ORIGINAL RESEARCH

ASSOCIATION OF GAMMA GLUTAMYL TRANSFERASE WITH ACUTE CORONARY SYNDROME AND CORRELATION WITH IN HOSPITAL OUTCOMES

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Received: 22 June, 2023 Accepted: 28 July, 2023

ABSTRACT

Introduction Sudden onset chest pain is one of the commonest causes for presentation to the hospital casualty. Even though acute onset chest pain is very often assumed to be acute coronary syndrome (ACS), after further workup only 15% to 25% of patients with acute chest pain have MI.

Aims & Objectives: To determine the frequency of raised serum Gamma Glutamyl Transferase levels in cases presenting with acute coronary syndromes. To determine the possible association between raised serum GGT levels and different subsets of ACS.

Materials And Methods: patients admitted with an episode of Acute Coronary Syndrome in the intensive coronary care unit. History of any alcohol intake Surgical conditions causing obstructive jaundice.

Results: Out of 150 study population 92 patients were male and 58 were female 40 out of 92 males had a positive value for GGT (43.5%). 34 out of 58 females were positive for GGT (58.6%). The p value was .07. There was no significant correlation between gender and GGT.

Key Words: Gamma Glutamyl Transferase, Acute Coronary Syndrome, LDL oxidation, atherosclerotic plaque, MACE.

INTRODUCTION

Sudden onset chest pain is one of the commonest causes for presentation to the hospital casualty. Even though acute onset chest pain is very 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 challenge is to differentiate patients with ACS or other life-threatening conditions from patients with non-cardiovascular, benign causes of chest pain. The diagnosis of ACS is overlooked in about 2% of patients, which can lead to negative consequences. The acute coronary syndromes constitute a range of heart diseases from unstable angina to ST elevation myocardial infarction. The basic pathophysiology is similar for the entire spectrum in the form of a 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. 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 ACS ranging from LDH and myoglobin to creatine phosphokinase and troponins. The current management particulars are centered around the measurements of troponins which are both highly specific and sensitive 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 (CAD). GGT shows promise as a new tool in the risk stratification of various types of acute myocardial infarction.

AIMS & OBJECTIVES

To determine the frequency of raised serum Gamma Glutamyl Transferase levels in cases presenting with acute coronary syndromes.To determine the possible association between raised serum GGT levels and different subsets of ACS. To determine the association between raised serum GGT levels and in-hospital adverse cardiovascular outcomes. To determine the association between raised GGT and risk factors for acute coronary syndrome.

MATERIALS AND METHODS

STUDY AREA:- Patients admitted to Intensive coronary care unit in Mahatma
Gandhi Memorial Hospital, Kakatiya Medical College, Warangal, Telangana

STUDY POPULATION:- Patients with Acute Coronary Syndrome

INCLUSION CRITERIA:- All patients admitted with an episode of Acute Coronary Syndrome in the intensive coronary care unit of Mahatma Gandhi Memorial Hospital, Warangal.

EXCLUSION CRITERIA:-

History of any alcohol intake
History of Hepatobiliary disease
Surgical conditions causing obstructive jaundice
Alanine Transaminase(ALT)>40U/L
Coarse liver echotexture on ultrasonography
History of taking drugs such as barbiturates, phenytoin, anti tubercular drugs

STUDY PERIOD:-November 2018 to January 2020

STUDY TOOLS: Pretested semi structured questionnaire, Validation of questionnaire was done by experts and necessary changes were made at the time of the study.

DATA COLLECTION

Method adopted to obtain data has been the "interview technique, prior to conducting the study, permission was obtained from the Ethical Committee of our Medical institute, Kakatiya medical college, Warangal (annexure I) The interview schedule in English was translated to local language Telugu and back translated to English for analysis. For all participants an oral consent and a written informed consent was taken. The study subjects were interviewed by the investigator personally.

PROCEDURE

A questionnaire was prepared to note the duration, symptoms of ACS. Questions were asked in relation to chest pain, dyspnoea, syncope, and cough. All previous clinical records of the patients were analyzed in detail. Based on the degree of effort needed to elicit symptoms patients were assigned to NYHA (New York Heart Association) class I to IV. A detailed history, physical examination was conducted to assess patients' volume status (rales, edema, and jugular venous distension), blood pressure changes.

INVESTIGATIONS

The following investigations were done in all the patients entering into the study:
Complete Blood Picture
Renal Function Test
Lipid Profile
FBS and PPBS
Cardiac Troponin T(qualitative)
Creatine Kinase-MB (CK-MB)
Liver Function Tests
Gamma Glutamy l Transferase levels
12 lead Electrocardigram
2D ECHO with Doppler
Ultrasonography for liver echotexture

LABORATORY METHODS

GAMMA GLUTAMYL TRANSFERASE levels were measured using a standardized photometric method with the normal value noted as 0-45 IU/L**.**

Pilot study was conducted in the selected population and details regarding individuals were collected.

Ethical Clearance: Institutional ethical scientific committee approval was
taken.Informed consent obtained from all subjects. Patient confidentiality maintained.

METHODOLOGY

All the patients presenting with ACS were included in the study. Serum GGT levels were measured in all the patients using a standardized photometric method with the normal value noted as 0-45IU/L. Blood samples were taken uniformly six hours from the time of presentation. Cases were divided into three subsets based on electrocardiographic and Troponin T measurement:
1. ST Elevation MI
2. Non ST Elevation MI

3. Unstable Angina

Patients were followed up for 5 days in the hospital from admission into ICCU for in-hospital outcome. Major adverse cardiovascular events (MACE) were recorded in the form of re-infarct, cardiogenic shock requiring inotropic support, ventricular arrhythmias requiring cardioversion, pulmonary edema and cardiac death.

Changes in serum GGT levels in ACS and its prognostic value on the development of MACE were studied.

STATISTICS

The data was entered in Windows Excel format. Frequency tables and measures of central tendency (mean) and measures of dispersion (Standard Deviation) were calculated by using the statistical package SPSS statistics software 23.0 Version.

Correlation was assessed using the Chi-Square Test .In the above statistical tools the probability value 0.05 is considered as significant level.

P value- Highly significant at P < or = .01

P value- Significant at 0.01 < P < or = .05

P value- Not Significant at P > .05

RESULTS

DISTRIBUTION OF THE STUDY POPULATION ACCORDING TO GENDER AND CORRELATION WITH GGT

Out of 150 study population 92 patients were male and 58 were female.

SEX		GGT	TOTAL	P value	
Positive	Negative				
MALE	Count	40	52	92	0.07
% within sex	43.50%	56.50%	100%		
FEMALE	Count	34	24	58	
% within sex	58.60%	41.40%	100%		
TOTAL	Count	74	76	150	
% within sex	49.30%	50.70%	100%		
% within GGT	100%	100%	100%		

40 out of 92 males had a positive value for GGT (43.5%). 34 out of 58 females were positive for GGT (58.6%). The p value was .07. There was no significant correlation between gender and GGT in this study.

DISTRIBUTION OF THE STUDY POPULATION ACCORDING TO DIABETIC STATUS AND CORRELATION WITH GGT

TABLE: 2 CORREL ATION BETWEEN DIABETES AND GGT

		GGT	TOTAL	P value		
POSITIVE	NEGATIVE					
DIABETES	YES	Count	40	30	70	0.073
% within Diabetes	57.10%	42.90%	100%			
NO	Count	34	46	80		
% within Diabetes	42.50%	57.50%	100%			
TOTAL	Count	74	76	150		
% within Diabetes	49.30%	50.70%	100%			

Out of 150 study population 70 patients were diabetics and 80 non-diabetics. 40 patients out of the diabetic group were positive for GGT. P value was 0.07. There was no significant correlation between diabetic status and GGT levels in this study.

DISTRIBUTION OF THE STUDY POPULATION BASED ON SMOKING STATUS AND CORRELATION WITH G G T.

		GGT	TOTAL	P value		
POSITIVE	NEGATIVE					
SMOKING	YES	Count	34	26	60	0.14
% within smoking	56.70%	43.30%	100%			
NO	Count	40	50	90		
% within smoking	44.40%	55.60%	100%			
TOTAL	Count	74	76	150		
% within smoking	49.30%	50.70%	100%			

60 subjects in the study population were chronic smokers. 34 of them turned out to be positive for GGT. The p value is 0.142. There is no significant correlation between smoking and rise in GGT.

DISTRIBUTION OF THE STUDY POPULATION BASED ON TYPE OF ACUTE CORONARY SYNDROME AND CORRELATION WITH GGT.

In our study of 150 patients 60 had ST Elevation in their ECGs, 48 subjects suffered from NSTEMI and 42 patients had Unstable Angina. 46 out of 60 patients with STEMI were positive for GGT. 28 out of 48 patients with NSTEMI were positive for GGT while none of the unstable angina subset had a positive GGT value. P value is 0.00001. Therefore there is a highly significant correlation between type of ACS and GGT levels with STEMI and NSTEMI showing positive values compared to unstable angina. In the study group of 150, people with TROP T positive were 108. Out of 108 subjects, 74 of them were positive for GGT. P value is 0.00001. It shows a highly significant correlation between TROP T positivity and GGT positivity. Out of 150 study subjects 90 had demonstrable RWMA of the ventricular wall on 2DECHO. Out of this subset, 70 patients had positive GGT values accounting for 78%. The p value is 0.00001. Therefore there is highly significant correlation between RWMA on 2DECHO and GGT levels. 90 out of 150 study subjects had systolic LV dysfunction on 2DECHO as evidenced by an ejection fraction on ECHO <50%. 70 patients out of that subset had a positive GGT value. The p value is <0.01. In this study there is significant correlation between presence of LV dysfunction and high GGT values. Out of the study population of 150, 36 subjects suffered from MACE within their five day in-hospital period in the form of one of the following: reinfarct, ventricular tachycardia or fibrillation requiring defibrillation, cardiogenic shock requiring inotropic support and death. All 36 patients had significantly positive GGT values. P value is <0.01. There is a significant correlation between incidence of MACE and GGT levels. 18 subjects suffered from one of the major adverse cardiovascular events. The mean value for these patients is 90.22. The mean GGT value for patients without MACE is a significantly less 46.44. The p value is significant with <0.01 There is no significant correlation between increasing age and GGT positivity in this study. The p value is 0.799 .In comparing the total cholesterol levels with GGT, the p value is significant <0.001, therefore there is a highly significant correlation between total cholesterol and GGT. In comparing LDL cholesterol levels and GGT, the p value is <0.001, therefore there is a highly significant correlation between LDL levels and GGT positivity.

In comparing HDL cholesterol levels and GGT, the p value is 0.183, therefore there is no correlation between HDL levels and GGT positivity. In comparing BMI of the study subjects and GGT, the p value is 0.049, therefore there is moderate correlation between high BMI values and GGT positivity. ANOVA test was used to look for correlation between the three types of ACS with their respective mean GGT values. The mean GGT values for STEMI, NSTEMI and UA subsets were respectively 74.03, 54.88 and 34.90 respectively. The p value was significant for this test, <0.001 . Therefore the difference in GGT values in the three subsets was statistically relevant. A post hoc test was calculated to compare each type of ACS with the other two types and statistically correlate the difference between them. The p value was highly significant while comparing the difference in GGT levels in STEMI with both NSTEMI and UNSTABLE ANGINA. Likewise the p value was significant while comparing NSTEMI and unstable angina with the other two subsets.

DISCUSSION

This study is a single centre cross sectional hospital based study done at Mahatma Gandhi Memorial Hospital, Warangal. Our study population included patients admitted to the Intensive Coronary Care Unit of our hospital with Acute Coronary Syndrome during the period from November 2018 to January 2020. All the cases were divided into three subsets; ST elevation MI, non ST elevation MI and unstable angina based on

electrocardiographic and Troponin T 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 correlation.

Age and Sex

In our study majority of patients were males (61%) and females accounted for 39% with a male: female ratio of approximately 3:2. 43.5% of males and 54.1% females had an elevated GGT value. However there was no significant correlation between gender and GGT in this study. The age group of our patients ranged from 37 to 84 and the mean age was 60.3 with peak incidence in the fifth and sixth decades. In this study there was no statistical correlation between age and GGT. In the study conducted by Emiroglu MY et al52 comparing CRP and GGT, published in the North American Journal of Medical Sciences in 2010, the majority of the patients in each subset of ACS were males and male sex showed a positive correlation with GGT values. However the same study showed no correlation between age and GGT. In the study conducted by **Jain Jyoti et al50**, statistically significant association of raised GGT in male patients with ACS in comparision to female patients was found which were similar as reported by Puukka et al.53

In the study conducted by Alexander M Strasak et al54, the age of participants significantly modified the relation between GGT change and CVD mortality, with markedly stronger associations to be observable for younger individuals.

Chakraborty et al55, showed significant correlation of raised GGT with increasing age.

CONCLUSIONS

Gamma glutamyl transferase levels are significantly elevated above normal in patients presenting with acute coronary syndrome. GGT levels were independently correlated with STEMI and NSTEMI but had no correlation with unstable angina. There is a significant correlation between GGT levels and incidence of left ventricular systolic LV dysfunction The mean value of GGT was significantly elevated in patients who suffered from major adverse cardiovascular events. Patients with significantly elevated GGT values may, in future, be referred for early invasive revascularization procedures like PCI/CABG. In conclusion, as concerns ischemic heart disease, GGT assay seems to have the features of a good prognostic marker and it helps improve our ability to predict adverse events in CAD. Further its prognostic impact can be utilized in risk stratification and the need for urgent therapeutic
intervention.

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