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STUDIES ON THE LEVELS OF GAMMA GLUTAMYL TRANSFERASE IN FEMALES WITH METABOLIC SYNDROME AS A PREDICTOR OF FUTURE CARDIOVASCULAR RISK

Dr. K.P. Mekhala* Dr. P.Kalidas Dr. N. Prasada Rao*****

**Assistant Professor, Dept. of Biochemistry, Karpagam Faculty of Medical Sciences and Research, Coimbatore, Tamilnadu.*
***Professor and Head, Department of Community Medicine, Coimbatore Medical College, Coimbatore, Tamilnadu.*
****Professor and Head, Department of Biochemistry, Karpagam Faculty of Medical Sciences and Research, Coimbatore, Tamilnadu.*

Abstract

Metabolic syndrome is also known as CS syndrome – X, Insulin Resistance syndrome, Reaven's syndrome, which is a combination of medical disorders that increases the risk of developing cardiovascular diseases and diabetes. In our present study we analyzed the levels of Gamma glutamyl transferase, Uric acid, serum AST (SGOT), serum alkaline phosphatase, serum SGPT (ALT), serum urea, serum creatinine in women population in Tanjore district (Tamil Nadu) with metabolic syndrome, where we observed that the levels of these biomarkers were extremely abnormal in the affected population in comparison with control population, which is a prognosticator tool for cardiovascular risk.

Key Words: Gamma Glutamyl Transferase, AST, SGPT, Metabolic Syndrome, Cardiovascular Risk.

INTRODUCTION

Gamma-Glutamyl Transferase is a cell- surface protein contributing to exracellular catabolism of Glutathione, the main thiol antioxidant in humans. The enzyme is produced in many tissues but serum GGT is derived mainly from Liver (Emdin, 2005). Metabolic syndrome is a combination of medical disorders that increases the risk of developing cardiovascular diseases and diabetes. It affects a great number of people and prevalence increases with age. Metabolic syndrome is also known as CS syndrome – x, Insulin Resistance syndrome, Reaven's syndrome, CHAOS (Australia) or Metabo (Japan).

The enzyme is produced in many tissues, but most GGT in serum is derived from the liver. In the serum, GGT is primarily carried with lipoprotein and albumin. One hypothesis on the relation of GGT levels and vascular diseases hold that GGT itself is Pro-antherogenic (Emdin, 2005). GGT has been reported to occur in atherosclerotic plaques (Paolicchi, 2004), which might support this hypothesis. The origin of GGT could be attributed to the influx of lipoproteins. One of the products of GSH hydrolysis produced by GGT is cystenyl – glycine which can generate super oxide anion radicals through its interaction with free ions. This would promote atherogenesis *via* LDL oxidation. GCT is localized more in cell membrane and comparatively less in cytosol. These enzymes normally involved in transport of amino acids and peptides across cell membrane into cells and involved in glutathione metabolism.

Liver plays a major role in the regulation of carbohydrate homeostasis. Type 2 diabetes is associated with a large number of liver disorders including elevated liver enzymes, fatty liver disease, cirrhosis, hepatocellular carcinoma, and acute liver failure (Tolman *et al.,* 2007). Hepatocellular glycogen accumulation leads to hepatomegaly and liver enzyme abnormalities in poorly controlled diabetes patients. Signs and Symptoms of Metabolic syndrome includes fasting hyperglycemia – diabetes mellitus, Type II impaired fasting glucose, impaired glucose tolerance or insulin resistance, high blood pressure, central obesity (visceral, male pattern or apple shaped adiposity), over weight with fat deposits around the waist, decreased HDL – cholesterol and elevated triglycerides. Other associated diseases and signs are elevated uric acid, fatty liver (especially in concurrent obesity) progressing to non-alcoholic liver diseases, polycystic ovarian disease (PCOD), Haemochromatosis (Iron overload), and Acanthosis Nigricans (skin condition featuring dark patches). In hyperglycemic states, there will be intracellular glycogen accumulation in the hepatocytes due to increased glycogen synthesis, causing typical biochemical findings of mild to moderately elevated aminotransferases, normal liver synthetic function, with or without mild elevations of ALP. All these biochemical disturbances and hepatomegaly are found to be reversible with good glycemic control (Chatila and West, 1996).

Serum amino transferases such as ALT and AST indicate the concentration of hepatic intracellular enzymes that have leaked into the circulation. These are the markers for hepatocellular injury and are used as primary screening of NASH (Meybodi *et al*., 2008). Chronic mild elevations of ALT and AST are seen in type 2 diabetes patients. In a study done in United States by Erbey *et al.* 2000, reported that the prevalence of elevated ALT among type 2 diabetes is 7.8% compared to 3.8% in those without diabetes.

In type 2 diabetes reports have been inconsistent, that protein metabolism has been reported to be both unaffected and affected (Gougeon *et al*., 1997, 2000). In 1993, insulin resistance of protein metabolism", was firstly introduced in patients

with type 2 diabetes (Luzi *et al*., 1993; Tessari, 1994). It is defined as the defect in amino acid metabolism and suppression of protein breakdown which is correlated with insulin resistance (Halvatsiotis *et al*., 2002). Since then many studies have shown a negative nitrogen balance and loss of nitrogen from most organs in patients with type 2 diabetes (Almdal *et al*., 1986; 2009). Protein malnutrition is associated with an increased level of oxidative stress (Ahmed *et al*., 2009). Protein restriction in rats with type 2 diabetes, cause an accelerated oxidative stress (Bonatto *et al*., 2005; Calderon Guzman *et al.*, 2007). Children with kwashiorkor have a higher level of lipid preoxidation (Catal *et al*., 2007; Becker *et al*., 2005; Albrecht and Pelissier, 1995). Consistently protein malnutrition in intra uterine growth retardation pregnancies is the leading cause of oxidative stress in these patients (Toy *et al.*, 2009; Raab, 2009). Insulin resistance of protein metabolism could be impaired as one of the causes of protein malnutriton (Kahn, 1994). It often precedes the onset of type 2 diabetes by many years.

Giral *et al*. (2008) conducted a cross sectional study involving 1131 dyslipidemic patients of whom 26% presented with Metabolic syndrome and found that Plasma Gamma glutamyl transferase, major regulator of circulating concentrations of thiol compounds derived from Glutathione (GSH) cleavage i.e. cystine and cysteinyl glycine which exhibit a positive association with coronary artery disease, was equally elevated in Metabolic syndrome. They concluded that dyslipidemic patients exhibiting metabolic syndrome are characterized by elevated GGT activity resulting from perturbed metabolism of thiol compounds.

Anoop Shankar and Jialiang Li (2007), Studied the association between serum Gamma – Glutamyl Transferrase Level and Prehypertension (systolic B.P. 120-139 mm. Hg (or) diastolic B.P:80-89 mm. Hg) among U.S. adults, both men and women with a background of higher serum GGT levels, a marker of oxidative stress. Serum GGT levels were divided into 4 quartiles: Quartile 1 (< 13 u/1), Quartile 3 (19 - 29 u/1) & Quartile 4 (>29 u/1). Higher serum GGT levels were positively associated with pre-hypertension, independent of smoking, waist circumference, diabetes, cholesterol levels and other confounders. The multivariate odd's ration comparing quartile 4 of GGT (>29u/1) to quartile 1 (<3u/1) was 1.84 (P<0.001). Subjects with high GGT levels were older.

Sato *et al.* (2008) undertook a study employing multivariate models involving a population of 8,576 Japanese men (40-45 years) with a 4 year follow up period. The results revealed that nondrinkers with the highest GGT had the highest risk of type II Diabetes than moderate level drinkers (> or = 42.7gm ethanol/day).

Lee *et al.* (2008) carried out a comparative cross sectional study of Metabolic syndrome definitions in four populations of the Asia – Pacific region namely Australia, Japan, Korea and Samoa. It was seen that prevalence of Metabolic syndrome was the lowest among Japanese and the highest among Samoans. Age adjusted prevalences for the four definitions ranged from 16% to 42% in Australia, 3% to 11% in Japan, 7% to 29 percent in Korea and 17 to 60 percent in Samoa.

Eilat Adar *et al*. (2008) studied the relationship of 'Diet' to several characteristics of Metabolic syndrome and insulin resistance that carry increased risk of diabetes and heart disease. Their results showed that "Polyunsaturated fatty Acid" intake was associated with lower incidence of Metabolic syndrome in women (OR 0.69) but not in men and higher intake of simple carbohydrates intake was associated with increased levels of Metabolic syndrome in men but not so in women.

Andre *et al*. (2006) worked out Spearmans correlation coefficient, utilizing the data for 3 years period from DESIR cohort to elucidate the relationship between ɤ-Glutamyl Transferrese and Metabolic syndrome. Very highly significant correlations (P<0.0001) were observed in both men and women for the variables GGT with age, ALT, AST, BMI, fasting Insulin, wasit circumference, Triglycerides, FPO, Systolic blood pressure. The correlation between GGT and two of the variables namely bilirubin levels and HDL Cholesterol were not significant.

The concluded that components of metabolic syndrome were associated with increasing baseline GGT for four of the five components in both sexes – central obesity, high triglycerides, high arterial blood pressure and impaired fasting glycaemia.
Andre *et al*. (2007) studied the association of GGT with development of Metabolic syndrome and concluded that GGT was significantly associated with individual components of Metabolic syndrome, more in men (P=0.08) then on women (P=0.16). The association mainly related with insulin resistance but was in depended of other confounding factors.

Sciarret *et al.* (2007) carried out a study with 128 essential hypertension patients, 51 with metabolic syndrome and 77 without metabolic syndrome Echocardiagrphy and Doppler results revealed that cardiovascular damage was more frequent in hypertensive with Metabolic syndrome than in hypertensive without Metabolic syndrome.

Uric acid production and metabolism are complex processed involving various factors that regulate hepatic production, and

renal and gut excretion of this compounds. Uric acid is the end product of an exogenous pool of purines and endogenous purine metabolism. The exogenous pool varies significantly with diet, and animal proteins contribute significantly to this purine pool. The endogenous production of uric acid is mainly from the liver, intestines and other tissues like muscles, kidneys and the vascular endothelium. Uric acid formation from purine catabolism occurs by a series of enzymatic reactions that ultimately involve the xanthine oxidase enzyme. An intermediate production of this metabolism is inosine. This intermediate is converted by the purine nucleoside phosphorylase to hypoxanthine. Xanthine oxidase converts hypoxanthine to xannthine and subsequently to uric acid (Sowers *et al*., 2011; Jalal *et al*., 2013).

In the present study we enhanced the clinical relevance of diagnosis and management for metabolic syndrome for local women population in Thanjavur district of Tamil Nadu state.

METHEDOLOGY

The study was conducted in Thanjavur Medical College Hospital which included 100 females with metabolic syndrome according to 3/5 criteria of National Cholesterol Education Programme (NCEP) the syndrome group and control group of 40 normal women without Metabolic syndrome. Only female patients in the age group 30 to 75 years were used.

All the people in the study group were enquired to as per the following questionnaire; Name, age, gender, occupation, religion, complaints, past history suggestive of DM/BA/TB, PIH or GDM, H.O alcohol intake , menstrual history, family history of obesity, HT, stroke and CV diseases. Also collect the treatment history of anti-hypertensive drug. Height, Weight, Body Mass Index, Measurement, Waist circumference, systolic and diastolic blood pressure was measured as described elsewhere (Stern *et al*., 1992).

We excluded patients with liver diseases, renal diseases, alcoholism, drug in take (Anticoagulants), males (Prostatic GGT) on the other hand included the patients with obesity, hypertension, dyslipidemia (over 150 g/dl TAG blood), fasting blood sugar (more than 106 mg/dl) and HDL less than 50mg/dl.

The patients were identified as having metabolic syndrome according to the five different criteria (Elevated waist circumference ≥35 inches, Elevated Triglycerides ≥150 mg/ dl, Decreased HDL-C ≤ 50 mg/dl, Elevated Blood pressure ≥ 130/85 mm of Hg, Elevated fasting Glucose ≥ 100mg/dl).

The levels of Gamma glutamy transferase, Uric acid, serum AST (SGOT), serum alkaline phosphatase, serum SGPT (ALT), serum urea, serum creatinine, was carried out by the method described by Tietz (1976).

STATISTICAL ANALYSES

Unpaired ‘t’ test on the equality of group mean values, Coefficient of variation (CV%), Pearson’s simple correlation, multiple regression, Chi-square analyses, Co-efficient of mean square contingency group wise using Statistical analysis was carried out using the (Statistical Package Social Science) SPSS software, version 16.0.

RESULTS AND DISCUSSION

In our present investigation we evaluated the bio enzymatic level of GGT, SGOT, SGPT, ALKP, uric acid, urea and Creatinine. The results of the study on Gamma Glutamyl Transferase (GGT) in relation to uric acid and creatinine included some cardiovascular risk factors, in two populations, one consisting of 100 females with Metabolic syndrome referred to as the ‘Syndrome group’ hereinafter and the other consisting of 40 females without Metabolic syndrome taken as ‘Control group’ are discussed in the following pages.

Gamma – Glutamyl Transferase is a cell - surface protein, involved in the extracellular catabolism of Glutathione, the main thiol antioxidant in humans. The enzyme is produced in many tissues but serum GGT is derived mainly from Liver. GGT is carried primarily by lipoproteins and albumin.

The mean value of syndrome population (groups) in respect to control is represented in table 1. Analysis of the data showed a significant difference for all variables except for SGPT and Creatinine. The mean values of variables were comparatively higher in the syndrome population than that in the control group. The magnitude of increase in means between the control and syndrome groups was the highest for ALKP (16.06ul), followed by GGT (12.22 u/l), SGOT (6.75 u/l), Uric acid (2.01 u/l), SGPT (1.52 u/l) and Creatinine (0.03 u/l). The level of urea in control group was higher (28.07 u/l) than syndrome group (22.19 u/l) with of difference of (-5.9 u/l). Thus it can be inferred that the range of recorded values was wider in the syndrome group as compared to the control group, which can be attributed to the metabolic regulation with respect to the requirement and defection by the biological system.

Analysis of table 2 reveals that there is a strong association and significant elevation in the characters, which helps us to deduce that there exist a significant difference between the characters and extremely high range of values for GGT, SGOT, ALKP and Urea. The level of SGPT has extremely doubled in the given examination. The level of creatinine too doubled by 0.4 (u/l) for control group. When analyzing for syndrome population, an extreme range of values recorded for GGT (509 – 43.3 u/l), Uric acid (3.4 – 10.7u/l), SGOT (26.7 – 44.0), SGPT (13.6 – 13.0u/l). ALKP (112.0 – 243.0 u/l), Urea (13.0 – 35.0u/l) and least with creatinine of values ranging from 0.6 to 1.1 u/l. Thus there is a variation between the characters and between the control and syndrome group population.

Table 3a and 3b represents the GGT and Uric acid levels between the control and syndrome group. The GGT levels has been stratified into three levels of values such as Low (≤909(u/l)), Medium (10.0 – 14.9(u/l)) and High (20 – 24.9(u/l)). It has been observed that the total number of individuals in control in low and medium were 13 in number, which represents equitable numbers, and a slight increase in high level with 14 individuals within the reachable control population. Realizing the values of GCT in three stratifiable group of low (<15(u/l)), medium 15 – 25(u/l) and high > 25(u/l)), 9 person recorded the low stratified line, 36 group of people represented medium levels and 55 people recorded high stratum. It can be inferred that the syndrome group population had gradual and remarkable change in their GCT values ie., between the groups and the stratified levels.

The GGT and Creatinine level of control group is represented in table 4a. Here also the members in the study group had been stratified into three levels based on the values as low ≤9.9(u/l)), medium 10.0 – 14.9(u/l) and high (20 – 24.9(u/l). Similar observation as that of GGT and Uric acid obtained in respect to total number of individuals for each stratum. It has to be noted that the low and medium stratum engaged by 13 individuals and high stratum by 14 individuals out of 40 members in control group. When analyzing table 4b, it can be inferred that 45 members occupied low ≤25 (u/l) stratum, followed by medium (15 - 25(u/l)) of 46 members and high (>25 (u/l)) of 9 members, out of 100 members in syndrome group. This can be inferred that most of the people fall under low and medium level of GGT and Creatinine levels in syndrome group. Thus low in respect to syndrome, but in comparison with control, syndrome group exhibited extremely high range of values, due to metabolic effect of the biological system.

The syndrome and control groups significantly differed in respect of mean and variability for GGT and other variables like Uric acid, SGOT, SGPT, ALKP, Urea and creatinine in our study. The means values of variables were higher in Metabolic syndrome population than that in the control group except Urea. The magnitude of change in mean values between the control and syndrome group was the highest for the cardio vascular risk factors GGT (24.64u/l). There was also a very significant increase in uric acid levels (6.53) in the syndrome group.

In the Control group, all the individuals recorded values well within/below clinically normal levels for all characters except for a few marginally-above normal values in one case of uric acid (6.53 mg/dl).

On the other hand, in the Syndrome group a large proportion of individuals recorded values much higher than clinically normal levels in respect of GGT, SGOT, SGPT and ALKP evident form wider range coupled with higher maximum values and there was a significant elevation in serum GGT levels in the syndrome group ($P<0.001$) with a mean value of 24.6 u/1 compared to 12.42 u/1 in the control group, an increase of 97.58 per cent.

Ford *et al*. (2002) based on a cross sectional study in 1131 dyslipidemic patient of whom 26 percent presented with Metabolic syndrome, concluded that dyslipidemic patients exhibiting Metabolic syndrome are characterized by elevated GGT activity resulting from perturbed metabolism of thiol compounds. Similarly it was reported that serum GGT levels were higher in the metabolic syndrome group compared to the healthy group of Korean population and it was suggested that GGT levels may be a surrogate marker of insulin resistance, inflammation and metabolic syndrome.

El Friede Rittman *et al.* (2005) calculated survival cures with a cox proportional hazards model that was adjusted for sex, age, body mass index, systolic blood pressure, triglyceride, glucose, smoking, work status and year examination. They found that prevalence of elevated GGT was 21.9 percent in men and 15.6 percent in women, and the total mortality due to CVD was 2.1% for men and 1.6 percent for women. Thus, CVD mortality appeared to be parallel to GGT levels.

The nature of association between GGT and the other variables was similar in the control group also except that the correlation between GGT was non-significant. Such parallelism between control and syndrome groups in respect of the association of GGT and other variables pointing that the association holds good in the entire range of values of GGT levels observed.

Metabolic syndrome can be considered a coronary artery disease equivalent. Multiple pathophysiological mechanisms play a role in the increased risk of cardiovascular events in the Metabolic syndrome. These mechanism include hypertension, dyslipidemia etc.

Though the enzyme GGT is produced in many tissues, most of GGT in serum is derived from liver. GGT is primarily carried with lipoprotein and albumin. One hypothesis for relation of GGT levels and cardiovascular disease holds that GGT itself is proatherogenic. GGT has been reported to occur in atherosclerotis plaques which might support this hypothesis. The origin of GGT should be through influx of Lipo proteins that carry it to the lesions.

GGT being a cell – surface protein is involved in extra cellular catabolism of glutathione (GSH). One of the products of GSH hydrolysis produced by GGT is cysteinyl – Glycine, which can generate super oxide anion radicals through its interaction with free ions. This would promote atherogenesis *via* LDL oxidatation. Increased GGT activity may be a response to oxidative stress which can increase the transport of Glutathione precursors into cells. Therefore GGT has a role in the atherogenesis of Cardiovascular disease, Diabetes Mellitus and Metabolic syndrome.

An alternative hypothesis that appears to be consistent with the findings of Lee *et al.* (2007) is that elevation of GGT is a marker of presence of Metabolic syndrome. There is growing evidence that liver, the primary source of circulation of GGT is related to Hepatic Steatosis.

Another important association between GGT and Metabolic syndrome is the finding of higher GGT levels in obese individuals with abdominal obesity (Andre *et al.*, 2006). The connection between GGT and Metabolic syndrome extends to and association of higher GGT levels with Hyper Tension (HT) (Stranges *et al.*, 2004; Miura *et al.*, 1994) . Thus it appears that all major components of metabolic syndrome are linked to elevation of serum GGT levels.

In obesity particularly visceral (or) central, adipocytes secrete number of biological products like Tumor Necrosis factor – alpha, free fatty acids, adiponectin, leptin and interleukin-6 that modulate insulin secretion, insulin action, body weight and contribute to insulin resistance. These biological substances secreted by adipocytes increase the amount of inflammation which can cause build up of plaques in vessel walls. Eventually pieces of clots can break up and block blood vessels leading to myocardial infarction.

Persons with Metabolic syndrome have a threefold greater risk of coronary heart disease and four fold risk of cardiovascular mortality. The growth in prevalence of Metabolic syndrome parallels the dramatic rise in prevalence of obesity (Reaven, 1988) .

The mean serum uric acid level was 6.53 mg/dl in the syndrome group with a maximum of 10.70 mg/dl and a minimum of 3.41 mg/dl compared to a mean of 4.52 mg/dl with a range of 3.4 to 6.2 in the control group. Many in the syndrome group (36 percent) had serum uric acid levels between 6.00 – 6.90 mg/dl. GGT and uric acid showed a positive correlation at ($P<0.001$) level.

The major component of metabolic syndrome is insulin resistance which influences protein metabolism and uric acid, an end product of protein metabolism is elevated. In patients with metabolic syndrome, excretion of uric acid via kidney is also impaired.

Andréa Name Colado Simao *et al*. (2008) reported that metabolic syndrome is a cluster of risk factors for cardiovascular disease related not only to insulin resistance, but also to oxidative stress. Uric acid and gammaglutamyl transferase levels were also associated with Metabolic syndrome and oxidative stree in a study conducted with 88 adults (67 with Metabolic syndrome and 21 controls). The study confirmed that GGT is a strong predictor of Metabolic syndrome and lipid peroxide and GGT activity are reliable markers of oxidative stress in the syndromes.

In the present investigation, as already stated elsewhere, the mean serum GGT level was (24.64) units/litre with a maximum of 43.32 units/litre and a minimum of 5.90 units/litre. Among this, 46 percent showed high values of GGT ranging from 25.10 to 35.00 units/lit and 9 percent showed very high values (35.10 to 45.00 units / litre).

Even through GGT is expressed in several tissues, the main source of serum GGT is the Liver. GGT's central role is in intracellular glutathione homeostasis and extracellular glutathione metabolism. It enhances hydrolysis of gamma-glutamyl bond of glutathione releasing dipeptide cysteinyl-glycine which outside the cell reduces Fe^{3+} to Fe^{2+} and releases a free

thyolyl radical. This released free radical oxidizes LDL and promotes atherogenesis. In this way GGT acts as a pro-oxidant in extracellular space (Whitfield, 2001).

The results of the present study demonstrated a strong dose-response relationship of serum GGT to risk factors of coronary heart disease from the highly significant positive correlations, χ^2 and coefficient of mean square contingency values between GGT and the risk factors. This observation is similar to the observation of Nilsen *et al.* (2005).

Added to this the parallel nature of association with the variables exhibited by GGT in both control and syndrome populations, showing that the relationship between GGT and other variables holds good in the entire range of GGT values as evident from step wise multiple regression analysis, when considered along with parallelism between prevalence of elevated GGT . In many cases GGT is a universally standardized and available measurement that could be a clinical marker of the insulin resistance state and its changes may be an added advantage (Lee, 2004).

Thus elevation of serum GGT levels belong to the list of biomarkers linked to Metabolic syndrome. It appears to be largely a reflection of secondary hepatic inflammation. Although high level of GGT have been postulated to be directly atherogenic, Syndrome group" has strong associations with progressive Non-alcoholic fatty Liver Disease (NAFLD), age>45 years, obesity (BMI≥30), Diabetes mellitus, AST / ALT >1 etc., which increased the risk of developing significant fibrosis of liver.
The frequency of nonalcoholic fatty liver disease in the general population is given as 3-58%, where the great variability is attributed to socio-economic differences (average value 20-23 percent). The development of non-alcoholic fatty liver disease is more closely correlated with obesity than with alcohol abuse and simultaneously can be the cause for elevation of GGT levels in the serum (Grundy *et al.,* 2005).

Out of 100 female patients with metabolic syndrome and 40 normal women included in my study, none was an alcoholic as per our recorded statements. In a study conducted by Albert *et al*. (1999) it has been shown that GGT is more influenced by drinking intensity than drinking frequency. Thus, alcohol related elevation of GGT was effectively ruled out in my study for all practical purpose.
The transaminase levels are normal (or) slightly increased. Non alcoholic Steatohepatitis is mostly associated with obesity and (or) type II diabetes. Thus nonalcoholic Steatohepatitis is regarded as a hepatic manifestation of Metabolic syndrome. With nonalcoholic fatty liver disease, there is a rise in GGT levels (Sahsi *et al*., 2011).

CONCLUSION

In our study on serum GGT levels and related examination Uric acid, SGOT, SGPT, ALKP, Urea and creatinine in Metabolic syndrome was evaluated and about 56 percent showed elevation in Gamma-glutamyl-transferease levels which may be due to Non Alcoholic Fatty Liver Disease which is the hepatic manifestation of Metabolic syndrome. It will be an interesting and informative event to follow – up these patients for future progression in metabolic profiles.

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Table- 1. Mean values of variables studied in the Control and Syndrome population / groups

Variables	Mean values *		Difference	% Increase/ Decrease Over control	$S.E._D$	't' Values	'p' levels
	Control Group (N=40)	Syndrome Group (N=100)					
GGT	12.42	24.64	12.22	98.38	1.27	9.62	<.001
Uric Acid	4.52	6.53	2.01	44.47	0.25	8.03	<.001
SGOT	29.66	36.41	6.75	22.76	0.92	7.29	<.001
SGPT	23.64	25.16	1.52	6.39	0.78	1.93	.056
ALKP	160.92	176.98	16.06	9.98	5.43	2.96	.004
Urea	28.07	22.19	-5.89	-20.98	1.03	-5.69	<.001
Creatinine	0.80	0.83	0.03	3.75	0.02	1.64	.103

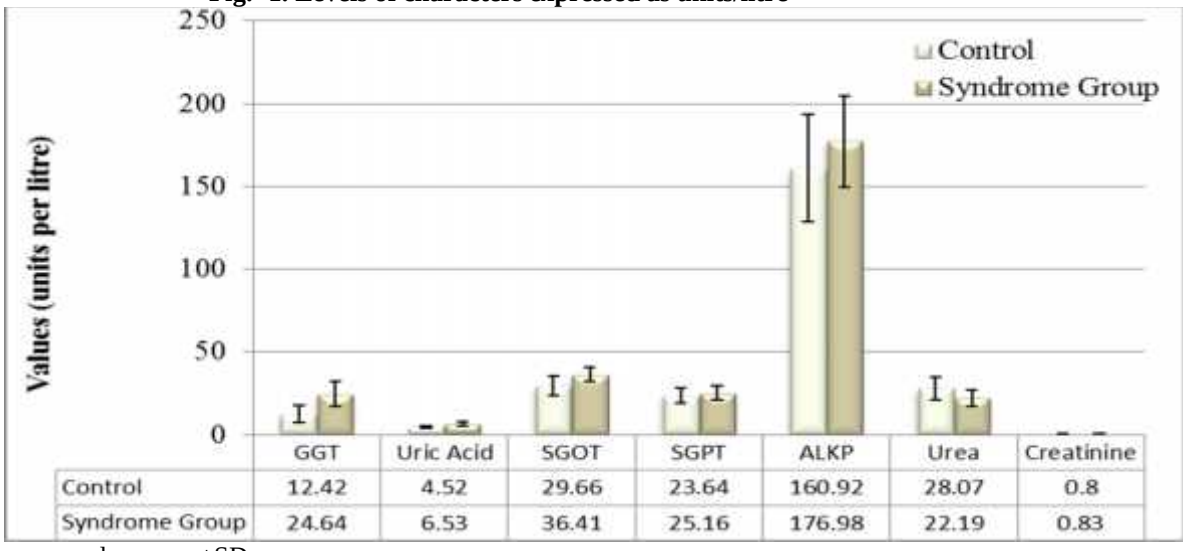
Table- 2. Variability for characters in the Control and Syndrome population.

Characters	Control Group					Syndrome population				
	Mini.	Max.	Mean	S.D.	C.V.%	Mini.	Max.	Mean	S.D.	C.V.%
GGT	4.2	20.2	12.42	4.99	40.21	5.9	43.3	24.64	7.38	30.0
Uric Acid	3.4	6.2	4.52	0.85	18.90	3.4	10.7	6.53	1.49	22.77
SGOT	18.0	44.0	29.66	5.93	20.00	26.7	44.0	36.41	4.50	12.35

SGPT	16.0	32.0	23.64	4.43	18.74	13.6	31.0	25.16	4.10	16.31
ALKP	106.0	212.0	160.92	32.63	20.28	112.0	243.0	176.98	27.51	15.59
Urea	17.0	40.0	28.07	6.82	24.28	13.0	35.0	22.19	4.93	22.21
Creatinine	0.6	1.0	0.80	0.13	16.18	0.6	1.1	0.83	0.12	13.76

*Values within clinically normal levels

Fig.- 1. Levels of characters expressed as units/litre



Values expressed as mean±SD

Table- 3 a. GGT and Uric Acid levels in control group

Uric Acid mg/dl / GGT (u/l)	≤4.0	4.1 – 5.0	≥5.1	Total
≤ 9.9	9	2	2	13
10.0 – 14.9	5	4	4	13
20 – 24.9	2	6	6	14
Total	16	12	12	40

X^2 d. f 4 = 8.347^{NS} ; P = 0.10;
NS –Not Significant
Coefficient of mean square contingency = 0.415

Table -3 b. GGT and Uric Acid levels in syndrome group

Uric Acid / GGT (u/l)	**<5 mg/ dl**	**5 – 7 mg/ dl**	**>7mg/ dl**	**Total**
<15	6	2	1	9
15 – 25	6	24	6	36
>25	4	28	23	55
Total	16	54	30	100

X^2 d .f 4 = 25.68**; P = 0.001
Significant at 1 % levels
CMSC – 0.452

Table -4a. GGT and Creatinine levels in Control group

Creatininine mg/dl / GGT (u/l)	0.6- 0.7	0.8 – 0.9	1.0 – 1.1	Total
≤ 9.9	7	5	1	13
10.0 – 14.9	5	6	2	13
20 – 24.9	2	10	2	14
Total	14	21	5	40

X^2 d. f 4 = 4.986^{NS} ; P = 0.30;
NS –Not Significant,

Table- 4 b. GGT and Creatinine levels in syndrome group

Creatinine / GGT	**≤0.7 mg/ dl**	**0.8 – 0.9 mg/ dl**	**1 – 1.1 mg/ dl**	**Total**
≤25	15	28	2	45
15 – 25	7	29	10	46
>25	1	4	3	9
Total	23	62	15	100

X^2 d .f 4 = 10.67*; P = 0.05
*Significant at 5 % levels ,
CMSC – 0.311.