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Association of Serum Gamma-Glutamyl Transferase with Metabolic Syndrome

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Abstract **Original Research Article**

***Background*:** Association between serum GGT and metabolic syndrome highlights the potential role of GGT as a biomarker in the early identification and management of this complex disorder. Further research is needed to elucidate the underlying mechanisms linking GGT and metabolic syndrome and to determine the clinical utility of GGT measurements in routine practice. Nonetheless, GGT holds promise as a valuable tool for assessing metabolic health and improving risk assessment in individuals at risk of metabolic syndrome. ***Objective*:** To assess the Association of Serum Gamma-Glutamyl Transferase with Metabolic Syndrome. ***Method*:** This Cross-sectional study was carried out at Outpatient department of Medicine, BSMMU, Shahbagh, Dhaka from March 2020 – July 2021. By non-probability sampling technique 36 diagnosed metabolic syndrome patients, 36 normal healthy subjects will be enrolled in the study. The purpose and procedure of the study was explained in detail and informed written consent was be taken from all the study subjects. ***Results*:** During the study, the mean values of Blood pressure, fasting plasma glucose, were increased from the first quartile to the fourth quartile ($p < 0.05$). However, there were no significant differences observed in terms of age, waist circumference, LDL-C, HDL-C, total cholesterol, and BMI ($p > 0.05$). A positive correlation was observed among Serum GGT, TG, fasting plasma glucose & blood pressure ($p<0.05$). A moderate positive correlation was observed between Serum GGT and waist circumference. However, there was no significant correlation with HDL cholesterol ($p>0.05$). Serum GGT is mainly influenced by levels of triglyceride ($\beta= 0.238$, $t= 2.002$, $p= 0.049$) and fasting plasma glucose ($\beta=0.355$, $t= 2.980$, $p= 0.004$). Logarithmic transformations of GGT, TG, and FPG were done to make the values normally distributed before conducting regression analysis. ***Conclusion*:** This study suggests that serum GGT is raised in metabolic syndrome group and GGT level raised with increased waist girth, blood pressure, and TG which are the features of metabolic syndrome according to NCEP-ATP III criteria. Hence, Serum GGT concentration might play a significant role in the early diagnosis of metabolic syndrome and to reduce the risk of cardiovascular disease by proper management.

Keywords: Clinical characteristics, metabolic syndrome, fasting glucose.

INTRODUCTION

Metabolic syndrome is a complex disorder characterized by a cluster of interconnected metabolic abnormalities, including abdominal obesity, insulin resistance, dyslipidemia, and hypertension. It is considered a major public health concern worldwide due to its association with an increased risk of cardiovascular disease, type 2 diabetes and other adverse health outcomes. Identifying reliable biomarkers that can aid in the early detection and management of metabolic syndrome is of great importance [1-4].

One such biomarker that has gained considerable attention in recent years is serum gamma-glutamyl transferase (GGT). GGT is an enzyme involved in the metabolism of glutathione, an important antioxidant in the body. While GGT is primarily found in the liver, it is also present in other tissues, including the kidneys, pancreas, and adipose tissue.

Several epidemiological studies have reported a significant association between elevated serum GGT levels and the presence of metabolic syndrome. Elevated GGT levels have been observed in individuals

with central obesity, insulin resistance, dyslipidemia, and hypertension, which are key components of metabolic syndrome. Moreover, GGT levels have been shown to increase progressively with the number of metabolic syndrome components present in an individual [5-7].

The underlying mechanisms linking GGT and metabolic syndrome are not fully understood, but several hypotheses have been proposed. It is believed that increased oxidative stress, chronic inflammation, and impaired liver function associated with metabolic syndrome may contribute to the elevation of GGT levels. Additionally, GGT has been suggested to play a role in the development of insulin resistance and endothelial dysfunction, both of which are central pathophysiological features of metabolic syndrome [8-11].

The association between serum GGT and metabolic syndrome has important clinical implications. Elevated GGT levels can serve as a valuable biomarker for identifying individuals at increased risk of developing metabolic syndrome and its associated complications. Furthermore, GGT can provide additional prognostic information beyond traditional risk factors, aiding in risk stratification and the implementation of targeted interventions [12].

OBJECTIVE

- To evaluate the Association of Serum Gamma-Glutamyl Transferase with Metabolic Syndrome.

METHODOLOGY

This Cross-sectional study was carried out at Outpatient department of Medicine, BSMMU, Shahbagh, Dhaka from March 2020 – July 2021. By non-probability sampling technique 36 diagnosed metabolic syndrome patients, 36 normal healthy subjects will be enrolled in the study. The purpose and procedure of the study was explained in detail and informed written consent was be taken from all the study subjects.

Collected data was checked and edited (to remove the outliers) and then processed with the help of a software statistical package for social science (SPSS) and analyzed. Statistical analyses were done by using SPSS 25.0. Quantitative data will be expressed as mean (±SD) or median (inter-quartile range) as appropriate. The crosstabs and descriptive procedures were used to produce frequencies of categorical variables. Comparisons between metabolic syndrome and healthy individuals were performed by unpaired t-test. Subjects were divided into four groups according to the number of components of the MetS (0, 1, 2, and 3 or more components). Comparisons between groups classified by quartiles of serum GGT and the number of components of the MetS were performed using one-way ANOVA analysis. Spearman correlation coefficient between serum GGT and other parameters was performed. To assess which components of the Metabolic Syndrome contribute to the change in serum GGT, we performed linear regression using serum GGT as the dependent variable and all the different components of the Metabolic Syndrome as the covariates. Serum GGT level has non-normal distribution, thus we used a logarithmic transformation. The level of significance used for all of the above analyses was two-tailed, $p < 0.05$. The SPSS statistical package was used to perform all statistical evaluations (SSPS Inc., Chicago, IL, USA).

RESULTS

Table-1 shows age distribution of the study group. The mean ± SD of age of metabolic syndrome and healthy individuals were 47.88± 9.69 and 43.43 ±12.68 years respectively. There was no significant difference in age, between the Metabolic syndrome & healthy group (p =0.098).

Table 1: Age distribution of study subjects (n=71)

Variables	Metabolic Syndrome (n = 41) (Mean± SD)	Healthy group (n = 30) (Mean± SD)	p- value
Age of the study subjects (years)	47.88± 9.69	43.43 ±12.68	0.098

Unpaired student's t-test was done.

Table-2 shows gender distribution. Among 71 participants, 41 identified as Metabolic Syndrome (M=16, F=25), and 30 identified as healthy individuals (M=11, F=19). Gender has no significant efeect on these two groups (p= 0.697).

Table 2: Gender distribution of study subjects (n=71)

Gender distribution	Metabolic Syndrome	Healthy group	p-value
Male	16	11	0.697
Female	25	19	
Total	**41**	**30**	

A Chi-square test was done to find out the level of significance.

Figure-1 shows quartiles of GGT. The study subjects were divided into four groups according to the quartile of serum GGT. Serum GGT were 8-18, 19-29, 30-46 & 47-184 U/L in 1st, 2nd, 3rd, and 4th group respectively.

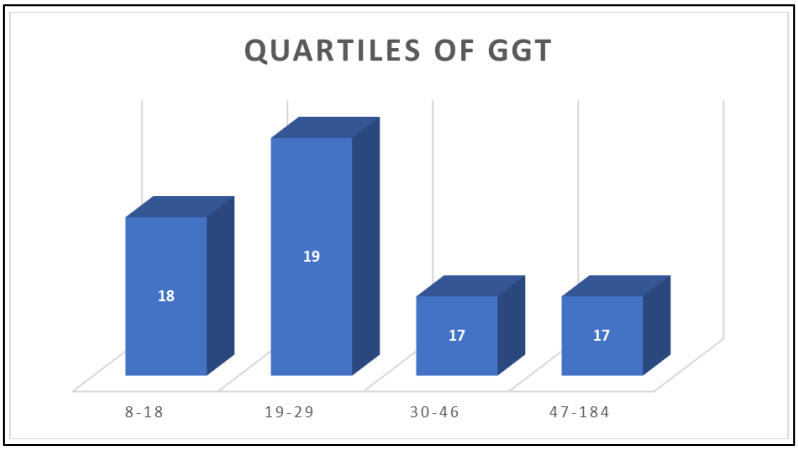

Figure 1: Distribution of study subjects according to quartiles of GGT (n=71)

Table-4 showed a comparison of clinical characteristics according to quartiles of serum GGT to see the statistical significance. The mean values of Blood pressure, fasting plasma glucose, were increased from the first quartile to the fourth quartile ($p < 0.05$). However, there were no significant differences observed in terms of age, waist circumference, LDL-C, HDL-C, total cholesterol, and BMI ($p > 0.05$).

Table 4: Characteristics of study subjects according to quartiles of GGT (n=71)

Characteristics	Quartiles of GGT				P-value
	8-18	19-29	30-46	47-184	
Age (years)	41.11 ± 13.07	45.89 ± 11.25	48.71 ± 9.31	48.59 ±9.75	0.147
WC (cm)	78.61 ± 4.41	81.05 ± 6.96	81.94 ± 4.76	82.59 ± 6.25	0.189
SBP (mmHg)	115.56±6.16	119.47 ± 7.80	122.35 ± 6.64	129.41±10.29	0.000
DBP (mmHg)	73.89 ± 6.08	74.21± 6.93	77.94 ± 5.88	82.94 ± 8.30	0.001
Fasting plasma glucose(mmol/L)	6.64 ± 2.93	9.16 ± 4.35	9.22 ± 4.16	10.94 ±3.71	0.015
LDL-C (mg/dl)	103.66±33.17	111.75±41.80	105.32±35.36	103.12±29.61	0.874
HDL–C (mg/dl)	42.61 ±8.95	41.74 ±9.67	40.88 ± 8.62	46.06 ± 8.42	0.354
TG (mg/dl)	187.94±171.61	187.26±68.02	294.53±145.00	284.71±162.03	0.033
TotalCholesterol (mg/dl)	179.33 ± 46.24	191.63±50.72	203.24 ± 43.18	199.24 ± 34.99	0.404
BMI ($kg/m^{2)}$	25.27 ± 2.10	25.53 ± 2.40	25.05 ± 1.70	25.58 ± 2.20	0.876

ANOVA test was done.

BMI- body mass index, **SBP**- systolic blood pressure, **DBP**- diastolic blood pressure, HDL-C- high-density lipoprotein cholesterol, **LDL-C**- low-density lipoprotein cholesterol, **TG** – Triglycerides, **ALT**- alanine aminotransferase

Table-5 shows correlation of serum GGT with metabolic syndrome parameters (n=71)**.** A positive correlation was observed among Serum GGT, TG, fasting plasma glucose & blood pressure ($p<0.05$). A moderate positive correlation was observed between Serum GGT and waist circumference. However, there was no significant correlation with HDL cholesterol ($p>0.05$).

Table 5: Correlation of serum GGT with metabolic syndrome parameters (n=71)

Variables	r value	p-value
GGT (U/L)	1.000	-
WC (cm)	.282	.017
SBP (mmHg)	.516	.000
DBP (mmHg)	.458	.000
Fasting plasma glucose (mmol/L)	.503	.000
HDL-C (mg/dl)	.087	.471
TG (mg/dl)	.435	.000

Spearman's correlation coefficient was done.

GGT- Gamma-glutamyl transferase, **WC**- waist circumference, **SBP**- systolic blood pressure, **DBP**- diastolic blood pressure, **HDL-C**- high-density lipoprotein cholesterol, **TG** – Triglycerides

Table-5 shows Association between components of the metabolic syndrome as the independent variables and serum GGT as the dependent variable (n=71).

A linear regression model was performed by using the individual components of the MetS as the independent variable, and serum GGT as the dependent variable. Serum GGT is mainly influenced by levels of triglyceride (β= 0.238, t= 2.002, p= 0.049) and fasting plasma glucose (β=0.355, t= 2.980, p= 0.004). Logarithmic transformations of GGT, TG, and FPG were done to make the values normally distributed before conducting regression analysis.

Table 5: Association between components of the metabolic syndrome as the independent variables and serum GGT as the dependent variable (n=71)

Coefficients					
Model	**Unstandardized Coefficients**		**Standardized Coefficients**	**t**	**Sig.**
	B	**Std. Error**	**Beta**		
(Constant)	.625	.389		1.605	.113
Log TG	.252	.126	.238	2.002	.049
Log FPG	.528	.177	.355	2.980	.004
HDL-C(mg/dl)	.007	.004	.223	1.704	.093
SBP (mmHg)	.007	.004	.250	1.785	.079
DBP (mmHg)	.010	.005	.290	2.185	.032
Waist circumference (cm)	.008	.005	.180	1.613	.111
a. Dependent Variable: Log GGT					

A linear regression model was performed.

DISCUSSION

Some studies have shown that serum GGT was correlated positively with male genders, body mass index, high blood pressure, high blood cholesterol, high LDL-C, low HDL-C, and high fasting glucose [11-14]. But we found a strong positive correlation between Serum GGT and TG, fasting plasma glucose, and high blood pressure ($p<0.05$). A moderate positive correlation was observed between Serum GGT, age, and waist circumference. However, there was no significant correlation with male genders, BMI, HDL-C, and LDL-C ($P>0.05$).

There were some large population-based studies to assess the relationship between serum GGT and the concept metabolic syndrome. (Rantala *et al.*, 2000), first investigated this relationship in a study of 1045 Caucasians. Serum GGT was correlated significantly with the components of MetS and the correlation coefficient between serum GGT and triglyceride was the highest ($r = 0.39$, $p = 0.0001$) which was also evident in our study but the correlation coefficient between serum GGT and components of metabolic syndrome was the highest ($r = 0.597$, $p = 0.000$) followed by TG ($r = 0.435$, $p = 0.000$). In our study, serum GGT was significantly correlated with waist circumference, triglyceride, fasting plasma glucose, and the number of components of MetS which is also supported by other large-scale studies [10-12].

In the linear regression model, serum GGT is mainly influenced by levels of triglyceride (β= 0.238, t= 2.002, p= 0.049) and fasting plasma glucose (β=0.355, t= 2.980, p= 0.004) with high statistical significance, which findings are consistent with the results of previous studies [13, 14].

It has been suggested that the elevation of serum GGT could be a marker of excess deposition of fat in the liver, which is closely related to obesity and visceral fat deposition and may be the first possible mechanism of the relationship between GGT and insulin resistance (Marchesini *et al.*, 2001). Recently, one study reported that elevated serum GGT levels predict glucose intolerance probably via insulin resistance and this may be primarily related to hepatic insulin resistance and increased intrahepatic lipids [14].

In our study, we also found that hypertriglyceridemia and fasting plasma glucose abnormality were the main components of MetS associated with serum GGT levels, suggesting that serum GGT might be more related to hepatic insulin resistance regardless of the presence of nonalcoholic fatty liver disease. These findings mean that elevated serum GGT is not simply the outcome of the fatty infiltration of the liver and serum GGT concentrations might be associated with hepatic insulin resistance and disturbances in the glucose metabolism in the absence of overt liver disease. Another possible mechanism is that GGT has been known to play an important role in antioxidant defense systems and might be an early marker of oxidative stress [15].

Elevated GGT could reflect subclinical inflammation, which would represent the underlying mechanism. In addition, certain mechanisms related to oxidative stress might play a role because cellular GGT has a central role in glutathione homeostasis by initiating the breakdown of extracellular glutathione, a

critical antioxidant defense for the cell [11, 12]. Increases in serum GGT activity may be a response to oxidative stress, making increased transport of glutathione into cells. Therefore, systemic inflammation is thought to be closely involved in the pathogenesis of MetS [14, 15].

CONCLUSION

This study suggests that serum GGT is raised in metabolic syndrome group and GGT level raised with increased waist girth, blood pressure, and TG which are the features of metabolic syndrome according to NCEP-ATP III criteria. Hence, Serum GGT concentration might play a significant role in the early diagnosis of metabolic syndrome and to reduce the risk of cardiovascular disease by proper management.

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