ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Is it important to analyse serum liver enzymes in patients with established metabolic syndrome? A Pilot study to tie the knot

Saumyajit Maiti[1], Arun Kumar[2]

[1]Assistant Professor, [2]Professor and Head, Department of Biochemistry, Krishna Mohan Medical College & Hospital, Mathura, Uttar Pradesh, India

Submitted: 23-02-2017 Revised: 28-03-2017 Published: 01-05-2017

ABSTRACT

Background: Metabolic Syndrome (MetS) is one of the emerging health problems which is the major area of concern as it is not only a potential risk factor for some many diseases but it also affecting globally. It is a common multi-factorial disorder of metabolic derangements and prominent etiological factors for the development and progression of atherosclerotic vascular disease and type 2 diabetes. The relation between elevated serum gamma-glutamyl tranferase and metabolic syndrome, however, have been not well explored in a developing country like India. **Aims and Objectives:** The current study was designed to estimate the levels of alanine transaminase (ALT), aspartate transaminase (AST), and gamma-glutamyl transferase (GGT) in metabolic syndrome patients with age-sex matched healthy controls. Furthermore the relation of liver function status with the various biochemical parameters of metabolic syndrome was explored. **Materials and Methods:** In this present only patients of metabolic syndrome were selected based on inclusion and exclusion criteria of selecting cases. All the biochemical parameters were analysed using standard methods. Data collected were analysed using Statistical Package for the Social Sciences (version 20.0). P value ($p < 0.05$) was considered to be significant. **Results:** Of the 200 cases and controls selected, the differences in serum GGT ($p < 0.001$) and ALT ($p = 0.048$) were statistically significant. In case of male subjects, study and controls groups were compared only for serum GGT level ($p = 0.032$) and in case of female subjects, study and controls were compared for serum ALT ($p = 0.027$) and serum GGT level ($p < 0.001$)and the differences were found to be highly significant. When male and female subjects of study group were compared, significant differences were observed in their serum ALT and GGT levels. **Conclusion:** Patients suspected of metabolic syndrome must also get their liver profile enzymes analysed as liver function is also affected with metabolic syndrome and it could be an additional risk factor additive of metabolic syndrome. Early detection and management can be preventive and can have a better treatment modalities is managing patients with metabolic syndrome. It not only prevent disease progression but also prevents additional cost burden beard by the patients.

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v8i3.16766
E-ISSN: 2091-0576
P-ISSN: 2467-9100

Key words: Metabolic syndrome, Central obesity, Diabetes, Lipid profile, Hypertension, Liver function test, Gamma-glutamyl transferase

INTRODUCTION

Metabolic syndrome (MetS), also known as insulin resistance syndrome, is one of the most important risk factors for the development of cardiovascular disease (CVD), cerebrovascular disease and diabetes.[1] As its prevalence is increasing rapidly across the globe, it have become a major area of concern to health care professionals in the past few decades.[2,3] International Diabetes Federation (IDF) states the criteria of MetS emphasizes the presence of central obesity, raised triglycerides, low HDL concentration, raised fasting serum glucose levelsand hypertension.[4]

Address for correspondence:
Dr. Saumyajit Maiti, Assistant Professor, Department of Biochemistry, Krishna Mohan Medical College & Hospital, Pali Dungra, Sonkh Road, Mathura, UP, 281123. **E-mail:** dr.saumyajitmaiti@gmail.com, **Phone:** +91 9831603139

It is well known that gamma-glutamyl transferase (GGT) is an important biomarker of hepatobiliary disease and in alcohol consumption or abuse.[5] GGT alteration is important in detecting abnormalities of extrahepatic tissues like kidney, epididymis, fibroblasts, lymphocytes, and lung.[6-8] GGT reduces oxidative stress by promoting intracellular glutathione (GSH) resynthesis and enhancing the availability of cysteine.[6, 9, 10] By oxidation, GGT lowers circulating low-density lipoprotein cholesterol (LDL).[11] It is expressed in the atheromatous core of coronary plaques, where it co-localizes with oxidized LDL and form cells.[12] GGT may also act as a pro-inflammatory factor, because it mediates interconversion of the glutathione-containing inflammatory mediator leukotriene C4 into leukotriene D4.[13]

There are some evidences from epidemiological studies which suggests that increased serum GGT is related with development of CVD risk factors, including diabetes, hypertension, dyslipidemia,[14-17] and also metabolic syndrome.[14] GGT levels correlate positively with novel cardiovascular risk factors such as C-reactive protein (CRP), fibrinogen, and F2-isoprostanes.[18] Though most of the studies conducted are from abroad, so this study is first of its kind to focus on the serum GGT levels in MetS patients in the eastern part of India.

AIMS AND OBJECTIVES

Aims and objectives of this present study was to estimate the parameters of liver function test among the patients attending in hospital with metabolic syndrome and to compare them with liver function test of healthy controls. Secondly the study aimed to analyze the relation of parameters of liver function tests with the various biochemical parameters of Metabolic Syndrome.

MATERIALS AND METHODS

A cross-sectional, observational hospital-based case-control study was conducted for a period from September 2013 to August 2014, in Hi-Tech Medical College and Hospital, Bhubaneswar, by Department of Biochemistry in collaboration with Department of Medicine. This study included 200 subjects of which 100 were in study group and rest were in the control group. According to International Diabetes Federation (IDF),[4] cases were recruited from the patients of metabolic syndrome, attending outpatient department (OPD) of Department of Medicine of Hi-Tech Medical College & Hospital for treatment. Age-sex matched healthy controls were recruited from relatives and peers of the patients, persons attending OPD for routine health checkups in the same institution.

Patients with pregnancy, trauma, thyroid dysfunction, malignant disease, severe renal insufficiency, cirrhosis, active liver disease attributable to viral infection (positive serology for virus hepatitis B and C), alcohol consumption, and consumption of drugs which interferes liver functions were excluded from this study.

Methods of Collection of Biochemical Data

A five milliliter of blood sample were withdrawn from every subjects both from study and control groups after 12 hours of overnight fasting for the measurement of lipid profile, liver function tests enzymes viz; [Alanine transaminase (ALT), aspartate transaminase (AST) and gamma-glutamyltrasferase (GGT)], fasting blood sugar (FBS) and glycosylated hemoglobin (HbA1c). After 2 hours post-prandial again 2 ml of blood was drawn for the estimation of post-prandial blood sugar (PPBS). In both the cases, blood was drawn from each of them by venipuncture of the antecubital vein under strict aseptic condition using dry disposable syringe and needle. Plasma glucose was measured using the glucose oxidase-peroxidase method, glycosylated hemoglobin (HbA1c) was estimated by the Bio-Rad D-10 Dual Program, serum total cholesterol by CHOD-PAP method, serum triglycerides by GPO-PAP method, serum HDL cholesterol by modified Polyvinyl Sulfonic acid (PVS) and Polyethylene Glycol – Methyl Ether (PEGME) coupled classical precipitation method and serum LDL and VLDL were estimated by Friedewald's formula.

ALT, AST and GGT were assessed with a Roche 902 using the companion's original kits (Roche Diagnostics, GmBH, Mannheim, Germany). Reference ranges for ALT, AST and GGT were < 40 U/l, 1-31 U/l and 1-32 U/l, respectively.

Methods of Collection of Other Data

A pre-designed, pre-tested, semi-structured questionnaire was used to collect various socio-demographic data like name, age, sex, address along with data about physical examination and clinical history.

Body heights of every subject were measured with a commercial standiometer in their standing position, and fraction values were approximated to the nearest centimeter. A digital weighing machine, with an accuracy of ±100 g, was used to measure body weight (BW), and fractions were approximated to its nearest kilogram. These machines were checked and calibrated regularly. Body Mass Index (BMI) or the "Quetelet Index" was calculated as per the formula of Adolphe Quetelet which is calculated by dividing weight (in kilograms) by the square of height (in meters).

According to World Health Organization's protocol,[19] the waist circumference (WC) was measured in a horizontal

plane, midway between the inferior margin of the last palpable ribs and the superior border of the iliac crest, using a stretch-resistant tape that provides a constant 100 g tension. Body mass index (BMI) (kg/m^2) was calculated by dividing weight (in kilograms) by the square of height (in meters). Hip circumferences (HC) were measured around the widest portion of the buttocks. In these measurements, the tape was parallel to the floor. For both measurements, the individual was stood with feet close together, arms at the side and body weight evenly distributed, and little clothing to be put on. The subjects were relaxed, and the measurements were taken at the end of a normal expiration. Each measurement was repeated twice; if the measurements were within 1 cm of one another, the average was calculated. If the difference between the two measurements exceeds 1 cm, the two measurements were repeated.[20]

Waist-Hip Ratio (WHR) is used as a measurement of obesity, which in turn is a possible indicator of other more serious health conditions. WHO STEPS states that abdominal obesity is defined as a waist–hip ratio above 0.90 for males and above 0.85 for females, or a body mass index (BMI) above 30.0.[21]

Blood pressures were recorded by regularly calibrated mercury sphygmomanometer after resting at least 5 min in a chair, with feet on the floor, and arm supported at heart level. An appropriate-sized cuff (cuff bladder encircling at least 80% of the arm) was used to ensure accuracy. Systolic blood pressure was measured at the point where the first of two or more sounds was heard, and diastolic blood pressure before the disappearance of sounds.

Statistical Analysis

The data collected was checked for error, cleaned and double entered into MS-Excel spread sheets and checked for any entry error. Then the whole data was imported into IBM SPSS Statistics (version 20.0) and further analysis was done. Data was first summarized and then analyzed for test of significance e.g. chi-square test, independent sample student t-test wherever applicable using the software package. P value less than 0.05 was taken as significant.

Ethical Issues

There was no associated risk or chance of harm to study subject other than the minimal risk associated with phlebotomy. However phlebotomy was done using disposable syringe and needle with complete aseptic measures and under direct supervision to minimize risks. Every subject was observed for an hour for any complication after phlebotomy.

The protocol of the study was approved by the Institutional Ethics Committee (IEC) for Human Research, Hi-Tech Medical College & Hospital, Bhubaneswar. Voluntary informed consent was taken from all participants in a consent form that was reviewed and approved by the IEC. Consents were taken by principal researcher himself. All participants were clearly explained that they reserve the right to withdraw from the study at any time they choose. A copy of the consent form was given to each participant. The study was continuously being monitored by the IEC during the study period.

No internal/external funding/grant were received for the study. It was solely funded by principal investigator himself. No conflict of interest was there to be declared.

RESULTS

This present study was conducted in the Department of Biochemistry in collaboration with Department of Medicine, Hi-Tech Medical College & Hospital, Bhubaneswar, Odisha. According to IDF criteria guideline, 100 metabolic syndrome patients were recruited as case group and age-sex matched another 100 healthy individuals were recruited as control group. In the cases, 37 were males and 63 were females whereas in control group, male participants were 40 and the rest 60 were females. Mean age group (±SD) of cases were 51.4 (±3.5) years and in controls it was 52.2 (±3.1) years.

In Table 1, diabetic profiles (FBS, PPBS, and HbA_{1c}), lipid profiles (serum TC, TG, HDL, LDL, and VLDL), waist and hip circumferences, and liver function tests (serum AST, ALT, and GGT) of both case and control groups were summarized.

Table 1: Summarized data and comparison of the parameters of metabolic syndrome and liver function tests between case and control groups

Parameters	MetS cases (n=100)	Healthy controls (n=100)	p-value
FBS (mg/dl) (±SD)	138.4±20.3	112.1±8.9	<0.001
PPBS (mg/dl) (±SD)	192.6±42.7	138.9±10.5	<0.001
HbA_{1c} (%)(±SD)	7.6±0.48	6.2±0.12	<0.001
Serum TC (mg/dl) (±SD)	212.4±41.7	178.6±10.2	<0.001
Serum TG (mg/dl) (±SD)	229.3±118.4	118.9±20.1	<0.001
Serum HDL (mg/dl) (±SD)	40.2±3.8	52.9±7.9	<0.001
Serum LDL (mg/dl) (±SD)	131.8±20.8	92.0±4.2	<0.001
Serum VLDL (mg/dl) (±SD)	46.7±24.0	25.5±3.7	<0.001
WC (cm) (±SD)	91.7±7.3	78.9±4.7	<0.001
HC (cm) (±SD)	101.5±6.9	98.2±5.2	<0.001
SBP (mm of Hg) (±SD)	136.8±7.2	128.4±5.9	<0.001
DBP (mm of Hg) (±SD)	86.1±5.4	81.9±7.2	<0.001
Serum AST (U/L) (±SD)	29.2±6.9	29.7±5.7	0.102
Serum ALT (U/L) (±SD)	26.8±9.1	22.6±3.9	0.048
Serum GGT (U/L) (±SD)	42.7±10.2	23.2±6.0	<0.001

All the data regarding metabolic syndrome like diabetic profile, lipid profile, waist circumference, hip circumference, systolic and diastolic blood pressure were higher and statistically significant in case group in comparison to those of control group. Mean serum AST level was slightly higher in control group and was not statistically related with case group, but other two parameters i.e., serum ALT and GGT levels were lower in control groups and that was statistically significant in comparison to case group.

Gender wise distributed data were summarized in below two tables (Table 2 and Table 3). In Table 2 male MetS cases were compared to male control group and similarly in Table 3 female MetS cases were compared to female control group.

From Table 2, it was resulted that only serum GGT levels were statistically related when these were compared in case and control groups. But in females, serum ALT and GGT levels both were statistically related here (Table 3).

From Table 2 and Table 3, it was noted, in both male and female control groups, serum AST levels were a little bit in higher side, but in case of serum ALT and GGT, these were on lower side when they were compared to case group.

Now the data of liver function tests of male MetS and female MetS patients were summarized and compared, which was stated in a tabular form below in Table 4.

From Table 4, it is observed that, levels of serum AST, ALT, and GGT were more in female MetS patients and statistically related when these were compared to male MetS case.

Table 2: Summarized data and comparison of the parameters of liver function tests between male case and male control groups

Parameters	Male MetS cases (n=37)	Male controls (n=40)	p-value
Serum AST (U/L) (±SD)	26.7±6.4	27.1±6.1	0.188
Serum ALT (U/L) (±SD)	25.4±8.3	25.2±7.9	0.312
Serum GGT (U/L) (±SD)	39.7±11.8	20.9±6.8	0.032

Table 3: Summarized data and comparison of the parameters of liver function tests between female case and female control groups

Parameters	Female MetS cases (n=63)	Female controls (n=60)	p-value
Serum AST (U/L) (±SD)	34.8±8.7	35.1±8.0	0.232
Serum ALT (U/L) (±SD)	29.6±10.4	18.2±4.7	0.027
Serum GGT (U/L) (±SD)	44.6±12.5	27.7±7.2	<0.001

Table 4: Summarized data and comparison of the parameters of liver function tests between male case and female case groups

Parameters	Male MetS cases (n=37)	Female MetS cases (n=63)	p-value
Serum AST (U/L) (±SD)	26.7±6.4	34.8±6.7	<0.001
Serum ALT (U/L) (±SD)	25.4±8.3	29.6±10.4	<0.001
Serum GGT (U/L) (±SD)	39.7±11.8	44.6±12.5	<0.001

DISCUSSION

In this present study, the hepatic enzyme levels in subjects with metabolic syndrome and those with age/sex matched controls in the eastern part of Indian population were compared. The study observed metabolic syndrome (MetS) subjects had significantly elevated liver enzymes especially, serum GGT and in some cases serum ALT.

In the study conducted by Kasapoglu et al in 2010 from Turkey included 442 MetS patients with age/sex matched 466 healthy controls, the levels of ALT, AST and GGT were significantly elevated among MetS patients when compared to the healthy controls.[22] Their study concluded elevated liver enzymes, play a central role in early diagnosis of fat overflow to the liver.

In another study on Roma patients conducted by Peter Jarčuška et al in Slovakia emphasized the strong link of serum GGT with metabolic syndrome.[23] Yet another study conducted elsewhere reveals an association of circulating GGT and transaminases activities also observed significantly elevated enzymes in MetS patients. [24, 25]

In other study by Nannipieri et al highlighted an association with mild elevations in liver function tests and metabolic syndrome in their study.[26] In a study conducted in China by Dong Wei et al observed significantly elevated serum GGT and ferritin levels MetS patients when compared controls.[27] Similarly, Rantala et al investigated the relationship between GGT and MetS and revealed highly significant relationship between GGT and the biochemical, clinical and physical components of the metabolic syndrome even after adjustment for age, body mass index and alcohol consumption.[14] Study conducted by Sakugawa et al also conforms a correlation between serum GGT level and components of MetS.[28]

One epidemiological study conducted by Devers et al also suggested that higher serum GGT levels was associated with development of various CVD risk factors, including diabetes, hypertension, and the metabolic syndrome.[29]

The Framingham heart study conducted by Douglas S. Lee et al. with 3451participants examined the relationship of GGT with CVD risk factors. GGT was positively associated with body mass index, blood pressure, LDL-C, TG, and blood glucose. Their study also has similar conclusion of increase serum GGT predicts onset of metabolic syndrome, incident CVD, and death suggesting that GGT is a marker of metabolic syndrome and cardiovascular risk.[30]

In a cohort study conducted in China by Villegas et al (2001) examined the liver enzymes in metabolic syndrome in 3978 urban Chinese men (40-74 yrs) also observed elevation of liver enzymes in metabolic syndrome. They predicted the involvement of liver injury associated with obesity and type II diabetes.[31]

Similar observations were also concluded from a study conducted in Thailand among Thai adults.[32]

Comparing the findings of the current study with the findings of study conducted earlier clearly highlights the association of liver enzymes alternation with Metabolic syndrome, hence it is suggested to call for liver function tests in also cases diagnosed with metabolic syndrome. So far we knew that lipid profiles were mainly associated with Metabolic syndrome but now it is proven than even liver enzymes gets altered in MetS. Right management of patients with MetS can overcome the additional cost of stay in hospital and prevents loss of economy in health care.

CONCLUSION

Metabolic syndrome is a major worldwide health problem leading to markedly increased mortality and serious morbidity. The need for early sensitive serum indicators of MetS complications is essential to prevent late complications and their deleterious effects. Estimation of these parameters of liver function test especially serum GGT helps in early intervention, thereby delaying the chronic complications of metabolic syndrome in the early stages. The estimation of serum GGT is a cost effective procedure and efficient enzyme as a good marker for predicting metabolic syndrome and its complications.

Limitation of this Study

This study was conducted in a single center, which is situated in eastern zone of India. However, large sample size is required to establish the findings of the current study. Another fact in this study is, the age group of female group is mostly in postmenopausal phase. It is recommended to compare the liver enzymes in pre- and post-menopausal women to establish the facts established in this study.

REFERENCES

1. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al for the American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/ National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005; 112(17):2735–2752.
2. Grundy SM, Brewer HB, Cleeman JI, Smith SC and Lenfant C. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation2004;109:433-438.
3. Lorenzo C, Okoloise M, Williams K, Stern MP and Haffner SM. The metabolic syndrome as predictor of type 2 diabetes: the San Antonio Heart Study. Diabetes Care2003; 26: 3153-3159.
4. www.idf.org/metabolic_syndrome, website of the International Diabetes Federation. Last accessed on April 21, 2016.
5. Whitfield JB. Gamma glutamyltransferase. Crit Rev Clin Lab Sci 2001;38:263–355.
6. Karp DR, Shimooku K and Lipsky PE. Expression of gamma-glutamyltranspeptidase protects ramos B cells from oxidation-induced cell death.J BiolChem 2001;276:3798 –3804.
7. Albert Z, Orlowska J, Orlowski M and Szewczuk A. Histochemicalandbiochemical investigations of gamma-glutamyl transpeptidase in thetissues of man and laboratory rodents. ActaHistochem1964;18:78–89.
8. Tate SS and Meister A. Gamma-Glutamyltranspeptidase: catalytic, structural and functional aspects. Mol Cell Biochem 1981;39:357–368.
9. Hanigan MH and Ricketts WA. Extracellular glutathione is a source of cysteine for cells that express gamma-glutamyl transpeptidase. Biochemistry1993;32:6302– 6306.
10. Hochwald SN, Harrison LE, Rose DM, Anderson M and Burt ME. Gamma-glutamyl transpeptidase mediation of tumor glutathione utilization invivo. J Natl Cancer Inst 1996; 88:193–197.
11. Paolicchi A, Emdin M, Passino C, Lorenzini E, Titta F, Marchi S, et al. A beta-Lipoprotein- and LDL-associated serum gamma-glutamyl transferase in patients with coronary atherosclerosis. Atherosclerosis 2006;186:80–85.
12. Paolicchi A, Emdin M, Ghliozeni E, Ciancia E, Passino C, Popoff G, et al. Images in cardiovascular medicine. Human atherosclerotic plaques contain gamma-glutamyl transpeptidase enzyme activity. Circulation2004;109:1440.
13. Anderson ME, Allison RD and Meister A. Interconversion of leukotrienescatalyzed by purified gamma-glutamyl transpeptidase: concomitant formation of leukotriene D4 and gamma-glutamyl amino acids. Proc Natl Acad Sci U S A 1982;79:1088 –1091.
14. Rantala AO, Lilja M, Kauma H, Savolainen MJ, Reunanen A and Kesaniemi YA. Gamma-glutamyl transpeptidase and the metabolic syndrome. J Intern Med 2000;248:230 –238.
15. Lee DH, Ha MH, Kim JR, Gross M and Jacobs DR. Gamma glutamyl transferase, alcohol, and blood pressure. A four year follow-up study. Ann Epidemiol 2002;12:90 –96.
16. Lee DH, Ha MH, Kim JH, Christiani DC, Gross MD, Steffes M, et al. Gamma-glutamyl transferase and diabetes–a 4year follow-up study. Diabetologia2003;46:359 –364.
17. Perry IJ, Wannamethee SG and Shaper AG. Prospective study of serum gamma glutamyl transferase and risk of NIDDM. Diabetes Care1998;21:732–737.
18. Lee DH, Jacobs DR, Gross M, Kiefe CI, Roseman J, Lewis CE, et al. Gamma-glutamyl transferase is a predictor of incident diabetesand hypertension: the Coronary Artery Risk

Development in Young Adults (CARDIA) Study. Clin Chem 2003;49:1358 –1366.

19. STEPwise approach to surveillance (STEPS)". World Health Organization. Last accessed on April 21, 2016.
20. Waist Circumference and Waist-Hip Ratio, Report of a WHO Expert Consultation. World Health Organization. 8–11 December 2008. Last accessed on April 21, 2016.
21. http://whqlibdoc.who.int/publications/2011/9789241501491_eng.pdf. Last accessed on April 21, 2016.
22. Kasapoglu B, Turkay C, Bayram Y and Koca C. Role of GGT in diagnosis of metabolic syndrome: A clinic-based cross-sectional survey. Indian J Med Res 2010;132: 56-61.
23. Jarčuška P, Janičko M, Dražilová S, Senajová G, Veselíny E, Fedačko J, et al. Gamma glutamyl transpeptidase level associated with metabolic syndrome and proinflammatory parameters in the young Roma population in eastern Slovakia: A population based study. Cent Eur J Public Health, Supplement 2014; 22: S43–S50.
24. Onat A, Hergenc G, Karabulut A, Turkmen S, Dogan Y, Uyarel H, et al. Serum gamma glutamyl transferase as a marker of metabolic syndrome and coronary disease likelihood in non-diabetic middle-aged and elderly adults. Prev Med 2006; 43: 136-139.
25. Music M, Dervisevic A, Pepic E, Lepara O, Fajkic A, Ascic-Buturovic B, et al. Metabolic Syndrome and Serum Liver Enzymes Level at Patients with Type 2 Diabetes Mellitus. Med Arh 2015; 69(4): 251-255.
26. Nannipieri M, Gonzales C, Baldi S, Posadas R, Williams K, Haffner SM, et al. Mexico City diabetes study: Liver enzymes, the metabolic syndrome, and incident diabetes; the Mexico City diabetes study. Diabetes Care 2005; 28: 1757-1782.
27. Wei D, Chen T, Li J, Gao Y, Ren Y, Zhang X, et al. Association of Serum Gamma-Glutamyl Transferase and Ferritin with the Metabolic Syndrome. Journal of Diabetes Research 2015; Article ID 741731, 10 pages.
28. Sakugawa H, Nakayoshi T, Kobashigawa K, Nakasone H, Kawakami Y, Yamashiro T, et al. Metabolic syndrome is directly associated with gamma glutamyltranspeptidase elevation in Japanese women. World J Gastroenterol 2004; 10: 1052-1055.
29. Devers MC, Campbell S, Shaw J, Zimmet P and Simmons D. Should liver function tests be included in definitions of metabolic syndrome? Evidence from the association between liver function tests, components of metabolic syndrome and prevalent cardiovascular disease. Diabet Med 2008; 25: 523-529.
30. Lee DS, Evans JC, Robins SJ, Wilson PW, Albano I, Fox CS, et al. Gamma Glutamyl Transferase and Metabolic Syndrome, Cardiovascular Disease, and Mortality Risk. Arterioscler Thromb Vasc Biol 2007;27:127-133.
31. Villegas R, Xiang YB, Elasy T, Cai Q, Xu W, Li H, et al. Liver Enzymes, Type 2 Diabetes, and Metabolic Syndrome in Middle-Aged, Urban Chinese Men. Metabolic Syndrome and Related Disorders 2011; 9(4): 305–311.
32. Perera S, Lohsoonthorn V, Jiamjarasrangsi W, Lertmaharit S and Williams MA. Association Between Elevated Liver Enzymes and MetabolicSyndrome Among Thai Adults. Diabetes Metab Syndr 2008; 2(3): 171–178.

Authors Contribution:
SM- Concept and design of the study, manuscript preparation, statistically analyzed and interpreted; **AK-**Critical revision of manuscript, Manuscript Preparation and Editing, Final Approval.

Work attributed to:
Department of Biochemistry, Hi-Tech Medical College and Hospital, Bhubneshwar.

Orcid ID:
Dr. Saumyajit Maiti: http://orcid.org/0000-0002-1418-7991
Dr. Arun Kumar: http://orcid.org/0000-0002-8800-0296

Source of Support: None, **Conflict of Interest:** None declared.