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METABOLIC SYNDROME;
GAMMA GLUTAMYLTRANSFERASE IN PATIENTS

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ABSTRACT… Objective: To determine the role of gamma glutamyltransferase as a biochemical marker for the diagnosis of metabolic syndrome. **Study Design:** Cross sectional descriptive study. **Period:** One year. **Setting:** Department of Medicine, Liaquat University Hospital Hyderabad / Jamshoro. **Methods:** All the patients with metabolic syndrome visited at OPD / admitted in the ward were further evaluated for serum gamma-glutamyltransferase level. The data was analyzed in SPSS 16 and the frequency and percentage was calculated. **Results:** During one year study period, total one hundred patients (23 males and 77 were females) with metabolic syndrome were recruited and study for gamma glutamyl transferase level. The mean age ±SD for overall population was 56.84±6.52 whereas it was 48.92±5.82 and 58.61±7.73 in male and female population respectively. The mean ± SD of systolic and diastolic blood pressure (mmHg), triglycerides (mg/dl), high density lipoprotein pressure (mg/dl) and fasting blood sugar (mg/dl) in overall population was 161.20 ± 16.74 and 95.60 ± 8.34, 176.38 ± 11.93, 29.44 ± 2.90 and 108.42± 6.25. The mean gamma glutamyl transferase level in overall population was 86.75±7.74 while it was 84.83±5.32 and 89.52±6.84 in male and female population respectively. The gamma-glutamyltransferase was raised in 75 patients of which 13 were males and 62 were females (p=0.02) and majority of patients were 50-59 year age group (p <0.01). **Conclusions:** It is concluded that GGT is a good diagnostic tool in metabolic syndrome with statistical significant results.

Key words: Gamma glutamyltransferase, metabolic syndrome, Gamma GT, dyslipidemia, Lipid profile, Lipoproteins, HDL, Triglycerides, LDL and Cholesterol.

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INTRODUCTION

The metabolic syndrome also called syndrome X, insulin resistance syndrome) has certain metabolic abnormalities that are responsible for cardiovascular and cerebrovascular disorders.[1] The main components of the metabolic syndrome include central obesity, low high-density lipoprotein (HDL) cholesterol, hypertriglyceridemia, hypertension and hyperglycaemia.[2] The prevalence of obesity rises in Asia and an alarm for the burden of atherosclerotic cardiovascular disease (ASCVD).[3] Worldwide prevalence for metabolic syndrome is 20-25% (IDF) and together with type 2 diabetes the cardiovascular events are responsible for morbidity and mortality while others include systemic inflammation, dyslipidemia, hypertension and thrombotic tendency.[4] Recently all these factors / disorders compiled under the heading of metabolic syndrome and in this sense and represent a multiplex cardiovascular risk factor.[5] The metabolic syndrome does not include but associated with complications of obesity, i.e. fatty liver, gallstones, obstructive sleep apnoea, and polycystic ovarian syndrome.[6]

There has been a role of biochemical markers to predict and diagnose the onset of metabolic syndrome and early intervention can be taken by means of lifestyle changes, drug therapy and reduction in cardiovascular morbidity and mortality.[7] Studies are lacking in context to markers in the adult Pakistani population, the adiponectin have been studied previously as a measure of increased adipose tissue by somewhere else but not proved to be easily available and cost effective.[8,9] SO a prompt, easily available and cost effective biochemical marker is required to predict and evaluate the onset of this syndrome.

Gamma Glutamyl Transferase (GGT) is one such marker which is easily available, cost effective and performed as part of liver function tests.[10] Increase in levels of GGT has been associated with increased risk of atherosclerotic cardiovascular disease (ASCVD).[11] Former literature reported that baseline serum GGT concentration is a risk factor for the development of coronary artery disorders, diabetes mellitus, CVS and hypertension.[12]

The present study was conducted at Liaquat University Hospital Hyderabad; the purpose of present study was to detect the role of GGT as an early diagnostic tool for the metabolic syndrome.

PATIENTS AND METHODS

This cross sectional descriptive study of one year was conducted in the department of medicine at Liaquat University Hospital Hyderabad / Jamshoro. All the patients of, ≥20 years of age, either gender with metabolic syndrome evaluated by central obesity - waist circumference ≥90cm for men and ≥80 cm for women with any two of the following parameters: (a) Raised TG level ≥150mg/dl (b) Reduced HDL cholesterol<40mg/dl (c) Raised blood pressure systolic ≥130 diastolic ≥85 or known case of hypertension and (d) Raised FPG≥100mg/dl or known case of type II diabetic were recruited, enrolled and entered in the study while the patients with hypothyroidism, renal insufficiency, malignancy, chronic alcoholic, on drugs (erythromycin, cimetidine, antiepileptics, oral contraceptive agents, trimethoprim, sulphamethoxazole) were excluded from the study. The informed consent was taken from the every patient to participate in the study while the data was collected by structured proforma. The detail history was taken and clinical examination was done. The relevant investigations advised were, liver function tests (including GGT), viral markers, fasting lipid profile, fasting and random plasma glucose, HbA1C, rhyroid profile, renal function tests and ultrasound abdomen. All the patients with metabolic syndrome were assessed for gamma glutamyl transferase by taking 2cc venous blood sample and sent to laboratory for analysis. The references value of GGT for male was <55 IU/L and female was <38 IU/L. The data was entered, saved and analyzed in SPSS 16. The frequency and percentage (%) was calculated while the mean ± SD was calculated for numerical variables. The stratification was done for age, gender, GGT and metabolic syndrome, the chi-square test was applied on categorical variables and independent sample t-test was applied to compare the mean at 95% confidence interval and the p-value ≤0.05 was considered as statistical significant.

RESULTS

During one year study period, total one hundred patients with metabolic syndrome were recruited and study for gamma glutamyl transferase level. The mean age ±SD for overall population was 56.84±6.52 whereas it was 48.92±5.82 and 58.61±7.73 in male and female population respectively. The mean ± SD of systolic and diastolic blood pressure (mmHg), triglycerides (mg/dl), high density lipoprotein pressure (mg/dl) and fasting blood sugar (mg/dl) in overall population was 161.20 ± 16.74 and 95.60 ± 8.34, 176.38 ± 11.93, 29.44 ± 2.90 and 108.42± 6.25. The mean gamma glutamyl transferase level in overall population was 86.75±7.74 while it was 84.83±5.32 and 89.52±6.84 in male and female population respectively. The age in relation to gender and gamma glutamyl transferase is shown in Table I and II while the gender in relation to gamma glutamyl transferase is shown in Table III. The mean ± SD of waist circumference, systolic and diastolic blood pressure, triglycerides, high density lipoprotein (HDL) and fasting blood sugar (FBS) in relation to patients with raised gamma glutamyl transferase (GGT) is shown in Table IV-IX.

		GENDER		Total	P-value
		Male	Female		
AGE	20-29	2	3	5	
		8.7%	3.9%	5.0%	
	30-39	5	6	11	
		21.7%	7.8%	11.0%	
	40-49	10	19	29	
		43.5%	24.7%	29.0%	0.02*
	50-59	3	36	39	
		13.0%	46.8%	39.0%	
	60 +	3	13	16	
		13.0%	16.9%	16.0%	
Total		23	77	100	
		100.0%	100.0%	100.0%	

Table-I. The age in relation to gender

**P-value is statistically significant*
Pearson chi-square value = 11.43; df = 4

		GGT		Total	P-value
		Normal	Raised		
AGE	20-29	4	1	5	<0.01*
		16.0%	1.3%	5.0%	
	30-39	6	5	11	
		24.0%	6.7%	11.0%	
	40-49	6	23	29	
		24.0%	30.7%	29.0%	
	50-59	5	34	39	
		20.0%	45.3%	39.0%	
	60 +	4	12	16	
		16.0%	16.0%	16.0%	
Total		25	75	100	
		100.0%	100.0%	100.0%	

Table-II. The age in relation to gamma glutamyl transferase

**P-value is statistically significant*
Pearson chi-square value = 16.56; df = 4

		GGT		Total	P-value
		Normal	Raised		
GENDER	Male	10	13	23	0.02*
		40.0%	17.3%	23.0%	
	Female	15	62	77	
		60.0%	82.7%	77.0%	
Total		25	75	100	
		100.0%	100.0%	100.0%	

Table-III. The gender in relation to gamma glutamyl transferase

**P-value is statistically significant*
Pearson chi-square value = 5.43; df =

Gender	N = 75	Mean ±SD	P-value
Male	13	102.00 ± 4.12	0.01*
Female	62	106.16 ± 5.60	

Table-IV. The mean ± SD of waist circumference in patients with raised gamma glutamyl transferase

**P-value is statistically significant*

Gender	N = 75	Mean ±SD	P-value
Male	13	153.07 ± 14.51	0.05*
Female	62	162.90 ± 16.78	

Table-V. The mean ± SD of systolic blood pressure in patients with raised gamma glutamyl transferase

**P-value is statistically significant*

Gender	N = 75	Mean ±SD	P-value
Male	13	91.15± 3.62	0.03*
Female	62	96.53 ± 8.75	

Table-VI. The mean ± SD of diastolic blood pressure in patients with raised gamma glutamyl transferase

**P-value is statistically significant*

Gender	N = 75	Mean ±SD	P-value
Male	13	170.38 ± 8.33	0.04*
Female	62	177.64 ± 12.24	

Table-VII. The mean ± SD of triglycerides in patients with raised gamma glutamyl transferase

**P-value is statistically significant*

Gender	N = 75	Mean ±SD	P-value
Male	13	30.92 ± 3.12	0.04*
Female	62	29.12 ± 2.79	

Table-VIII. The mean ± SD of high density lipoprotein in patients with raised gamma glutamyl transferase

**P-value is statistically significant*

Gender	N = 75	Mean ±SD	P-value
Male	13	104.23 ± 3.46	<0.01*
Female	62	109.30 ± 6.36	

Table-IX. The mean ± SD of fasting blood sugar in patients with raised gamma glutamyl transferase

**P-value is statistically significant*

DISCUSSION

The need for the early diagnosis of metabolic syndrome is necessary to reduce the morbidity and mortality due to CVD. The role of GGT as a diagnostic tool of metabolic syndrome has been assessed in present study. In our study, one hundred subjects of metabolic syndrome were recruited and the subjects in the present study were found to be clustered in the fifth decade of life with 39% cases belonging to this category. There were 23 males and 77 females in the study group. In a study conducted by Kasapgolu B, et al, [13] the mean age was 54.42±32.21 and the gender distribution showed 62% females and 38% males in the study group. This suggested a higher incidence of metabolic syndrome in female population. In our study 90% patients

were from the urban area whereas 10% belonged to the rural community. The observation may be due to selection of patients from a tertiary care hospital but is consistent with former studies referring it to as the disease of urban population. The mean waist circumference in the study group was 102.00 ± 4.12 and 106.16 ± 5.60cm in the male and female population whereas the mean BMI was 31.95±53.62, the finding indicates that obesity and increased central adiposity have a role in the pathogenesis of metabolic syndrome. The mean systolic and diastolic blood pressure in male and female population was 153.07 ± 14.51 / 162.90 ± 16.78 and 91.15± 3.62 / 96.53 ± 8.75. The finding suggested that raised blood pressure is a major contributing factor as far as metabolic syndrome is concerned. The observations are consistent with the study by Kasapgolu B, et al[13] while another study done by A O Rantala AO, et al[14] had detected higher values (SBP 160.2±20.3 and DBP being 98.2±10.2) in subjects with metabolic syndrome. The mean fasting blood sugar was 104.23 ± 3.46 and 109.30 ± 6.36 in male and female population respectively while the mean HbA1C was 9.81±3.32 in overall population with metabolic syndrome. The finding suggested a high prevalence of type II diabetes in patients with metabolic syndrome. The values in relation to lipid profile were somewhat different than the former literature where mean TG was 279.84±29.21 and HDL was 40.52±5.73. This difference may be due to variations in diet, life style and familial metabolic parameters in specific geographic distributions. Hypertriglyceridemia is the main lipid disorder found in subjects with metabolic syndrome maximum number of cases in the study, the similar observation was identified by the Grundy SM, et al study as well.[15] With regard to the liver function tests, GGT which is the marker evaluated in the current series with following values, the mean gamma glutamyl transferase level in overall population was 86.75±7.74 while it was 84.83±5.32 and 89.52±6.84 in male and female population respectively, in a similar conducted by Kasapgolu B et al.[13]The mean GGT in the study group was 72.92±9.83, Ruttmann E et al[16] showed that GGT activity was associated with cardiovascular mortality. Devers MC, et al[17] also suggested that higher serum GGT levels is associated with development of CVD risk factors, including diabetes, hypertension, and the metabolic syndrome. The former literature comprising 13% of the metabolic syndrome population was suffering from cerebrovascular disease, of which 6% had elevated GGT values suggesting that raised GGT levels is a risk factor for cerebrovascular disease.

The GGT values even in the upper limit of normal may have a predictive importance in diagnosing patients with metabolic syndrome.[18,19] The most predominant LFT abnormality in patients with diabetes was isolated elevation of GGT. Meisinger C, et al[20] observed that GGT is an important predictor for incident type II diabetes mellitus in general population. In other studies, conducted by Bruckert E et al[21] and Onat A et al, [22] it has been found that circulating GGT and transaminases activities are raised in subjects with metabolic syndrome. Nannipieri, et al[23] revealed an association with mild disturbance in LFT in patients with metabolic syndrome. Moreover, Wannamethee et al,[24] revealed that; raised levels of GGT and ALT are found to be the independent predictors of type II diabetes mellitus. Rantala, et al[14] investigated the association between GGT and MS and revealed a highly significant relationship between GGT and the components of the metabolic syndrome even regardless of the curable factors. In present study the components of MS and GGT were statistically significant and it is consistent with the study by Sakugawa, et al[25] in which the serum GGT level was found to be higher and significant with the components of the MS.

Therefore in present study, the GGT has the highest correlation with hypertriglyceridemia, HDL, FBS and hypertension, and all are the important risk factors for cardiovascular and cerebrovascular diseases. Considering the cardiovascular disease risk, the primary prevention should be emphasized in subjects with metabolic syndrome have high GGT values. Hence GGT probably has placed in the algorithms for the assessment of metabolic syndrome and CVD risk evaluation.

CONCLUSIONS

This study has evaluated the use of GGT as a diagnostic marker of metabolic syndrome with significant results. An elevated level of gamma glutamyl transferase was found to be associated with metabolic syndrome and is a strong predictor of cardiovascular risk. It is related with all the components of MS with statistical significance. Therefore there is need for considering the values GGT in the context of metabolic syndrome and CVD risk.

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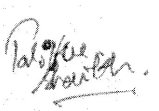
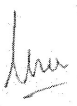
1	Dr. Tariq Zaffar Shaikh	Contriubtion to conception and deisng, acquision of data, analysis and terpretation of data	
2	Dr. Hamid Nawaz Ali Memon	Drafting the article and shares its expert research opinion and experience in finalizing the manuscript	
3	Dr. Nisar Ahmed Shah	Contributed in conection and interpretation fo data and give his expert view for manuscript designing	
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