ORIGINAL RESEARCH

To study the association of gamma glutamyl transferase levels in patients admitted with acute coronary syndrome

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ABSTRACT

Introduction: The diagnosis of ACS is overlooked in about 2% of patients, which can lead to negative consequences. The term acute coronary syndrome comprises unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment myocardial infarction (STEMI). ACS is often the first presentation of coronary artery disease (CAD), the leading cause of mortality and morbidity in many parts of the world.

Aims and objectives: 1. To find out the levels of serum Gamma glutamyl transferase (GGT) in patients admitted with acute coronary syndrome. 2. To determine the association of raised GGT levels with different sub types of ACS.

Material and methods: It is an observational study, constituted of 150 study cases presented with Acute Coronary Syndrome to the medicine intensive cardiac care unit Deptt. of Medicine at R.D. Gardi Medical College and C.R. Gardi Hospital, Ujjain from December 2017 to November 2018.

Observations and results: Out of one fifty study cases, ninety (60.0%) cases were STEMI and among them fifty four (60.0%) had raised GGT level while Thirty six (40.0%) case had normal GGT value. Forty five (30.0%) cases were NSTEMI and among them twenty four (53.3%) had raised GGT level while twenty one (46.7%) had normal. Fifteen (10.0%) cases were having Unstable angina and among them three (20.0%) had raised GGT level while twelve (80.0%) had it normal. Chi Square value 8.293, p value was 0.016. There was highly significant association of various sub types STEMI and NSTEMI of ACS with GGT levels.

Discussion: In present study majority ninety four (62.7%) patients were males and Fifty six (37.3%) females with a Male: Female ratio of 1.6:1. Males 55.3% and Females 48.2% had an elevated GGT value. However there was no significant Gender wise association with GGT levels (Chi square =0.176, p value = 0.674). The age group of our patients ranged from 35 to 90 years and the mean age was male 62.63+/-10.90 & female 57.79+/15.38 years with peak incidence in the sixth and seventh decades. In this study

there was no statistical age wise significant association with GGT levels. Similarly Emiroglu MY et al in 2010 obtained the male preponderance in cases of each subset of ACS with a positive age wise association with GGT values and that was not with gender wise.

Conclusion: GGT may have a role in diagnosing cases of myocardial infarction especially in the presence of a non-diagnostic ECG. This will help in preventing MI cases to be missed in the ED. In addition to its diagnostic role in MI, GGT also has a discriminatory capacity to differentiate between STEMI, NSTEMI and UA. GGT can hence be an important laboratory tool alongside Troponin I and the electrocardiogram in the categorization of MI. Further its prognostic impact could be utilized in the risk stratification and the need for urgent therapeutic intervention.

Keywords: GGT, ACS, STEMI

INTRODUCTION

Acute onset chest pain is one of the commonest causes for presentation to the medical emergency. Even though acute onset chest pain is often assumed to be acute coronary syndrome (ACS), after further workup only 15% to 25% of patients with acute chest pain have MI. The important diagnostic task is to differentiate patients with ACS from other life-threatening non-cardiovascular causes of chest pain like pulmonary embolism, aortic dissection, and tension pneumothorax.

The diagnosis of ACS is overlooked in about 2% of patients, which can lead to negative consequences. The term acute coronary syndrome comprises unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment myocardial infarction (STEMI). ACS is often the first presentation of coronary artery disease (CAD), the leading cause of mortality and morbidity in many parts of the world. The basic pathophysiology is similar for the entire spectrum in the form of thrombus overlying a plaque. The approach to treating all these diseases is fundamentally similar but with certain unique features depending on the type of acute coronary syndrome. Several recent advances, have enhanced the accuracy and efficiency of the evaluation of patients with acute chest pain, mainly owing to better biomarkers of cardiac injury.3 Cardiac markers are proteins released into the circulation when cardiac cells die. These are troponin I, troponin T, myoglobin and CK-MB. These cardiac markers play an essential role in diagnosing as well as stratifying acute coronary syndrome (ACS). A variety of molecules have been used to diagnose and prognosticate acute coronary syndromes ranging from LDH and myoglobin to creatine phosphokinase and troponins[1].

The current management particulars are centered around the measurements of troponins which are both highly specific and sensitivity to acute cardiac insult. However the search is still ongoing for other molecules and enzymes which will help in assessing the severity of various forms of myocardial infarction. Stratification of ACS into high and low risk is imperative not only regarding the adequacy of treatment but also in avoiding unnecessary costs and inconvenience to the patient.

Among the latest armamentarium of molecules being investigated for diagnosing and more importantly, prognosticating myocardial infarction is an enzyme called Gamma Glutamyl Transferase (GGT). Well recognized as a marker of alcohol induced liver injury, GGT has gained importance in recent years as a marker of acute cardiac injury and has shown correlation with a host of risk factors responsible for macrovascular diseases, primarily coronary artery disease. GGT shows promise as a new tool in the risk stratification of various types of acute myocardial infarction. The underlying cause of ACS is a sudden rupture of a pre-existing atherosclerotic plaque. Risk stratification is critical in managing patients with

ACS. Risk prediction models identify high-risk patients who would benefit from early revascularisation therapy[2].

Inflammation is implicated in arterial plaque formation, plaque rupture and clot formation during subclinical and symptomatic coronary events . Gamma-glutamyl transferase (GGT), catalyses the first step in the degradation of extracellular glutathione (GSH), allowing the precursor amino acids to be assimilated and reutilized for intracellular GSH synthesis. Thus in this way, GGT activity favours the cellular supply of GSH, the most important non-protein antioxidant of the cell. However, there is also clear evidence that the degradation of GSH can play a prooxidant role in selected conditions; low density lipoprotein (LDL) oxidation through GSH/GGT-dependent iron reduction has been suggested as a potential mechanism in atherosclerosis. Serum GGT has been proposed as a marker of oxidative stress[3]. GGT contributes to oxidative stress pathways in several organs systems, localizes to atheromatous plaques containing oxidized LDL, and is pro-inflammatory, further implicating this protein in atherogenesis.

The prevalence of CAD, as well as the incidence of acute coronary syndrome (ACS) is very high among Indians, and in fact India has the maximum burden of ACS in the world . Serum Gamma-glutamyl transferase (GGT) also known as gamma glutamyl transpeptidase is a second-generation hepatic function test which has been widely used as a diagnostic index of liver dysfunction, alcohol consumption and abuse , GGT is the key enzyme accountable for the extracellular catabolism of glutathione (GSH), the chief antioxidant in mammalian cells[4].

This degradation allows for precursor assimilation and recycling of amino acids for synthesis of intracellular glutathione. Meanwhile, the reactive thiol of cysteinylglycine moiety originated during GGT-mediated cleavage of glutathione on the cellular membrane or in the extracellular space may also cause the reduction of ferric (Fe3+) to ferrous (Fe2+) ion starting an iron dependent redox-cycling process resulting in the production of the reactive oxygen species particularly superoxide anion and hydrogen peroxide, both capable of stimulating prooxidant reactions. GGT mediated pro-oxidant reactions catalyse the oxidation of LDL lipoproteins (lipid peroxidation), likely contributing to the formation of inflammatory atheroma within the vascular endothelial wall . Therefore it has been put forward that GGT can be considered as a potent biochemical marker for preclinical development of atherosclerosis and the key advantages of GGT over other cardiac markers is its high sensitivity, accuracy and cost effectiveness[5].

AIMS AND OBJECTIVES

1. To find out the levels of serum Gamma glutamyl transferase (GGT) in patients admitted with acute coronary syndrome.
2. To determine the association of raised GGT levels with different sub types of ACS.

MATERIAL AND METHODS

It is an observational study, constituted of 150 study cases presented with Acute Coronary Syndrome to the medicine intensive cardiac care unit Deptt. of Medicine at R.D.Gardi Medical College and C.R.Gardi Hospital, Ujjain from December 2017 to November 2018.

INCLUSION CRITERIA

- Patients with an episode of Acute Coronary Syndrome.

EXCLUSION CRITERIA

- Patient with Atypical chest pain.
- Patients with Stable Angina.
- Patients with Alcohol intake.

- Patients with liver disease.
- Drugs History of such as barbiturates, phenytoin, anti-tubercular drugs.

All study cases subjected to detailed history, clinical examination, routine biochemical investigations, radiological investigation and special investigation like Gamma glutamyl tranferase levels were measured in all the patients using a standardized photometric method with the normal value noted as 15-73 IU/L for male and 12-43 IU/L for female.

STATISTICAL ANALYSIS

Data were entered and analyzed in SPSS data sheet version 23. Frequency tables and measures of central tendency (mean) and measures of dispersion (Standard Deviation) were calculated. Correlation was assessed using the chi-square test for comparing mean of different group independent sample t-test and ANOVA were applied. Karl Pearson correlation coefficient was calculated for measuring linear relationship between GGT level and other study variable.

OBSERVATIONS AND RESULTS

Table 1- Age wise distribution of study cases(n=150)

Age Group (in years)	No. of cases	Percentage
< 45	20	13.3
45 - 60	53	35.3
61 - 75	57	38.0
> 75	20	13.3
Total	**150**	**100.0**

In the present study youngest case was of 35 yrs while oldest was of 90 yrs. However the maximum fifty seven (38%) cases where in the age group of 61-75 yrs. while equal numbers twenty (13.3%) were present in the each study group of below the 45 yrs. & above 75 yrs (Table 1).

In the present study the GGT levels ranging from 12 to 30 IU/L was not present in males & female 1 case while from 31 to 50 IU/L was present in males 24 (48%) & female 26 (52%) & from 51 to 70 IU/L was present in males 29 (58%) & female 21(42%) , followed by from 71 to 90 IU/L was present in males 23 (82.1%) & female 5 (17.9%) & from 91 to 110 IU/L was present in males 12 (80%) & female 3(20%) and >110 IU/L was present only in males 6 (100%)(Table 2) (Graph 1).

Table 2-Age & Gender wise distribution of GGT level in study cases.(n=150)

GGT Levels(IU/L)	Total No.of cases	Femalecases		Male cases	
12 - 30	1	1	100.0%	0	0.0%
31 - 50	50	26	52.0%	24	48.0%
51 - 70	50	21	42.0%	29	58.0%
71 - 90	28	5	17.9%	23	82.1%
91 - 110	15	3	20.0%	12	80.0%
> 110	6	0	0.0%	6	100.0%
	150	56		94	

Graph 1-Age & Gender wise distribution of GGT level in study cases.(n=150)

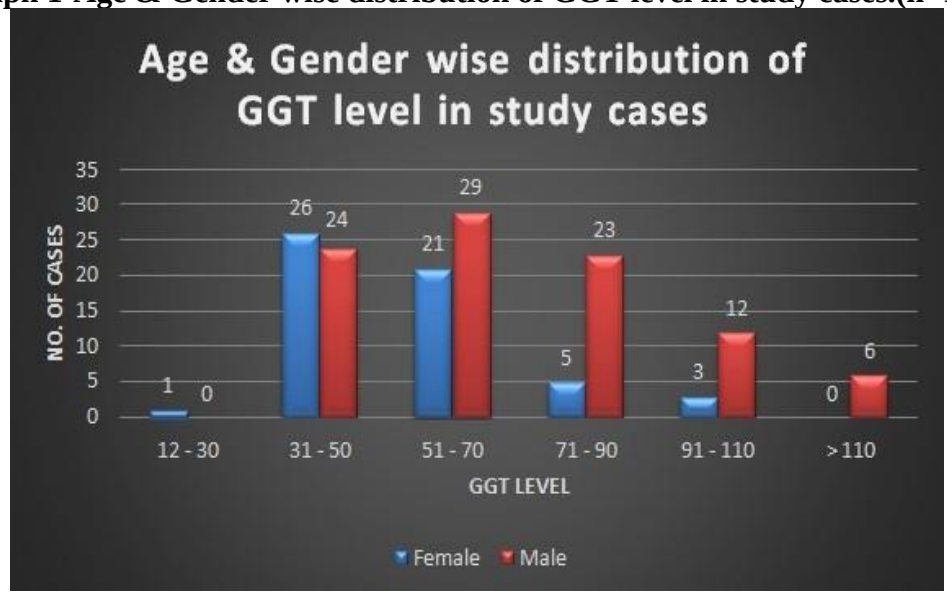

Table 3 - Association of GGT levels with various subtypes of ACS.

Subset of ACS	GGT levels		Total
	Normal	Raised	
NSTEMI	21	24	45
	46.7%	53.3%	100.0%
STEMI	36	54	90
	40.0%	60.0%	100.0%
UNSTABLE ANGINA	12	3	15
	80.0%	20.0%	100.0%
Total	69	81	150
	46.0%	54.0%	100.0%
Chi-Square = 8.293, p = 0.016			

Out of one fifty study cases, ninety (60.0%) cases were STEMI and among them fifty four (60.0%) had raised GGT level while Thirty six (40.0%) case had normal GGT value. Forty five (30.0%) cases were NSTEMI and among them twenty four (53.3%) had raised GGT level while twenty one (46.7%) had normal. Fifteen (10.0%) cases were having Unstable angina and among them three (20.0%) had raised GGT level while twelve (80.0%) had it normal. Chi Square value 8.293, p value was 0.016. There was highly significant association of various sub types STEMI and NSTEMI of ACS with GGT levels (Table 3).

DISCUSSION

All the cases were classified into three subsets; ST elevation MI, non ST elevation MI and unstable angina based on electrocardiographic and Troponin I measurements. Baseline gamma glutamyl tranferase levels were measured by a standardized method for all the patients. All the subjects were observed for the first five days of their hospital stay for episodes of re-infarcts, ventricular arrhythmias requiring defibrillation, cardiogenic shock requiring inotropic support, pulmonary edema and death. Multiple parameters including traditional risk factors of coronary artery disease as well as its complications were compared to GGT to look for association[6-8].

In present study majority ninety four (62.7%) patients were males and Fifty six (37.3%) females with a Male: Female ratio of 1.6:1. Males 55.3% and Females 48.2% had an elevated

GGT value. However there was no significant Gender wise association with GGT levels (Chi square =0.176, p value = 0.674). The age group of our patients ranged from 35 to 90 years and the mean age was male 62.63+/-10.90 & female 57.79+/15.38 years with peak incidence in the sixth and seventh decades. In this study there was no statistical age wise significant association with GGT levels. Similarly Emiroglu MY et al in 2010 obtained the male preponderance in cases of each subset of ACS with a positive age wise association with GGT values and that was not with gender wise[9-13].

Out of one fifty study cases, ninety cases were STEMI and among them fifty four (36 %) had raised GGT level. Forty five cases were NSTEMI and among them twenty four (16%) had raised GGT level. Fifteen cases were having unstable angina and among them three (2%) had raised GGT level Chi square value 8.293, the p value was 0.016. There was highly significant association of various sub types STEMI and NSTEMI of ACS with GGT levels. Comparable observation by Jain Jyoti et al in 2017 where obtained for the prevalence of raised GGT in STEMI 20.74%, 14.55 % in NSTEMI and 5.6% in Unstable Angina. But similar observation of prevalence raised GGT 19.4% in NSTEMI and 2.8 % in Unstable Angina were obtained by Asma kamal et al in 2012.Which resemble to those obtained in the present study. The mean value in unstable angina was within normal limits. Although the mean values in the other two subsets were elevated, the mean GGT in the STEMI subset was significantly higher than that of the NSTEMI subset. This revealed that GGT shows promise as a sensitive diagnostic marker of STEMI. Emiroglu MY et al in 2010, obtain positive association between types of ACS and GGT. However there was no association of STEMI subset with NSTEMI in this study and mean value of GGT in unstable angina subset was similar to that of control group. Dogan A et al 2012, observed mean GGT level was higher in ACS group than that of control group (32 vs. 16 U/L, P=0.001)[14-16].

CONCLUSION

Acute coronary syndrome is one of the most common presentations to the medical casualty. Despite major advances in the diagnosis and management of this serious disorder, there is still much scope for improvement in reducing mortality and morbidity. Further, around 2%-3% of myocardial infarction cases are still missed in emergency departments leading to unforeseen fatalities. In our study, GGT was significantly elevated in patients presenting with ACS. In addition, the mean GGT values of the three different groups of ACS were significantly different from one another. In comparing the correlation between types of ACS and level of GGT p value was 0.016. Gamma glutamyl transferase levels are significantly elevated in the study cases presenting with acute coronary syndrome and also reflect the burden of atherosclerotic changes. GGT levels were independently correlated with STEMI, NSTEMI and unstable angina. GGT levels were found significantly higher in acute coronary syndrome patient reflects the burden of atherosclerotic changes occurred in these cases. In ischemic heart disease, GGT assay showed be considered as a good prognostic marker with optimal sensitivity of the diagnostic assay and it helps improve our ability to predict adverse events in CAD. Therefore GGT may have a role in diagnosing cases of myocardial infarction especially in the presence of a non-diagnostic ECG. This will help in preventing MI cases to be missed in the ED. In addition to its diagnostic role in MI, GGT also has a discriminatory capacity to differentiate between STEMI, NSTEMI and UA. GGT can hence be an important laboratory tool alongside Troponin I and the electrocardiogram in the categorization of MI. Further its prognostic impact could be utilized in the risk stratification and the need for urgent therapeutic intervention.

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