Molecular Mechanism Research (2024) Volume 2 Issue 1
doi: 10.59429/mmr.v2i1.7097

ARTS AND SCIENCE
ARTS AND SCIENCE PRESS PTE. LTD

RESEARCH ARTICLE

Serum Gamma-Glutamyl Transferase as a Biomarker for Insulin Resistance and Metabolic Syndrome in Dhaka, Bangladesh: A Cross-Sectional Study

Abdinasir Ali Mohamud[1], Mohamed Nur Mohamed[2], Md. Ashiqur Rahman[3], Sadia Islam[4*]

[1] *Abdinasir Ali Mohamud, Department of Internal Medicine, University of Somalia, abdinasirali01@gmail.com*

[2] *Mohamed Nur Mohamed, Department of Public Health, World University of Bangladesh (WUB), mohamednuur9920@gmail.com*

[3] *Md. Ashiqur Rahman, Department of Laboratory Medicine, Novus Clinical Research Services Limited (NCRSL), Bangladesh, ararashiqur@gmail.com*

[4] *Sadia Islam, Department of Laboratory Medicine, Bangladesh Specialized Hospital, Bangladesh, sadia.buhs.6700@gmail.com*

***Corresponding author:** Sadia Islam
Department of Laboratory Medicine
Bangladesh Specialized Hospital PLC, Bangladesh
Email: sadia.buhs.6700@gmail.com
Orcid id: 0009-0007-7932-3804

ABSTRACT

Background: Gamma-glutamyl transferase is an enzyme found in various tissues, including the liver, kidney, pancreas, and intestine. Elevated serum GGT levels are linked to oxidative stress and cardiovascular risk factors. GGT plays a role in glutathione catabolism, potentially leading to metabolic disturbances like insulin resistance and metabolic syndrome. **Objective:** The study explores the link between serum GGT levels and insulin resistance in Dhaka, Bangladesh, aiming to assess serum GGT's potential as a biomarker for insulin resistance and metabolic syndrome. **Methods:** The study was conducted at a hospital in Dhaka, Bangladesh, involving 330 participants aged 20 to 60, with 147 diagnosed with metabolic syndrome (MetS) and 183 without. Anthropometric data were collected, and fasting blood samples were analyzed. Statistical analysis was performed using SPSS software, with results compared using unpaired Student's t-test and ANOVA, considering a p-value <0.05 as statistically significant. **Results:** In this study of 330 participants, individuals with metabolic syndrome exhibited significantly higher levels of BMI, waist circumference, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, insulin, HOMA-IR, and gamma-glutamyl transferase compared to those without MetS. Lipid profiles showed elevated total cholesterol and triglycerides, and reduced HDL cholesterol in the MetS group. Insulin resistance was associated with increased BMI, WC, BP, and elevated levels of FPG, insulin, HOMA-IR, and GGT, while ALT and uric acid levels did not differ significantly. Higher GGT tertiles were linked to increased BMI, WC, BP, FPG, insulin, HOMA-IR, ALT, TC, and TG, and lower HDL-C. Significant positive correlations between GGT and HOMA-IR were observed across all subjects, with a strong

ARTICLE INFO
Received: 18 September 2024 | Accepted: 01 November 2024 | Available online: 22 November 2024

CITATION
Mohamud A.A, Mohamed M.N, Rahman M.A, et al. Serum Gamma-Glutamyl Transferase as a Biomarker for Insulin Resistance and Metabolic Syndrome in Dhaka, Bangladesh: A Cross-Sectional Study. *Molecular Mechanism Research* 2024; 2(1): 7097. doi: 10.59429/vicr/v2i1.7097

association remaining after adjusting for other variables. The results suggest that elevated GGT levels are closely linked with insulin resistance and components of MetS. **Conclusion:** The study reveals a strong positive correlation between serum gamma-glutamyl transferase (GGT) and insulin resistance, metabolic syndrome (MetS), and HDL cholesterol, suggesting GGT as a valuable biomarker for monitoring MetS and insulin resistance.

Keywords: Gamma-glutamyl transferase; HOMA-IR; Metabolic syndrome; Biomarker; Lipid Profile

1. Introduction

Gamma-glutamyl transferase (GGT) is an enzyme found in various tissues, including the kidney, liver, pancreas, and intestine. Serum GGT, primarily from the hepatobiliary system, is a sensitive biomarker of oxidative stress and associated with cardiovascular risk[1]. It contributes to the extra cellular catabolism of glutathione, causing the reduction of ferric ion to ferrous ion[2] and the production of super oxide and hydrogen peroxide[3]. Elevated levels of GGT aggravate oxidative stress, causing inflammation and insulin resistance, leading to glucose intolerance and dyslipidemia. Serum GGT may be a significant predictor for metabolic syndrome, including T2DM and CVD[4]. Studies have shown that increased serum GGT is associated with hypertriglyceridemia, elevated blood glucose, and insulin resistance. Elevated or high normal serum GGT levels are strongly associated with the risk of developing hyperglycemia, dyslipidemia, hypertension, and obesity[6].

Insulin resistance (IR) is a common condition that contributes to MetS development and increases the risk of diabetes[7]. It is caused by genetic and environmental factors and involves impaired insulin sensitivity, reduced glucose uptake in skeletal muscle, impaired liver glucose production[8], and increased lipolysis in adipose tissue, leading to hyperglycemia and dyslipidemia[9]. IR is a significant factor in metabolic abnormalities associated with MetS. Studies have shown a positive correlation between gamma-glutamyl transferase (GGT) and insulin resistance (IR)[10]. The mechanisms linking GGT to insulin resistance are not fully understood, but may involve oxidative stress and inflammation. GGT is involved in the metabolism of glutathione, an antioxidant, which can lead to oxidative stress, impairing insulin signaling pathways[11]. Elevated GGT levels can also reflect increased oxidative stress and inflammation, which negatively affect insulin sensitivity[12]. Higher GGT levels have been observed in individuals with conditions associated with insulin resistance, such as obesity, metabolic syndrome, and type 2 diabetes. Some studies have found that serum GGT is an independent predictor of insulin resistance, suggesting its role as a marker for metabolic disturbances beyond liver function assessment[13]. Overall, the evidence suggests that elevated GGT levels are associated with increased insulin resistance, likely through mechanisms involving oxidative stress and inflammation.

MetS is a growing global public health issue due to urbanization and sedentary lifestyles. Bangladesh, a developing country with rapid economic growth, has seen a significant increase in non-communicable chronic diseases and associated mortality due to altered food habits, processed food, and less physical activity[14]. MetS is associated with non-communicable chronic diseases such as Type 2 Diabetes, coronary artery diseases, cerebrovascular diseases, and non-alcoholic fatty liver disease[15]. Recent studies suggest that MetS components are independently associated with several cancers[16]. Iron deficiency (IR) is a core component of T2DM and contributes to increased health system costs worldwide. Identifying individuals with MetS early is crucial for lifestyle interventions and treatment to prevent diabetes and cardiovascular diseases[17]. Serum GGT activity, a sensitive marker of oxidative stress, has been suggested to be associated with CVD and associated risk factors like insulin resistance, dyslipidemia, MetS[17], diabetes[18], and hypertension[19]. If such an association is observed, serum GGT could be used as a biomarker for MetS and

IR development, enabling clinicians to take necessary steps to prevent MetS complications. The aim of this study was to determine the association of serum GGT with IR.

2. Materials and methods

2.1. Study settings and study population

It was an analytical cross-sectional study conducted at the biochemistry department of a hospital in Dhaka, Bangladesh, from February 2021 to March 2023. Purposive easy sampling was the method used for sampling. For the study, 330 participants in total were enrolled. A total of 330 patients were enrolled, of which 147 had MetS and 183 did not. Age range of 20 to 60 years old and apparently healthy volunteers of both genders were the inclusion criteria. Exclusion criteria of study subjects: pregnant and lactating mothers; patients with-acute severe septic condition; cardiovascular disease; Liver disease; renal disease; pulmonary disease; chronic debilitating disease: such as malignancy, HIV, etc.; alcoholism, smoking; patients receiving drugs that affect liver enzymes; patient using insulin as well as subjects taking oral hypoglycemic agent.

2.2. Anthropometric sata collection

Height was measured using a metal tape from floor to marked point on a wall, with participants standing barefoot and upright. Weight was recorded using a digital scale with participants in light clothing, and BMI was calculated by dividing weight (kg) by height squared. Waist circumference was measured to the nearest centimeter at the midpoint between the iliac crest and lower ribs. Blood pressure (BP) was measured with a manual sphygmomanometer on the left arm in a seated position after five minutes of rest, with two readings taken five minutes apart and averaged.

2.3. Study procedure

Adult participants in this cross-sectional analytical study participated between February 2021 to March 2023. Purposively chosen study participants were those who visited the outpatient department (OPD) at a Hospital Dhaka, Bangladesh, as per the selection criteria. People who appeared to be in good health were chosen as subjects. All research participants provided informed written consent once the study's purpose was fully disclosed to them. Following appropriate counseling, each participant received a detailed explanation of the study's purpose, goals, and methodology. Only willing applicants were chosen to participate in the study. In addition to other pertinent data, sociodemographic information was gathered and entered into the data collecting sheet. A thorough physical as well as pertinent clinical evaluations were carried out and documented.

2.4. Blood sample collection and laboratory analysis

Fasting blood samples were collected from all participants. They were allowed to fast overnight (10–12 hours). Blood was collected from the antecubital vein after all aseptic precautions, 5 ml venous blood was taken by sterile disposable syringe. 2 ml of collected blood was taken in a test tube coated with dried sodium fluoride-potassium oxalate mixture and plasma was separated after centrifugation at 3000 rpm for five minutes for fasting glucose and insulin. The remaining 3 ml blood was collected in a plain tube. This tube was allowed to stand for 20 to 30 minutes so that blood was clotted properly. Then serum was separated after centrifuging at 3000 rpm for 10 minutes and was collected into Eppendorf tubes, labelled properly to measure serum GGT, lipid profile, ALT, uric acid. Samples were preserved in a deep freezer at-37^{0}C and were analyzed later. All the Biochemical tests were done in the biochemistry laboratory[20].

2.5. Data analysis

Data were analyzed using SPSS version 23, with results expressed as mean ± SD. Comparisons between MetS and non-MetS groups, as well as IR and non-resistance groups, were conducted using an unpaired Student's t-test, which was also applied for gender variations. Serum GGT levels were divided into tertiles for trend analysis, and ANOVA with post-hoc tests was used to compare these tertiles. A p-value <0.05 was considered statistically significant.

3. Results

In this study, 330 participants were selected, including 147 with MetS and 183 without MetS. **Table 1** presents the mean ± SD for age (years), BMI (kg/m²), WC (cm), SBP (mm Hg), and DBP (mm Hg) in relation to metabolic syndrome. The results showed that individuals with MetS had significantly higher BMI, WC, and BP compared to those without MetS (p<0.001). However, there was no significant difference in age between the two groups.

Table 1. Baseline characteristics of study subjects according to metabolic syndrome (n=330).

Variables	Subjects with MetS (n=147)	Subjects without MetS (n=183)	p-value
Age (years)	40.04±12.77	38.84±12.60	0.621
BMI (kg/m^2)	28.03±4.07	22.00±3.74	**<0.001***
WC (cm)	102.08±9.69	80.18±7.37	**<0.001***
SBP (mmHg)	127.76±13.23	110.00±9.13	**<0.001***
DBP (mmHg)	88.37±10.07	73.52±7.82	**<0.001***

Data were expressed as mean±SD

Unpaired student t-test was performed to compare between two groups

Table 2 presents the mean ± SD of biochemical parameters for the study subjects based on metabolic syndrome status. FPG, insulin, and HOMA-IR were significantly higher (p<0.001) in individuals with MetS compared to those without MetS. GGT levels were also significantly higher (p<0.001) in the MetS group; however, there was no significant difference in ALT and uric acid levels between the two groups. The lipid profile analysis revealed that TC and TG levels were significantly elevated, while HDL-C was significantly lower in subjects with MetS compared to those without MetS (p<0.001). There was no significant difference in LDL-C levels between the two groups.

Table 2. Biochemical parameters of study subjects according to metabolic syndrome (n=330).

Variables	Subjects with MetS (n=147)	Subjects without MetS (n=183)	p-value
FPG (mmol/L)	6.51±1.41	4.78±0.63	**<0.001***
FPI (μU/ml)	13.47±±5.80	7.39±3.41	**<0.001***
HOMA-IR	1.85±0.83	0.98±0.47	**<0.001***
GGT (U/L)	33.18±15.69	17.90±7.15	**<0.001***
ALT (U/L)	24.78±6.86	23.20±6.00	0.201

Variables	Subjects with MetS (n=147)	Subjects without MetS (n=183)	p-value
Uric acid (mg/dl)	3.96±2.60	3.86±1.75	0.814
TC (mg/dl)	189.47±29.59	168.11±21.11	**<0.001***
TG (mg/dl)	208.71±55.06	137.41±18.81	**<0.001***
HDL-C (mg/dl)	32.53±4.91	37.54±5.66	**<0.001***
LDL-C (mg/dl)	108.65±29.02	104.39±21.19	0.376

Data were expressed as mean±SD

Unpaired student t-test was performed to compare between two groups.

Table 3 displays the mean ± SD of various parameters for study subjects based on insulin resistance status. Individuals with insulin resistance had significantly higher BMI, WC, and BP compared to those without insulin resistance ($p<0.001$). There was no significant difference in age between the two groups. Serum GGT levels were notably higher in subjects with insulin resistance ($p<0.001$). All lipid profile components showed significant differences between the two groups. However, there were no significant differences in serum ALT and uric acid levels between those with and without insulin resistance.

Table-3. Characteristics of study subjects according to insulin resistance (n=330).

Variables	Subjects with IR (n=132)	Subjects without IR (n=198)	p-value
Age (years)	39.59±12.37	39.23±12.90	0.883
BMI (kg/m^2)	28.09±4.28	22.42±3.90	**<0.001***
WC (cm)	99.32±12.51	83.68±10.82	**<0.001***
SBP (mmHg)	127.73±13.57	111.36±10.36	**<0.001***
DBP (mmHg)	88.41±9.63	74.62±9.21	**<0.001***
FPG (mmol/L)	6.51±1.51	4.91±0.72	**<0.001***
Insulin (µU/ml)	15.30±4.63	6.63±2.50	**<0.001***
GGT (U/L)	34.07±15.33	18.47±8.50	**<0.001***
ALT (U/L)	24.57±6.57	23.45±6.32	0.375
Uric acid (mg/dl)	3.95±2.43	3.87±1.98	0.845
TC (mg/dl)	193.73±28.60	166.89±20.38	**<0.001***
TG (mg/dl)	206.75±57.90	144.12±29.66	**<0.001***
HDL-C (mg/dl)	31.73±4.28	37.70±5.59	**<0.001***
LDL-C (mg/dl)	112.77±27.43	101.97±22.34	**<0.05***

Data were expressed as mean±SD

Unpaired student t-test was done to compare between two groups.

Table 4 presents the characteristics of the overall study population, as well as separately for male and female subjects. The only significant gender difference observed was in BMI, which was higher in females ($p<0.05$). All other parameters showed no significant variation between genders.

Table 4. Characteristics of all study population, male subjects and female subjects (n=330).

Variables	Total (n=330)	Male (n=174)	Female (n=156)	p-value
Age (years)	39.37±12.63	41.07±12.94	37.48±12.13	0.138
BMI (kg/m^2)	24.68±4.91	23.63±4.27	25.86±5.33	**<0.05***
WC (cm)	89.94±13.81	92.62±11.85	88.69±16.20	0.147
SBP (mmHg)	117.91±14.20	118.10±12.31	117.50±16.19	0.825
DBP (mmHg)	80.14±11.54	80.52±10.33	79.52±12.77	0.652
FPG (mmol/L)	5.55±1.35	5.53±1.30	5.60±1.43	0.795
FPI (μU/ml)	10.10±5.51	10.63±5.90	9.51±5.04	0.287
HOMA-IR	1.37±0.79	1.44±0.77	1.29±0.80	0.341
GGT (U/L)	24.71±13.95	25.86±14.58	23.42±13.24	0.363
ALT (U/L)	23.90±6.42	23.98±6.67	23.81±6.19	0.887
Uric acid (mg/dl)	3.90±2.16	4.12±2.39	3.66±1.86	0.266
TC (mg/dl)	177.63±27.29	177.98±27.86	177.23±26.90	0.886
TG (mg/dl)	169.17±52.89	173.12±55.34	166.96±51.14	0.547
HDL-C (mg/dl)	35.31±5.88	34.46±6.82	36.07±4.81	0.153
LDL-C (mg/dl)	106.29±24.95	105.45±28.08	107.23±21.16	0.710

Data were expressed as mean±SD

Unpaired student t-test was done to compare between males and females.

Table 5 details the characteristics of study subjects categorized by tertiles of serum GGT. There were no significant age differences between subjects across the different GGT tertiles. However, those in the higher tertiles had significantly elevated levels of BMI, WC, BP, FPG, insulin, HOMA-IR, ALT, TC, and TG, along with lower HDL-C. Serum uric acid levels did not vary significantly among the different GGT tertiles.

Table 5. Characteristics of study subjects according to tertiles of serum GGT (n=330).

Variables	Serum GGT tertile (U/L)			p-value
	Tertile 1(<18) (n=111)	Tertile 2 (18-27) (n=111)	Tertile 3 (>27) (n=108)	
Age (years)	38.42±12.85	37.68±13.30	40.58±11.86	0.593
BMI (kg/m^2)	21.65±3.68	25.04±4.83	27.44±4.41	**<0.001***
WC (cm)	82.03±9.51	87.54±12.26	102.72±11.16	**<0.001***

Variables	Serum GGT tertile (U/L)			p-value
	Tertile 1(<18) (n=111)	Tertile 2 (18-27) (n=111)	Tertile 3 (>27) (n=108)	
SBP (mmHg)	108.11±10.76	115.68±6.03	130.00±14.69	**<0.001***
DBP (mmHg)	72.57±9.10	78.38±8.34	89.44±10.13	**<0.001***
FPG (mmol/L)	4.57±0.71	5.31±0.47	6.84±1.49	**<0.001***
FPI (μU/ml)	6.60±3.11	9.61±4.24	14.19±5.98	**<0.001***
HOMA-IR	0.84±0.44	1.29±0.54	1.99±0.85	**<0.001***
ALT (U/L)	21.24±5.50	25.16±6.66	25.33±6.34	**<0.05***
Uric acid (mg/dl)	3.57±1.67	4.02±2.20	4.12±2.55	0.506
TC (mg/dl)	171.05±22.86	175.22±21.89	186.86±33.90	**<0.05***
TG (mg/dl)	131.86±20.63	154.92±21.61	225.33±54.63	**<0.001***
HDL-C (mg/dl)	39.95±4.82	35.46±4.26	30.39±4.16	**<0.001***
LDL-C (mg/dl)	104.51±23.41	107.22±20.21	107.17±30.82	0.870

Data were expressed as mean±SD

ANOVA test was done to compare among three groups

Table 6 presents the results of comparisons between the tertiles using the Bonferroni test. It revealed that WC was significantly higher in tertile 3 compared to both tertile 1 and tertile 2, though there was no significant difference between tertile 1 and tertile 2. BP, FPG, HOMA-IR, ALT, and TG were significantly higher, while HDL-C was significantly lower in tertile 3 and tertile 2 compared to tertile 1. Except for ALT, these parameters also showed significant differences between tertile 2 and tertile 3.

Table 6. Post-hoc (Bonferroni test) for multiple comparison between groups based on GGT tertiles.

Variables	Post-hoc test		
	Tertile 1 vs Tertile 2 p-value	Tertile 1 vs Tertile 3 p-value	Tertile 2 vs Tertile 3 p-value
WC (cm)	0.102	<0.001	<0.001
SBP (mmHg)	<0.05	<0.001	<0.001
DBP (mmHg)	<0.05	<0.001	<0.001
FPG (mmol/L)	<0.01	<0.001	<0.001
HOMA-IR	<0.01	<0.001	<0.001
ALT (U/L)	<0.05	<0.05	1.000
TG (mg/dl)	<0.05	<0.001	<0.001
HDL-C (mg/dl)	<0.001	<0.001	<0.001

Table 7 displays the correlations between GGT and components of MetS as well as HOMA-IR. Significant correlations between GGT and HOMA-IR were found across all subjects, and these correlations were also significant within both male and female subjects.

Table 7. Correlation of serum GGT with HOMA-IR..

Variables	All subjects		Male		Female	
	r-value	p-value	r-value	p-value	r-value	p-value
WC (cm)	+.670	**<0.001**	+.731	**<0.001**	+.614	**<0.001**
SBP (mmHg)	+.735	**<0.001**	+.764	**<0.001**	+.729	**<0.001**
DBP (mmHg)	+.628	**<0.001**	+.557	**<0.05**	+.707	**<0.001**
FPG (mmol/L)	+.804	**<0.001**	+.820	**<0.001**	+.806	**<0.001**
TG (mg/dl)	+.823	**<0.001**	+.842	**<0.001**	+.793	**<0.001**
HDL-C (mg/dl)	-.619	**<0.001**	-.663	**<0.001**	-.656	**<0.001**
HOMA-IR	+.567	**<0.001**	+.511	**<0.05**	+.652	**<0.001**

Correlations were determined by Pearson's correlation coefficient test

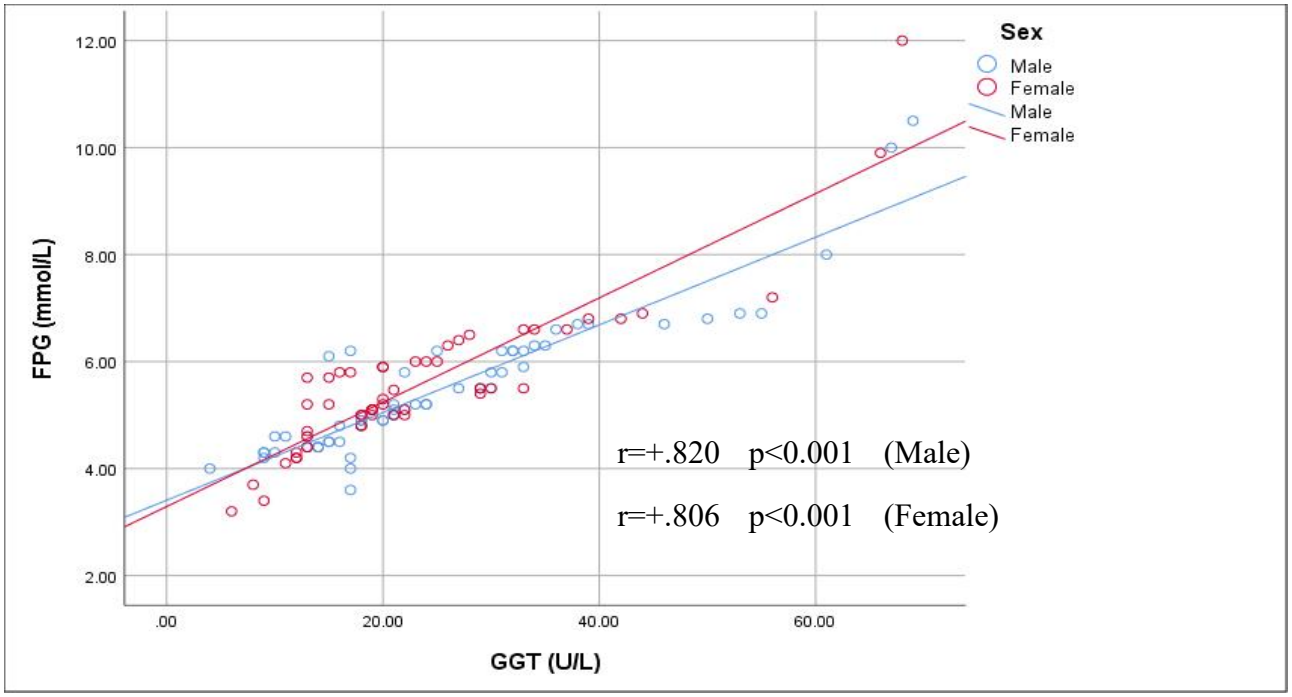

Figure 1. Correlation of serum GGT with FPG in male and female.

Figure 1 illustrates the correlation between GGT and FPG in both males and females. It is clear that these two variables are positively and significantly correlated (p<0.001) in both gender.

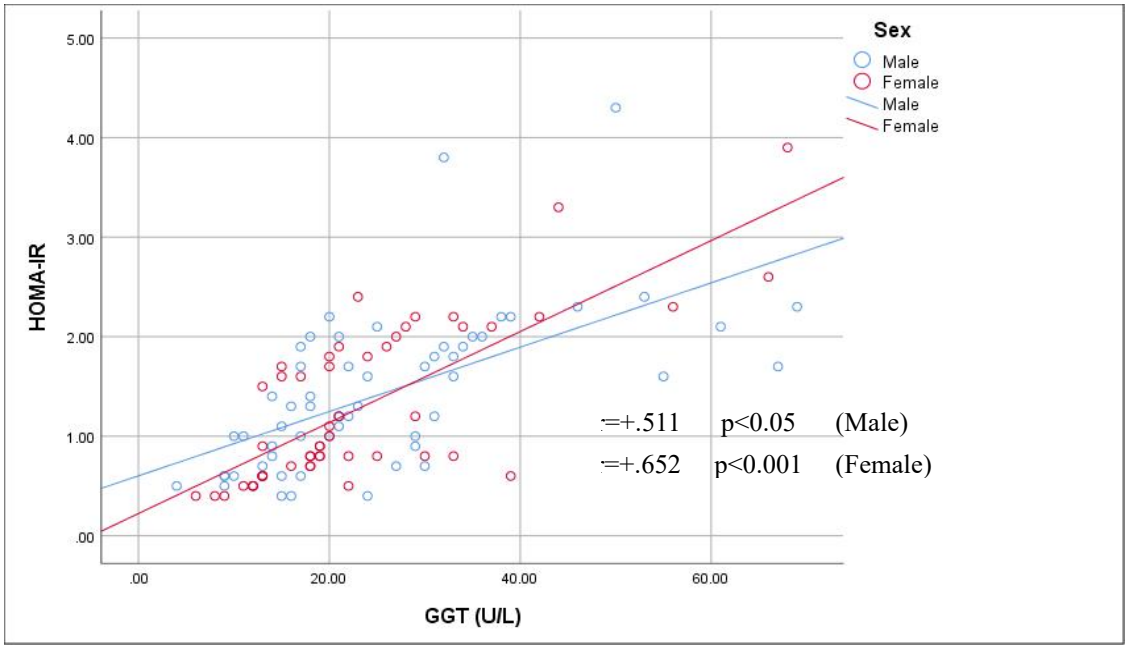

Figure 2. Correlation of serum GGT with HOMA-IR in male and female.

Figure 2 demonstrates the correlation between GGT and HOMA-IR in both males and females. It is evident that the two variables are positively and significantly correlated, with a significant correlation in males ($p<0.05$) and an even stronger one in females ($p<0.001$).

Table 8 presents the results of multiple linear regression analysis for HOMA-IR with various confounding independent variables. In model 1, a positive association was observed between HOMA-IR and both BMI ($p<0.05$) and TG ($p<0.05$). However, after including serum GGT in model 2, only BMI retained its significance ($p<0.05$), while serum GGT showed an independent linear association with HOMA-IR ($p<0.001$).

Table 8. Multiple Linear regression analysis of the relation between HOMA-IR and variables of interest in study subjects (n=330).

Variables	Model 1 (R^2=0.608)		Model 2 (R^2=0.606)	
	β	p-value	β	p-value
Age (years)	.004	0.327	.003	0.389
Sex	-.177	0.096	-.152	0.161
BMI (kg/m2)	.040	**<0.05***	.038	**<0.05***
WC (cm)	.013	0.059	.011	0.099
SBP (mmHg)	.004	0.518	.003	0.659
DBP (mmHg)	.006	0.385	.002	0.815
TC (mg/dl)	.010	0.221	.008	0.240
TG (mg/dl)	.014	**<0.05**	.011	0.071
HDL-C (mg/dl)	-.008	0.498	-.001	0.962
LDL-C (mg/dl)	.003	0.394	.001	0.874
ALT (U/L)	.002	0.832	.001	0.934
Uric acid (mg/dl)	.009	0.119	.009	0.117
GGT (U/L)			.022	**<0.001***

a. Dependent variable: HOMA-IR. The analysis was first conducted including all variables except serum GGT (Model 1), then repeated with serum GGT forced into the (Model 2). β for standardized coefficient. R^2 for adjusted R square (multiple coefficient of determination).

4. Discussion

Elevated GGT levels are linked to insulin resistance and metabolic syndrome (MetS). Serum GGT contributes to the extracellular catabolism of glutathione, a major thiol antioxidant. This leads to increased production of Reactive Oxygen Species (ROS), oxidative stress, inflammation, and impaired insulin signaling in the liver, muscle, and adipose tissue[21,22]. Insulin resistance causes reduced glucose clearance in skeletal muscle, impaired glucose production by the liver, and increased lipolysis in adipose tissue, leading to hyperglycemia and dyslipidemia. Elevated GGT is also linked to hepatic steatosis, which is strongly associated with MetS[23].

In this study, gender differences were generally not significant for most parameters, except for BMI, which was notably higher in females than in males (see **Table 4**). Individuals with Metabolic Syndrome (MetS) had significantly elevated levels of GGT, BMI, waist circumference (WC), and blood pressure (BP) compared to those without MetS (**Tables 1 and 2**). Those in the higher tertiles of GGT also showed significantly increased BMI, WC, and BP (**Table 5**). A significant positive correlation was found between GGT levels and both WC and BP (**Table 7**). These findings indicate a connection between elevated GGT levels and both abdominal obesity and high blood pressure. This is consistent with the studies by Lawlor et al[24]. and Kawamoto et al[25], which also linked oxidative stress and insulin resistance—affected by serum GGT—with obesity and hypertension[22]. In individuals with MetS, serum levels of triglycerides (TG) and total cholesterol (TC) were significantly higher, while HDL cholesterol (HDL-C) levels were significantly lower compared to those without MetS (Table 2). Participants in higher GGT tertiles also had elevated TG and TC levels but lower HDL-C levels (**Table 5**). A significant positive correlation was observed between GGT concentration and TG, while a negative correlation was found with HDL-C **(Table 7)**. These results are in line with Masilamani et al[18]. Additionally, this study identified a linear relationship between serum GGT and insulin resistance (IR) (**Table 8**). Insulin resistance in adipose tissue may increase lipolysis[26], leading to an increased flow of free fatty acids to the liver, which stimulates higher hepatic TG synthesis. This results in increased secretion of VLDL from the liver into the bloodstream[27]. The low HDL-C levels observed in MetS are attributed to high TG levels in the blood. Elevated TG levels lead to the exchange of TG and cholesteryl esters between LDL, VLDL, and HDL particles facilitated by cholesteryl ester transfer protein (CETP), resulting in TG-rich HDL that are more prone to breakdown[16-19].

MetS components, except HDL-C, compared to those without insulin resistance (**Table 3**). Participants in higher GGT tertiles also had increased levels of fasting plasma glucose (FPG), insulin, and HOMA-IR (**Table 5**). Positive correlations between GGT and both FPG and HOMA-IR were observed **(Table 7**), supporting a link between elevated GGT levels and insulin resistance. These findings are consistent with Marchesini et al[28] and Kang et al.[29], who noted a strong relationship between GGT and hepatic insulin resistance. The study also highlighted that the association between GGT and MetS was significantly influenced by insulin resistance (HOMA-IR). After adjusting for factors such as age, gender, BMI, ALT, uric acid, and LDL-C, GGT's association with MetS diminished, becoming insignificant when HOMA-IR was also adjusted for. This indicates that GGT's relationship with MetS is primarily due to insulin resistance. Multiple linear regression analysis confirmed a significant independent link between GGT and HOMA-IR **(Table 8)**. Similar results were reported by Kawamoto et al[13]. and Kim et al.[16], who found that higher

serum GGT levels are a significant predictor of MetS, even when accounting for various demographic and lifestyle factors.

Serum GGT is a sensitive indicator of biliary obstruction and alcohol consumption, and its levels are elevated in various liver conditions, including primary biliary cirrhosis (PBC), viral hepatitis, fatty liver disease, and drug-induced liver injury. Given that these liver diseases can sometimes be asymptomatic[30], some participants in the study might have had undiagnosed subclinical liver conditions. However, the effect of these liver conditions on the study's results is likely minimal because PBC is rare and participants with a history of viral hepatitis were screened out. Furthermore, the link between serum GGT and MetS remained significant even after adjusting for ALT levels. The precise mechanism through which GGT reflects the risk of MetS and insulin resistance (IR) is not fully understood. Increased GGT activity leads to the breakdown of glutathione[31]. This breakdown produces reducing agents that convert ferric to ferrous ions, generating superoxide and hydrogen peroxide[17,24]. Elevated GGT levels thereby enhance oxidative stress, which triggers inflammation and impairs insulin signaling in the liver, muscle, and adipose tissue, contributing to MetS[24]. Additionally, high GGT levels, even within the normal range, are often associated with hepatic steatosis, which correlates with visceral fat accumulation and increased lipolysis[32]. Hepatic steatosis can lead to hepatic insulin resistance, and chronic hepatic IR can result in metabolic disturbances[33]. Moreover, inflammation induced by elevated GGT levels can disrupt insulin signaling in the liver and other organs[34].

5. Conclusion

In conclusion, this study highlights the significant association between elevated gamma-glutamyl transferase (GGT) levels and the prevalence of metabolic syndrome (MetS) and insulin resistance (IR) among the study population. The findings reveal that individuals with MetS exhibit higher levels of GGT, along with increased body mass index (BMI), waist circumference (WC), and blood pressure (BP). Moreover, a positive correlation was observed between GGT levels and various metabolic parameters, including triglycerides and fasting plasma glucose, indicating that elevated GGT may contribute to the development of dyslipidemia and impaired glucose metabolism. The relationship between GGT and MetS was found to be primarily mediated by insulin resistance, underscoring the importance of GGT as a potential biomarker for metabolic health. These results suggest that monitoring GGT levels could serve as an effective strategy for early detection and management of metabolic disturbances, potentially guiding interventions to prevent the progression of metabolic syndrome and its associated complications. Further research is warranted to elucidate the underlying mechanisms through which GGT influences metabolic pathways and to explore its role as a therapeutic target in managing metabolic disorders.

6. Acknowledgments

The authors are grateful to the participants of the study.

Funding

None

Conflict of interest

The authors have no conflict of interest to declare.

References

1. Scott, R., Donoghoe, M., Watts, G.F., O'Brien, R., Pardy, C., Taskinen, M.R., Davis, T.M., Colman, P.G., Manning, P., Fulcher, G. and Keech, A.C., 2011. Impact of metabolic syndrome and its components on cardiovascular disease event rates in 4900 patients with type 2 diabetes assigned to placebo in the FIELD randomised trial. *Cardiovascular Diabetology*, *10*(1), p.102.
2. International Diabetes Federation, 2006. The IDF consensus worldwide definition of the metabolic syndrome. *IDF Communications*, pp.1-23.
3. Singh, B. and Saxena, A., 2010. Surrogate markers of insulin resistance: A review. *World Journal of Diabetes*, *1*(2), p.36.
4. Burtis, C.A. and Bruns, D.E., 2014. *Tietz fundamentals of Clinical Chemistry and Molecular Diagnostics, 7th edn,* Elsevier, St. Louis, Missouri, USA.
5. Meisinger, C., Döring, A., Schneider, A. and Löwel, H., 2006. Serum γ-glutamyltransferase is a predictor of incident coronary events apparently healthy men from the general population. *Atherosclerosis*, *189*(2), pp.297-302.
6. Mason, J.E., Starke, R.D. and Van Kirk, J.E., 2010. Gamma-Glutamyl transferase: a novel cardiovascular risk BioMarker. *Preventive Cardiology*, *13*(1), pp.36-41.
7. Hotamisligil, G.S., 2003. Inflammatory pathways and insulin action. *International Journal of Obesity*, *27*(S3), p.S53.
8. Park, Y.W., Zhu, S., Palaniappan, L., Heshka, S., Carnethon, M.R. and Heymsfield, S.B., 2003. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988-1994. *Archives of Internal Medicine*, *163*(4), pp.427-436.
9. Kavsak, P., 2017. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics,* edited by Nader Rifai, Andrea Rita Horvath and Carl T. Wittwer,6th edn, Elsevier, St. Louis, Missouri, USA.
10. Nestel, P., Lyu, R., Low, L.P., Sheu, W.H.H., Nitiyanant, W., Saito, I. and Tan, C.E., 2007. Metabolic syndrome: recent prevalence in East and Southeast Asian populations. *Asia Pacific Journal of Clinical Nutrition, 16*(2), pp.362-367.
11. Mainuddin, A.K.M., Choudhury, K.N., Ahmed, K.R., Akter, S., Islam, N. and Masud, J.H.B., 2013. The metabolic syndrome: comparison of newly proposed IDF, modified ATP III and WHO criteria and their agreements. *Cardiovascular Journal*, *6*(1), pp. 17-22.
12. Chowdhury, M.Z.I., Anik, A.M., Farhana, Z., Bristi, P.D., Al Mamun, B.A., Uddin, M.J., Fatema, J., Akter, T., Tani, T.A., Rahman, M. and Turin, T.C., 2018. Prevalence of metabolic syndrome in Bangladesh: a systematic review and meta-analysis of the studies. *BMC Public Health*, *18*(1), p.308.
13. Borai, A., Livingstone, C. and Ferns, G.A., 2007. The biochemical assessment of insulin resistance. *Annals of Clinical Biochemistry*, *44*(4), pp.324-342.
14. Lee, D.H., Blomhoff, R. and Jacobs, D.R., 2004. Review is serum gamma glutamyltransferase a marker of oxidative stress. *Free Radical Research*, *38*(6), pp.535-539.
15. Nakanishi, N., Suzuki, K. and Tatara, K., 2004. Serum γ-glutamyltransferase and risk of metabolic syndrome and type 2 diabetes in middle-aged Japanese men. *Diabetes Care*, *27*(6), pp.1427-1432.
16. Inoue, K., Hirohara, J., Nakano, T., Seki, T., Sasaki, H., Higuchi, K., Ohta, Y., Onji, M., Muto, Y. and Moriwaki, H., 1995. Prediction of prognosis of primary biliary cirrhosis in Japan. *Liver*, *15*(2), pp.70-77.

17. Whitfield, J.B., 2001. Gamma glutamyl transferase. *Critical Reviews in Clinical Laboratory Sciences*, *38*(4), pp.263-355.
18. Lee, D.H., Ha, M.H., Kim, J.H., Christiani, D.C., Gross, M.D., Steffes, M., Blomhoff, R. and Jacobs, D.R., 2003. Gamma-glutamyltransferase and diabetes—a 4 year follow-up study. *Diabetologia*, *46*(3), pp.359-364.
19. Chanda M, Biswas T, Roy MN, Sampa SR, Saha P, Sharna RJ, Islam S, Mahbub A, Rahman MA. Association of Liver Enzymes and Lipid Profile in Adults at Tertiary Level Hospitalin Bangladesh. J Natl Inst Lab Med Ref Bangladesh. 2021;1(1):17-24.
20. Kim, J.Y., Dhananjay, D., Ahn, S.V., Koh, S.B., Son, J.W., Lee, J.W., Youn, Y.J., Ahn, M.S., Ahn, S.G., Yoo, B.S. and Lee, S.H., 2016. Ps 11-70 A Prospective study Of serum γ-glutamyltransferase levels and incident of Metabolic Syndrome: The Arirang Study. *Journal of Hypertension*, *34*, p.352.
21. Marchesini, G., Avagnina, S., Barantani, E.G., Ciccarone, A.M., Corica, F., Dall'Aglio, E., Dalle Grave, R., Morpurgo, P.S., Tomasi, F. and Vitacolonna, E., 2005. Aminotransferase and gamma-glutamyl transpeptidase levels in obesity are associated with insulin resistance and the metabolic syndrome. *Journal of Endocrinological Investigation*, *28*(6), pp.333-339.
22. Kawamoto, R., Kohara, K., Tabara, Y., Miki, T. and Otsuka, N., 2009. Serum gamma-glutamyltransferase levels are associated with metabolic syndrome in community-dwelling individuals. *Journal of Atherosclerosis and Thrombosis, 16*(4), pp.355-362.
23. Xie, J., Zhang, S., Yu, X., Yang, Y., Liu, Z., Yuan, G. and Hu, S., 2018. Association between liver Enzymes with metabolically unhealthy obese phenotype. *Lipids in Health and Disease*, *17*(1), p.198.
24. Lawlor, D.A., Sattar, N., Smith, G.D. and Ebrahim, S., 2005. The associations of physical activity and adiposity with alanine aminotransferase and gamma-glutamyltransferase. *American Journal of Epidemiology*, *161*(11), pp.1081-1088.
25. Masilamani, V., Gopinath, P., Kandasamy, S. and Kumar, A., 2016. Association of Gamma-glutamyl transferase with Metabolic syndrome. *Medicine and Healthcare, 3*(100), pp.5498-5502
26. Sakugawa, H., Nakayoshi, T., Kobashigawa, K., Nakasone, H., Kawakami, Y., Yamashiro, T., Maeshiro, T., Tomimori, K., Miyagi, S., Kinjo, F. and Saito, A., 2004. Metabolic syndrome is directly associated with gamma glutamyl transpeptidase elevation in Japanese women. *World Journal of Gastroenterology*, *10*(7), p.1052.
27. Gorter, P.M., Olijhoek, J.K., van der Graaf, Y., Algra, A., Rabelink, T.J., Visseren, F.L. and SMART Study Group, 2004. Prevalence of the metabolic syndrome in patients with coronary heart disease, cerebrovascular disease, peripheral arterial disease or abdominal aortic aneurysm. *Atherosclerosis*, *173*(2), pp.361-367.
28. Kolovou, G.D., Anagnostopoulou, K.K. and Cokkinos, D.V., 2005. Pathophysiology of dyslipidaemia in the metabolic syndrome. *Postgraduate Medical Journal*, *81*(956), pp.358-366.
29. Kang, Y.H., Min, H.K., Son, S.M., Kim, I.J. and Kim, Y.K., 2007. The association of serum gamma glutamyltransferase with components of the metabolic syndrome in the Korean adults. *Diabetes Research and Clinical Practice, 77*(2), pp.306-313.
30. Marchesini, G., Brizi, M., Bianchi, G., Tomassetti, S., Bugianesi, E., Lenzi, M., McCullough, A.J., Natale, S., Forlani, G. and Melchionda, N., 2001. Nonalcoholic fatty liver disease: a feature of the metabolic syndrome. *Diabetes*, *50*(8), pp.1844-1850.

31. Kerner, A., Avizohar, O., Sella, R., Bartha, P., Zinder, O., Markiewicz, W., Levy, Y., Brook, G.J. and Aronson, D., 2005. Association between elevated liver enzymes and C-reactive protein: possible hepatic contribution to systemic inflammation in the metabolic syndrome. *Arteriosclerosis, Thrombosis, and Vascular biology*, *25*(1), pp.193-197.
32. Lindsay, R.S., Funahashi, T., Hanson, R.L., Matsuzawa, Y., Tanaka, S., Tataranni, P.A., Knowler, W.C. and Krakoff, J., 2002. Adiponectin and development of type 2 diabetes in the Pima Indian population. *The Lancet*, *360*(9326), pp.57-58.
33. Lomonaco, R., Ortiz-Lopez, C., Orsak, B., Webb, A., Hardies, J., Darland, C., Finch, J., Gastaldelli, A., Harrison, S., Tio, F. and Cusi, K., 2012. Effect of adipose tissue insulin resistance on metabolic parameters and liver histology in obese patients with nonalcoholic fatty liver disease. *Hepatology*, *55*(5), pp.1389-1397.
34. Abdiaziz AA, Hossain MB, Mahbub A, Islam S, Rahaman S, Rahman MA. Prevalence of Abnormal Lipid Profile Among Obese People in Mogadisho, Somalia. Asian Journal of Medicine and Health. 2024 Jun 26;22(7):194-203.