUE	P VALUE	PERCENT
WAIST CIRCUMFERENCE & GGT	0.376	<0.001	13%
GGT & FBS	0.400	<0.001	16%
GGT & HDL	-0.162	0.078	2%
GGT & TGL	0.242	<0.01	5%
GGT & SBP	0.282	<0.01	7%
GGT & DBP	0.305	<0.01	9%

As per table 3, the association between serum GGT and components of metabolic syndrome was derived using correlation coefficient. We observed a significant positive correlation between waist circumference and serum GGT, fasting blood glucose and serum GGT, serum triglycerides and serum GGT, systolic blood pressure and serum GGT, diastolic blood pressure and serum GGT in the study group. In the present study, no significant correlation was found between serum GGT and HDL in the study population (Table No.3).

In our study group, 78% no of patients with increased serum GGT levels had non alcoholic fatty liver disease.

Discussion

We observed in our study that 28.3% of patients with metabolic syndrome having increased serum GGT activity, a marker of nonalcoholic fatty liver disease. The present study shows that 62% of metabolic syndrome patients are having nonalcoholic fatty liver disease. Metabolic syndrome may be a cause or consequence of nonalcoholic fatty liver disease. In one hand, nonalcoholic fatty liver disease leads to decreased insulin sensitivity and in other hand insulin resistance causes nonalcoholic fatty liver disease in several ways i.e activation of adipocytokines secretion from adipocytes, alter rates of triglycerides synthesis in hepatocytes, increased hydrolysis of triglycerides to free fatty acids. This leads to increased free fatty acids levels in liver[15-16].

In the present study, we have found a positive significant correlation between serum GGT and waist circumference. Several studies have suggested that abdominal obesity plays a key role in the elevated cardiovascular risk associated with metabolic syndrome. Hence the waist circumference is a robust marker of abdominal obesity[2,17].

This study shows a positive significant correlation between fasting blood glucose and serum GGT, serum triglycerides and serum GGT. Ikai E et al have obtained a significant correlation between serum GGT and plasma insulin levels[18]. Previous studies have confirmed the association of hyperinsulinemia with metabolic syndrome[19]. Insulin resistance leads to impaired suppression of fatty acid oxidation. Which results in elevated free fatty acids which in turn causes increased de-novo synthesis of triglycerides[20-21].

Nitric oxide is a potent vasodilator. In the oxidative stress condition, nitric oxide is rapidly destroyed by the free radicals. Decreased nitric oxide causes prolonged vasoconstriction which results in hypertension. With the help of GGT, glutathione is required for antioxidant enzymes to scavenge the free radicals. Pedro Botet et al observed decreased antioxidant enzyme activity (superoxide dismutase and glutathione peroxidase) and increased free radicals in hypertensive patients[22-24].

In our study we observed a positive correlation between serum GGT levels and individual components of metabolic syndrome so serum GGT can be considered as a eligible marker which is inexpensive, determined easily and as an important role for diagnosing metabolic syndrome. [25-26].

Conclusion

The results from this study indicate that metabolic syndrome patients with non alcoholic fatty liver disease are having increased serum GGT levels. Elevated serum GGT levels may be early biomarker for the development of metabolic syndrome. Due to smaller sample size, our study is unable to analyze clearly the association between serum GGT, non alcoholic fatty liver disease and components of metabolic syndrome.

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