Original Research Article

Role of gamma glutamyl transferase as a diagnostic marker of metabolic syndrome

Abhinay Tibdewal[1], Sangamesh Asuti[2,*], Arun Narayan[3]

[1]Dept. of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India
[2]Dept. of Medicine, Gadag Institute of Medical Sciences, Gadag, Karnataka, India
[3]Dept. of Medicine, M.S. Ramaiah Medical College, Bengaluru, Karnataka, India

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ABSTRACT

Introduction: In an era of a cardiovascular epidemic, there is ongoing re search for more sensitive and specific markers of sub-clinical inflammation, atherogenesis, and increased adiposity. This study attempted to see the utility of serum gamma glutamyl transferase (GGT) as an ideal endogenous substance for the diagnosis of metabolic syndrome.

Materials and Methods: 180 patients attending medicine outpatient or inpatients in a tertiary care hospital of Bangalore were chosen comprising 90 cases of metabolic syndrome and equal number of controls. Study period was 2 years from September 2011–September 2013. GGT estimation and other biochemical parameters were obtained. Descriptive and analytical statistical tests were applied accordingly.

Results: In this study, 69% cases had higher GGT levels whereas another 25% were in the upper limit of normal in patients with metabolic syndrome. The sensitivity and specificity of GGT to diagnose patients with metabolic syndrome was found to be 67% and 100% in males and 94% and 98% in females respectively.($p<0.001$)

Conclusion: Hence study revealed elevated level of GGT among people with metabolic syndrome. The sensitivity of the test to diagnose metabolic syndrome was better in females; but specificity had no gender bias. Hence GGT as a marker can be proposed in the algorithm used for the evaluation of metabolic syndrome.

1. Introduction

The metabolic syndrome (syndrome X, insulin resistance syndrome) comprises of cluster of meta bolic abnormalities that promote risk of acquiring cardiovascular disease (CVD) and cerebrovascular disease.[1] Since the original definition by the World Health Organization in 1998, the criteria for the metabolic syndrome have evolved and are reflecting growing clinical evidence and analysis by a variety of consensus conferences and professional organizations. Central obesity, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol, hyperglycaemia, and hypertension are the major features of the metabolic syndrome.[1]

The prevalence of metabolic syndrome worldwide is 20-25% (IDF) . In India the overall prevalence is around 31.4%.[2] The upsurge in the prevalence of diabetes, obesity etc. is seen concomitantly with the rise in the number of patients with metabolic syndrome. In this sense, metabolic syndrome can considered as a cardiovascular risk factor. This syndrome not only includes, but is also strongly associated with, other complications of obesity, fatty liver, cholesterol gallstones, obstructive sleep apnoea, and polycystic ovarian syndrome.[3]

Several markers like adiponectin have been studied as a measure of increased adipose tissue but have not proven to be cost effective and easily available. Currently, the focus is on the pocket friendly and feasible biochemical marker is required to predict an early onset of this syndrome. Gamma Glutamyl Transferase (GGT) is one such marker which is cost effective, easily available and is routinely done as part of liver function tests.[4]

* Corresponding author.
E-mail address: drsagameshasuti@gmail.com (S. Asuti).

High levels of GGT have been associated in populations with increased risk of atherosclerotic cardiovascular disease (ASCVD).[5] Several prospective studies reported baseline serum GGT concentration as an independent risk factor for the development of non-communicable diseases like coronary artery disease (CAD), hypertension, diabetes mellitus and stroke.[6]

The purpose of this study is to evaluate the utility of GGT as a diagnostic marker of metabolic syndrome.

2. Materials and Methods

2.1. Study design

2.2. Case control study

2.3. Study area

The patients availing the medicine outpatient & inpatient services at MS Ramaiah Hospital were considered for the study.

2.4. Inclusion criteria

Satisfying the IDF criteria[7] as mentioned below:

1. Patients aged above 18 years
2. Central obesity – defined as waist circumference>=90cm for men and>=80 cm for women(Indian population)

And any two of the following four factors:-

1. Raised TG level>=150mg/dl or specific treatment for this lipid abnormality
2. Reduced HDL cholesterol<40mg/dl or specific treatment for this lipid abnormality
3. Raised B.P systolic>=130 diastolic>=85 or treatment for previously diagnosed hypertension
4. Raised FPG>=100mg/dl or previously diagnosed type 2 diabetic

2.5. Exclusion criteria

Hypothyroidism, malignant diseases, severe renal insufficiency, acute and chronic liver disease, chronic alcohol consumption and drugs like antiepileptics, oral contraceptive agents, trimethoprim, sulphamethoxazole, erythromycin and cimetidine.

2.6. Study period

A period of two years from September 2011 – September 2013

2.7. Sample size

It was estimated using N-master software considering sensitivity of GGT for the diagnosis of MS to be 0.77.

Relative precision (allowable error) was considered to be 10% and with the confidence interval of 95%, sample size was estimated to be approximately a minimum of 70. An equal number of age group and sex matched normal controls were recruited to compare the GGT levels. Hence the study was done on a total of 180 patients inclusive of both groups.

3. Method of data collection

Ethical clearance was obtained from the M S Ramaiah Medical College ethics committee prior to the start of study was taken. Data was collected by pretested semi structured questionnaire; clinical examination and necessary investigations (involved in IDF criteria) after taking written informed consent from the patients. An estimation of GGT was done for all the study subjects including cases and controls. The two groups were compared to fulfill the study objective. Reference range for normal GGT values at M S Ramaiah Hospital laboratories:

Males < 55 IU/L
Females<38 IU/L

3.1. Statistics

Data were entered serially in MS Excel and were analyzed using SPSS software version 20. Descriptive statistics, unpaired t test and fischer exact test were applied wherever necessary. p<0.05 was considered as statistically significant. Results were expressed in the form of text, figure and tables.

On comparison of the biochemical parameters among cases and control higher/raised values were seen among cases. Table 1

Among cases, 68.9% had GGT values above the reference range and also statistically significant. Table 2

The sensitivity was 69% and specificity was 100%. The positive predictive value of the test was 100% and negative predictive value was 76.2 %. There were 31% false negatives and nil false positives. Table 3

To calculate the best possible value for validity measure of GGT in males ROC curve analysis was done. The sensitivity and specificity through this analysis was computed as 90.7% and 97.6% respectively. The cut-off value of GGT for normal, through this analysis was 50 IU/L. Figure 1

To calculate the best possible value for validity measure of GGT in females ROC curve analysis was done. The sensitivity and specificity through this analysis was computed as 100% and 93.9% respectively. The cut-off value of GGT for normal, through this analysis was 36 IU/L.Figure 2

Table 1: Biochemical parameters of the cases and controls

|	Group	N	Mean	SD	Min	Max	't' value	'p' value
GGT(IU/L)	Case	90	52.49	6.004	37	61	279.420	<0.001
	Control	90	34.58	8.202	23	51		
FBS (mg/dl)	Case	90	142.25	59.792	64	315	69.709	<0.001
	Control	90	88.93	9.730	68	108		
HBA1C (%)	Case	90	8.414	2.2171	5.2	13.8	83.467	<0.001
	Control	90	6.204	.5923	5.2	7.8		
Triglyceride	Case	90	194.54	83.023	116	449	109.134	<0.001
	Control	90	100.52	19.936	92	144		
HDL Cholesterol	Case	90	37.89	10.358	17	54	58.717	<0.001
	Control	90	47.46	5.752	38	63		

Table 2: Serum GGT levels in cases and controls (above normal values)

Variable		Case (N=90)		Control (N=90)		X2 value #	'p' value
		n	%	n	%		
GGT(IU/L)	<55/38	28	31.1%	90	100%	94.576	<0.001
	≥55/38	62	68.9%	0	0%		

fischer exact test

Table 3: Sensitivity and specificity of GGT in diagnosis of metabolic syndrome

GGT result	Patients with metabolic syndrome (IDF criteria)	Patients without metabolic syndrome	Total
Positive(≥55/38 IU/L)	62	0	62
Negative(<55/38 IU/L)	28	90	118
Total	90	90	180
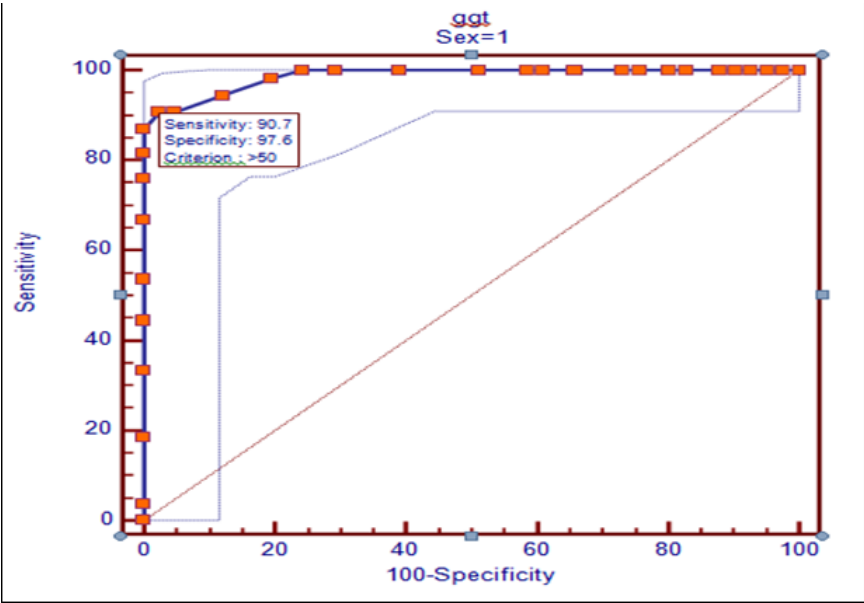
Fig. 1: ROC curve analysis for sensitivity and specificity of GGT in males
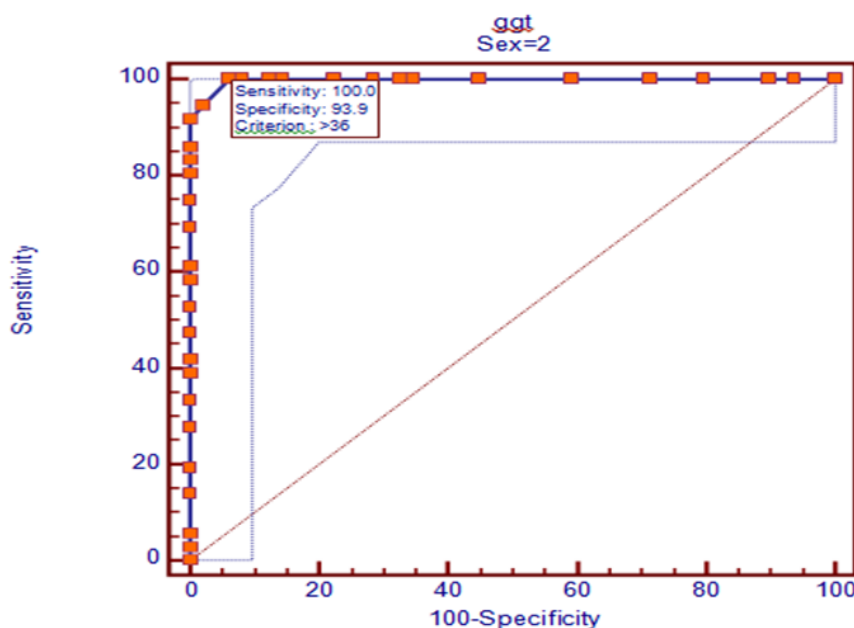
Fig. 2: ROC curve analysis for sensitivity and specificity of GGT in females

4. Results

A total of 180 patients (90 cases and 90 controls) were recruited in the study. Of the enrolled patients, the mean age of cases 52.8±5.89 years and controls was 54.1±12.484 years. Out of cases, 54(60%) were males and 36(40%) females and in control group, 49(54.4%) were females, 41(45.6%) were males. Mean BMI and waist/hip ratio of cases was 29.96± 2.56 kg/m² and 1.04±0.70 and control group was 24.17±0.76 kg/m² and 0.7 4±0.51 respectively. The SBP, DBP of cases were 135±15.17 mm of Hg and 86.44±6.30 mm of Hg respectively and control group were 120.22±7.74 mm of Hg and 73.31±4.78 mm of Hg.

5. Discussion

In our study, 180 subjects were recruited comprising 90 cases of metabolic syndrome and 90 age and sex matched controls. The mean age in the study group was 54.1±5.895 years and 52.8±12.4 years in the control group. In a similar study done by B Kasapgolu et al[4] and Harini G L et al,[8] the mean age was 51.3±3.2 years and 50.76±10.36 in cases and 50.78± 10.58 in controls respectively

Out of cases, 54(60%) were males and 36(40%) females and in control group, 49(54.4%) were females, 41(45.6%) were males. In a similar study done by B Kasapgolu et al,[4] the gender distribution showed 62% females and 38% males in the study group. Another study done by Vijayalakshmi Masalmani et al[2] included 42% males and 58% females in cases and 47% males and 53% females in the control group.

The mean BMI was 29.9±2.5 kg/m² in the study group and 24.17±0.76 kg/m² in the control group. The mean

waist-hip ratio was 1.04±0.07 in the study group and 0.74±0.05 in controls. The reference study[5] showed almost similar results; the mean waist circumference and BMI were 104.1±9.8 and 30.8±4.1 kg/m² respectively. Comparable findings were also seen in the study by R Shanmuga Priya et al[9] where the mean BMI was 26±4.47 in the study group and 23.46±3.06 in the control group. The above observation indicates that obesity and increased central adiposity are pivotal to the pathogenesis of metabolic syndrome.

The SBP, DBP of cases were 135±15.17 mm of Hg and 86.44±6.30 mm of Hg respectively and control group were 120.22±7.74 mm of Hg and 73.31±4.78 mm of Hg. In another study done by A O Rantala et al[10] higher values were observed with SBP being 160.2±20.3 and DBP being 98.2±10.2 which was significantly different from our study.

The mean HbA1C was 8.41±2.21, with 26% in the IGT group (HbA1C 5.7-6.4) and 74% in the diabetes group (HbA1C>6.5). Similar results were seen in a study done by Kishor phepale et al [13] where 73.6% of cases had HbA1C more than 6.5 whereas among controls only 24% had HbA1C more than 6.5 These observations suggest a high prevalence of type 2 diabetes in patients with metabolic syndrome.

The mean total cholesterol was 173.6±45.6, triglyceride was 194.5±83, HDL was 37.89±10.35, and LDL was 105.86±38.3. A total of 68 out of 90 cases had TG>150 including 40 males and 28 females. A total of 56 out of 90 cases had HDL <40mg/dl for males and <50mg/dl for females. The values in our study with respect to lipid profile were lower than the reference study wherein mean TG was 273.8±25.2, LDL was 131.4±8.9 and HDL was 42.1±9.7.

A similar finding was noted in the reference study[4] as well.

In the evaluation of liver function tests, GGT which is the biomarker being evaluated in this study had the following results. The mean GGT in the study group was 52.49 ± 6.04 and that in the control group was 34.58 ± 8.20. A total of 62 out of 90 cases had values of GGT (≥55 (males)/≥38 (females) IU/L) including 29 males and 33 females, comprising 69% of the study group (P<0.001). In the control group none of the subjects had GGT levels above the normal range. In a similar study done by B.Kasapgolu et al[4] the mean GGT among cases was 40.9 ± 10.2 and it was 21.0 ± 7.1 in the controls. In a study done by Gurjar BS[14] GGT values were 53.39 ± 19.12 among cases and 32.78 ± 10.71 in control group and similarly a study done by Vijayalakshmi Masalmani et al[4] showed 74.77 ± 15.36 and 40.91 ± 8.3

The sensitivity and specificity of GGT to diagnose metabolic syndrome was found to be 67% and 100% in males and 94% and 98% in females respectively in our study. Comparable findings were seen in the study done by Harini GL et al[8] where the overall sensitivity was 92% and specificity was 88% and in study done by Kishor phepale et al[11] the overall sensitivity was 84% and specificity was 91.2%.

Thus, study showed that elevated level of GGT among people with metabolic syndrome. The sensitivity of the test to diagnose metabolic syndrome was better in females; but specificity had no gender bias. Considering the CVD risk primary prevention may be emphasized in patients of metabolic syndrome with high GGT values. Hence GGT as a marker can be proposed in the algorithm used for the evaluation of metabolic syndrome.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Author biography

Abhinay Tibdewal Assistant Professor

Sangamesh Asuti Assistant Professor

Arun Narayan Professor