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The Study of Serum Gamma Glutamyl Transferase Level in Patients with Metabolic Syndrome

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ABSTRACT

Gamma Glutamyl Transferase (GGT) belongs to Transferase enzymes. It is used as a diagnostic marker for liver disease.[1] Gamma Glutamyl Transferase was found to elevated in Metabolic Syndrome patients along with mildly elevated liver enzymes to the upper limit. The aim is to study the level of Serum Gamma Glutamyl Transferase in Metabolic Syndrome patients and to analyse for any association between serum GGT levels and parameters of Metabolic Syndrome. The study population is of 114 who are diagnosed as Metabolic Syndrome. Waist circumference, Body Mass Index (BMI), blood pressure, lipid profile, liver function test, fasting blood glucose of the subjects were recorded. Mean serum Gamma Glutamyl Transferase was 92.7 ± 52.5. An elevated GGT was found to be associated with Metabolic Syndrome subjects. Also there was a positive correlation between GGT and waist Circumference, triglycerides, erythrocyte sedimentation rate, liver function test.

Key words: Gamma Glutamyl Transferase, metabolic syndrome, waist circumference, triglycerides.

INTRODUCTION

The Metabolic Syndrome is a group of metabolic abnormalities that confers increased risk of cardiovascular diseases and diabetes mellitus[1]. The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low high-density lipoprotein, cholesterol, hyperglycemia, and hypertension.[1] The raise in the prevalence of obesity in India is threatening to increase the burden of Atherosclerotic cardiovascular disease (ASCVD).

The prevalence of metabolic syndrome worldwide is 20-25%.[2,3] There has been a consistent effort to evaluate biochemical markers to predict an early onset of Metabolic Syndrome and subsequently intervene appropriately by means of lifestyle changes and drug therapy and thereby reduce cardiovascular morbidity and mortality. Studies are lacking in the adult Indian population.

Markers like adiponectin have been studied as a measure of increased adipose but have not proven to be cost effective and easily available. Clearly a cost effective and easily available 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[5].High levels of GGT have been associated in populations with increased risk of Atherosclerotic cardiovascular diseases (ASCVD) [2,6]. Several prospective studies reported that baseline serum GGT concentration was an independent risk factor for the development of coronary artery disease (CAD), diabetes mellitus, stroke and hypertension[7].The purpose of this study is to evaluate the utility of GGT as an early marker in Metabolic Syndrome.

Objective

1. To study the level of Serum Gamma Glutamyl Transferase in Metabolic Syndrome patients.

2. To analyse for any association between serum GGT levels and parameters of Metabolic Syndrome

MATERIALS AND METHODS

A Hospital based cross sectional study done on patients with central obesity, hypertriglyceridemia, low HDL cholesterol, hypertension, type 2 diabetes mellitus at Sri Manakula Vinayagar Medical College and Hospital after clearance from institution research and ethics committee. Sample size is calculated as 114 using the reference article.[5]

Inclusion criteria: Those who are having three or more of the following were included in study,

1. Central obesity: waist circumference > 90 cm(M), > 80cm(F)
2. Hypertriglyceridemia: Triglycerides ≥ 150 mg/dl or specific medication.
   Low HDL cholesterol: < 40 mg/dl (male), < 50 mg/dl (females) or specific medication.
3. Hypertension: ≥ 130 mm of Hg Systolic or ≥ 85 mm of Hg Diastolic
4. Fasting plasma glucose level: ≥100 mg/dl or previously diagnosed type 2 diabetes mellitus

Exclusion criteria

1. Alcohol intake,
2. Liver and biliary diseases,
3. Use of hepatotoxic drugs (erythromycin, cimetidine, anti-epileptics, oral contraceptives),
4. Familial hyperlipidemia.

Data collection

After selecting appropriate patients written informed consent from the patient is obtained. Questionnaire was used to obtain clinical information. Body Mass Index (BMI) was calculated. Blood pressure, waist circumference were measured. 5 ml venous blood sample obtained after overnight fasting and following investigations were done:-

1) Serum total cholesterol,
2) HDL and LDL cholesterol,
3) Triglycerides,
4) Fasting glucose,
5) GGT
6) Liver function test.

Gamma glutamyl transferase analysis

Sampling, reagent delivery, mixing, processing, and printing of results are automatically performed by the dimension system. Reference range for normal GGT values at Sri Manakula Vinayagar Medical College and Hospital laboratories is 11- 50 IU/L.

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software.

RESULTS

Table 1: Age distribution of subjects with Metabolic Syndrome

		Count	%
Age	<40 Years	7	6.2%
	41 to 50 years	29	25.7%
	51 to 60 years	38	33.6%
	61 to 70 years	29	25.7%
	>70 years	10	8.8%

Table 2: Gender distribution of subjects

		Count	%
Gender	Female	59	52.2%
	Male	54	47.8%

Table 3: History of DM and HTN among Metabolic Syndrome subjects

		Count	%
DM	No	5	4.4%
	Yes	108	95.6%
HTN	No	25	22.1%
	Yes	88	77.9%

Table 4: Duration of DM and HTN

		DM		HTN	
		Count	%	Count	%
Duration	<5 years	31	28.7%	42	47.7%
	6 to 10 years	62	57.4%	43	48.9%
	>10 years	15	13.9%	3	3.4%
	Mean ± SD	7.73 ± 3.59		6.30 ± 3.56	

Table 5: Mean and SD of all the parameters measured in Metabolic Syndrome subjects

	Mean	SD
Waist Circumference	92.7	4.8
BMI	32.1	2.8
TC	187.2	51.6
TG	193.1	125.2
LDL	112.5	42.0
VLDL	32.5	13.1
HDL	37.9	7.8
FBS	171.2	80.1
HB%	11.1	2.3
WBC	9746.0	4207.9
Platelets	279150.4	125771.4
ESR	37.6	33.3
Blood Urea	30.9	20.1
Serum Creatinine	1.0	.8
Total Bilirubin	.8	.2
Direct Bilirubin	.3	.2
Indirect Bilirubin	.6	.1
SGOT	24.9	13.8
SGPT	23.5	16.7
Alkaline Phosphate	125.5	58.3
Total Protein	7.8	5.5
Serum Albumin	4.0	.6
GGT	92.7	52.5

Table 6: Mean and SD of all the parameters in comparison with GGT levels in Metabolic Syndrome subjects

	GGT Classification						SD
	<50		51 to 100		>100		
	Mean	SD	Mean	SD	Mean	SD	
Waist Circumference	91.9	4.9	91.4	4.3	93.6	4.8	0.112
BMI	33.4	3.1	30.9	1.6	31.5	2.6	0.001*
TC	197.4	53.2	193.5	60.6	178.2	46.9	0.170
TG	198.4	160.0	200.1	67.3	187.4	110.8	0.890
LDL	119.4	41.4	108.1	42.1	109.0	42.6	0.441
VLDL	32.4	12.8	37.4	11.9	31.3	13.5	0.258
HDL	38.4	5.4	37.5	11.0	37.6	8.3	0.867
FBS	179.3	79.4	183.7	70.6	161.8	83.3	0.461
HB%	11.3	1.8	11.9	2.1	10.7	2.6	0.162
WBC	9885.0	3319.1	9887.5	3702.9	9608.8	4902.1	0.942
Platelets	293100.0	149522.6	288437.5	132615.2	266754.4	105052.4	0.572
ESR	37.5	33.4	33.4	25.1	38.9	35.6	0..850
Blood Urea	29.2	15.2	27.7	7.2	33.0	24.9	0.525
Serum Creatinine	0.9	0.6	0.8	0.3	1.2	1.0	0.108
Total Bilirubin	0.8	0.1	0.8	0.2	0.9	0.3	0.161
Direct Bilirubin	0.3	0.1	0.3	0.2	0.3	0.2	0.960
Indirect Bilirubin	0.5	0.1	0.6	0.1	0.6	0.1	0.002*
SGOT	22.4	13.5	24.6	11.0	26.8	14.6	0.296
SGPT	20.9	12.4	27.2	12.4	24.3	19.9	0.390
Alkaline Phosphate	122.9	46.3	111.9	56.0	131.1	66.1	0.483
Total Protein	7.4	0.7	7.4	.8	8.2	7.7	0.759
Serum Albumin	3.9	0.5	4.0	.5	4.0	.6	0.772

In the study there was no significant difference in mean values of all the parameters measured in comparison with GGT levels except for BMI and Indirect Bilirubin. Mean BMI among those with GGT <50 was 33.4 ± 3.1, among those with GGT 51 to 100 was 30.9 ± 1.6 and among those with GGT >100 was 31.5 ± 2.6. Mean BMI was significant higher among those with normal GGT than with abnormal GGT. Were as Indirect bilirubin was lowest among those with GGT <50 and highest among those with abnormal GGT.

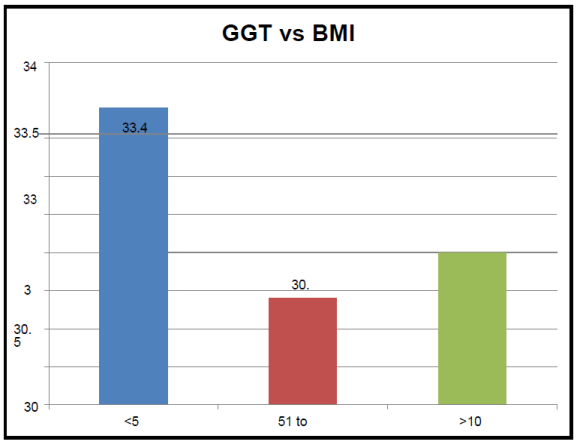

Figure 1: Bar diagram showing Mean BMI in comparison with GGT levels in Metabolic Syndrome subject

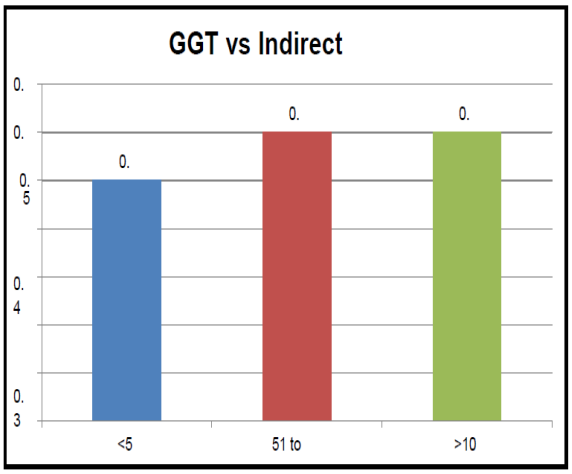

Figure 2: Bar diagram showing Mean Indirect Bilirubin in comparison with GGT levels in Metabolic Syndrome subjects.

Table 7: Correlation between GGT and Duration of DM and HTN

		GGT	DM	HTN
GGT	Pearson Correlation	1	-0.118	0.015
	P value		0.225	0.886
	N	113	108	88

In the study there was negative correlation between GGT and duration of DM i.e. with increase in Duration of DM there was decreased in GGT and vice versa. But the correlation was not statistically significant.

Were as there was positive correlation between GGT and duration of HTN i.e. with increase in duration of HTN there was increase in GGT. But the correlation was not statistically significant.

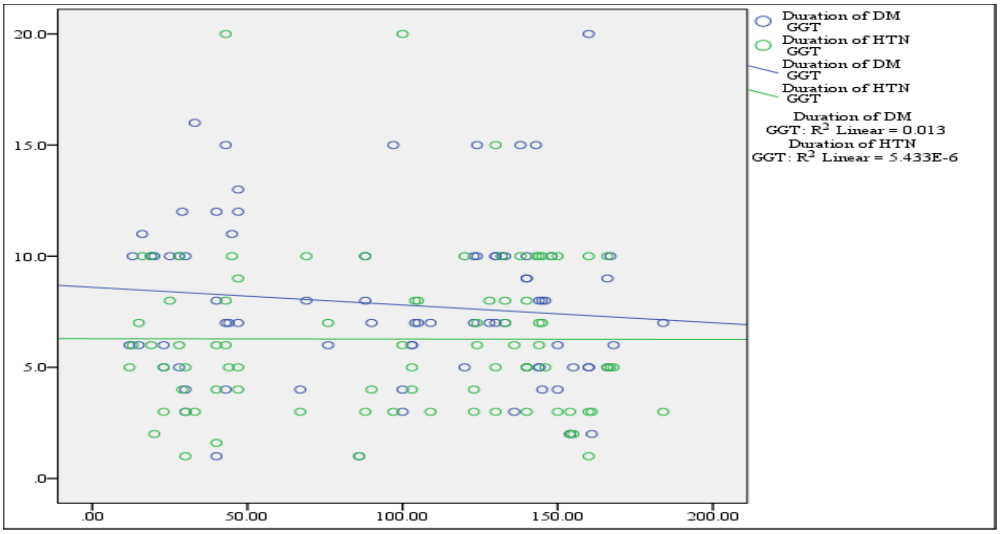

Figure 3: Scatter Plot showing Correlation between GGT and Duration of DM and HTN

Table 8: Correlation between GGT and Anthropometric measurements

		GGT	Waist Circumference	BMI
GGT	Pearson Correlation	1	0.196*	-0.209*
	P value		0.037*	0.026*
	N	113	113	113

In the study there was positive correlation between GGT and Waist Circumference i.e. with increase in Waist circumference there was increase in GGT and vice versa. This positive correlation was statistically significant.

In the study there was negative correlation between GGT and BMI i.e. with increase in BMI there was decrease in GGT and vice versa. This negative correlation was statistically significant.

In the study there was negative correlation between GGT and Lipid profile parameters, i.e. with increase in TC, TG, LDL, VLDL and HDL there was decrease in GGT and vice versa.

Among these parameters significant correlation was seen between GGT and TC. With other parameters there was no significant correlation.

Table 9: Correlation between GGT and Lipid Profile

		GGT	TC	TG	LDL	VLDL	HDL
GGT	Pearson Correlation	1	-0.190*	-0.078	-0.134	-0.044	-0.101
	P value		0.044	0.413	0.157	0.642	0.288
	N	113	113	113	113	113	113

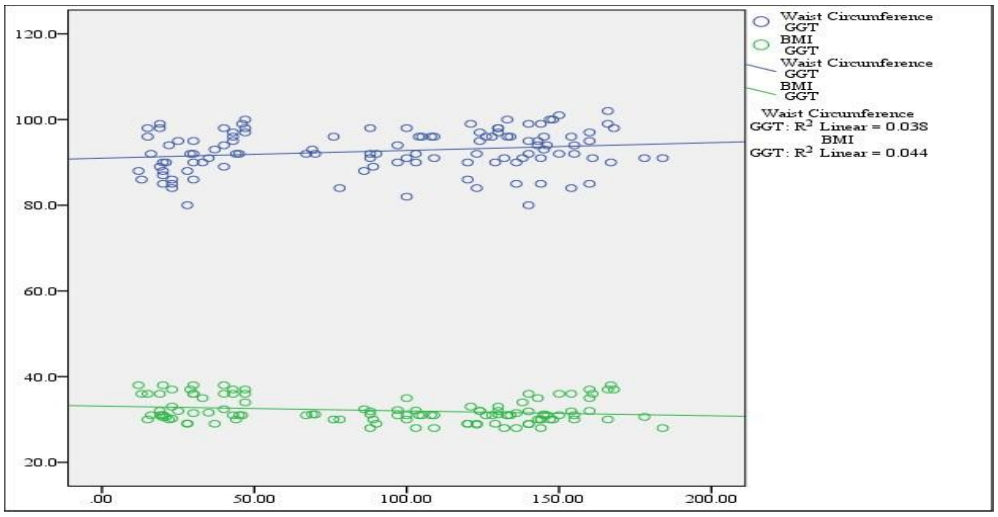

Figure 4: Scatter Plot showing Correlation between GGT and Anthropometric measurements

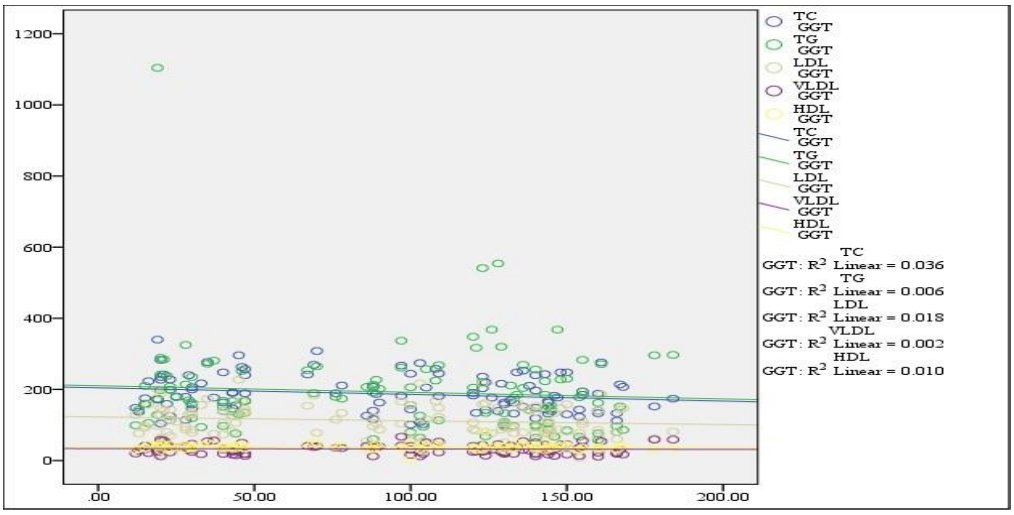

Figure 5: Scatter plot showing Correlation between GGT and Lipid Profile Table 10: Correlation between GGT and FBS

Table 10: Correlation between GGT and FBS

		GGT	FBS
GGT	Pearson Correlation	1	-0.088
	P value		0.356
	N	113	112

In the study there was negative correlation between GGT and FBS i.e. with increase in FBS there was decrease in GGT and vice versa. This negative correlation was not statistically significant

There was insignificant negative correlation between GGT and HB%, WBC and Platelet count. Insignificant positive correlation was observed between GGT and ESR.

Table 11: Correlation between GGT and CBC parameters

		GGT	HB%	WBC	Platelets	ESR
GGT	Pearson Correlation	1	-0.081	-0.029	-0.106	0.013
	P value		0.393	0.764	0.266	0.893
	N	113	113	113	113	112

Table 12: Correlation between GGT and Renal Profile

		GGT	Blood Urea	Serum Creatinine
GGT	Pearson Correlation	1	0.088	0.142
	P value		0.357	0.133
	N	113	113	113

Insignificant positive correlation was observed between GGT and Blood Urea and Serum Creatinine. i.e. with increase in Blood urea and serum Creatinine there was increase in GGT and vice versa.

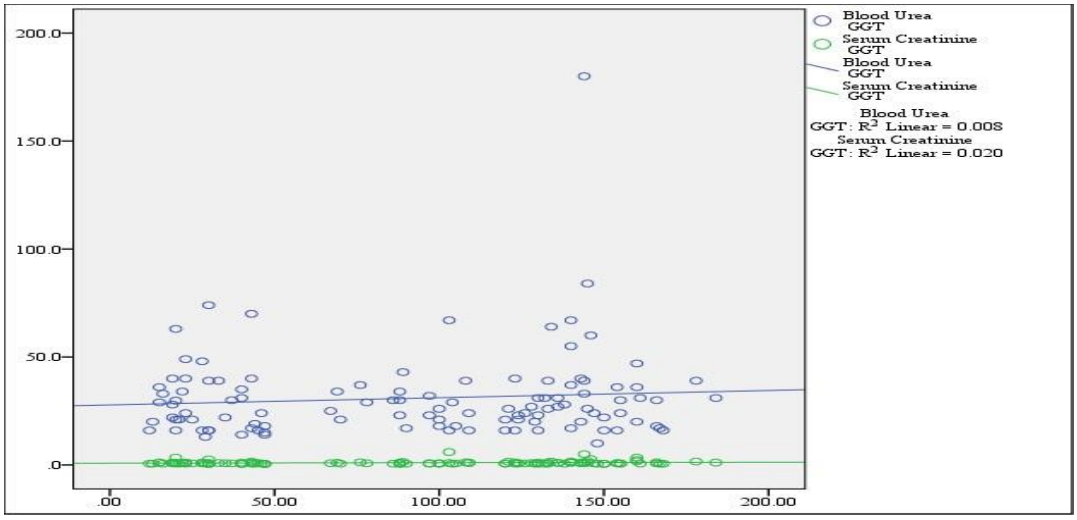

Figure 11: Scatter Plot showing Correlation between GGT and Renal Profile

Table 13: Correlation between GGT and Liver Function tests

		GG T	Total Bilirubin	Direct Bilirubin	Indirect Bilirubin	SGO T	SGP T	Alkaline Phosphate	Total Protein	Serum Albumin
GG T	Pearson Correlation	1	0.200*	0.027	0.328**	0.131	0.080	0.052	0.038	0.006
	P value		0.034*	0.773	<0.001*	0.167	0.401	0.586	0.689	0.950
	N	113	113	113	113	113	113	113	113	113

In the study there was positive correlation between GGT and all the liver function parameters i.e. with increase in GGT there was increase in Total Bilirubin, Direct Bilirubin, Indirect Bilirubin, SGOT, SGPT, Alkaline phosphate, total protein and serum albumin and vice versa. However significant correlation was seen with Total bilirubin, indirect bilirubin.

DISCUSSION

In our study, 114 subjects were recruited who has Metabolic Syndrome. Age distribution include all age group with predominant Age is between 51 to 60 years of 33.6 %, with mean Age is 56.6. There were 52.2 % Females and 47.8 % are Males. In a similar study done by B Kasapgoluet al[5], the mean age was 51 ± 32 and the gender distribution showed 62 % females and 38 % males in the study group. This difference may suggest a higher incidence of Metabolic Syndrome in Females in the Indian sub-continent. The mean Waist Circumference of the present study is 92.7 ± 4.8 and the mean Waist Circumference of the B Kasapgolu et al study is 104.1 ± 9.8. The mean BMI in the present study is 32.1 ± 2.8 and B Kasapgolu et al study BMI was 30.8 ± 4.1.The above observation shows that obesity and increased central adiposity are vital to the pathogenesis of Metabolic Syndrome. Mean BMI among those with GGT <50 was 33.4 ± 3.1, among those with GGT of 51 to 100 was 30.9 ± 1.6 and among those with GGT of >100 was 31.5 ± 2.6. Mean BMI was significant higher among those with normal GGT than with abnormal GGT. There was positive correlation between GGT and Waist Circumference i.e. with increase in Waist circumference there was increase in GGT and vice versa. This positive correlation was statistically significant. In the study there was negative correlation between GGT and BMI i.e. with increase in BMI there was decrease in GGT and vice versa. This negative correlation was statistically significant.

In our study, out of 114 subjects 108 subjects had Diabetes mellitus with 95.6 %. Less then, 5 years duration are 31 subjects of 28.7 % and 6 to 10 years of duration are 62 subjects of 57.4 % and greater than 10 years of duration are 15 subjects of 13.9 %. There was negative correlation between GGT and duration of DM i.e. with increase in Duration of DM there was decrease in GGT and vice versa. But the correlation was not statistically significant. The mean of fasting blood sugars in the study was 171.2 ±8.1.

In our study, out of 114 subjects 88 subjects had Hypertension (HTN) with 77.9 %. Less then, 5 years duration are 42 subjects of 47.7 % and 6 to 10 years of duration are 43 subjects of 48.9% and greater than10 years of duration are 3 subjects of 3.4%. There was positive correlation between GGT and duration of HTN i.e. with increase in duration of HTN there was increase in GGT. But the correlation was not statistically significant. The mean Total cholesterol was 187.2 ± 51.6, Triglycerides was 193.1 ± 125.2, HDL was 37.9 ± 7.8, LDL was 112.5 ± 42 and VLDL was 32.5 ± 13.1. Out of 114 subjects Triglycerides more than 150 mg/dl is 73 subjects of that 35 are males and 38 are females. The mean Triglycerides and mean HDL values in B Kasapgolu et al are 273 ± 25.2 and 42 ± 9.7 respectively which are more than the values in our study. This difference may suggest variations in diet and familial metabolic parameters in particular geographic distributions. Hypertriglyceridemia was found in around 50 % of subjects and also the predominant dyslipidemic abnormality. A similar finding was noted in the reference study.

In the evaluation of liver function tests, GGT which is the biomarker being evaluated in this study had the following results. The mean GGT of the study was 92.7 ± 52.5. Out of 114 subjects GGT more than 50 IU/L was 73 subjects which is 64.03%. In male subjects GGT more than 50 IU/L were 36 which is 49.31 % of the 73 subjects (GGT more than 50 IU/L). In female subjects GGT more than 50 IU/L were 37 which is 50.68 % of the 73 subjects (GGT more than 50 IU/L). This indicates GGT raised more in female subjects than male subjects. In a similar study done by B. Kasapgolu et al. the mean GGT was 40.9 ± 10.2

Comparison of GGT with parameters of metabolic syndrome

Gamma-Glutamyl Transferase (GGT) is a cell-surface protein contributing to the extracellular catabolism of glutathione (GSH)[8]. The enzyme is produced in many tissues, but most GGT in serum is derived from the liver. In the serum, GGT is carried primarily with lipoproteins and albumin[9]. Serum levels of GGT are determined by several factors: alcohol intake, body fat content, plasma lipid/lipoproteins and glucose levels, and various medications[10,11]. There was positive correlation between GGT and Waist Circumference i.e. with increase in Waist circumference there was increase in GGT and vice versa. This positive correlation was statistically significant. There was positive correlation between GGT and all the liver function parameters i.e. with increase in GGT there was increase in TB, DB, IDB, SGOT, SGPT, Alkaline phosphate, total protein and serum albumin and vice versa. However significant correlation was seen with Total bilirubin, indirect bilirubin.

In the study of Khubchandanl[12] on 25 diabetic subjects compared with 25 normal individual found significantly higher Serum GGT level in diabetics in comparison of normal individual. Possible mechanism for this significant difference in two groups might be in response to oxidative stress in diabetics which leads to increase in serum GGT level.

CONCLUSION

This study has critically evaluated the utility of GGT as a marker of Metabolic Syndrome, with good results. An elevated GGT was found to be associated with Metabolic Syndrome subjects. There was

positive correlation between GGT and duration of HTN i.e. with increase in duration of HTN there was increase in GGT. But the correlation was not statistically significant. There was positive correlation between GGT and Waist Circumference i.e. with increase in Waist circumference there was an increase in GGT and vice versa. Among lipid profile significant correlation was seen between GGT and Triglycerides. Positive correlation was observed between GGT and ESR. There was negative correlation between GGT and FBS, duration of diabetes mellitus, BMI. There was positive correlation between GGT and all the liver function parameters i.e. with increase in GGT there was increase in TB, DB, IDB, SGOT, SGPT, Alkaline phosphate, total protein and serum albumin and vice versa. However significant correlation was seen with total bilirubin, indirect bilirubin. GGT is probably has a position in algorithm for the evaluation of Metabolic syndrome and CVD risk assessment.

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