Estimation of gamma-glutamyl transferase with acute coronary syndrome

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Abstract

Introduction: Cardiovascular diseases (CVDs) are the leading cause of mortality in India attributing to a quarter of all mortality. Despite spectacular progress in disease prevention, detection and treatment over the last three decades; more CV deaths are caused by ischemic heart events. Considering the early mortality rate from acute myocardial infarction (AMI) (30-day), still, death from CVD Carries a higher burden. In several patients, the progressive phenomena of cardiac failure leading to ischemic cardiomyopathy reflects the burden of underlying coronary artery disease. Thus, identification of at risk patients who may be prone for future heart failure after the first myocardial infarction and detection of the extent of future heart failure is the cornerstone of secondary prevention strategies. This might help in prospective treatment in decreasing morbidity and mortality from heart failure following AMI.

Aim & Objective: To study the correlation between the rise in GGT levels and different subsets of Acute Coronary Syndrome. To study the correlation between GGT and the Risk of Major Adverse Cardiovascular Events (MACE).

Materials and Methods: This is a cross-sectional study conducted at Rajah Muthiah Medical College and Hospital. After obtaining clearance from institutional research and ethical committee, informed consent was obtained and patients of ACS in our CCU were selected. Using a standardized method GGT levels were measured and patients were followed up for five days in the hospital for adverse events. This study was done for some time between November 2019 to October 2021 and 75 patients with diagnosed ACS were included.

Results and Observations: In this study, there is a significant correlation between the presence of LV dysfunction and high GGT values. Serum levels of GGT were significantly higher in both the STEMI and NSTEMI patients but not in unstable angina patients. The patients who suffered complications has a mean GGT Value of 90.22. (IU/L) (SI units). The mean value for patients without MACE is significantly less than 46.44 (IU/L) (SI units).

Conclusion: Gamma-glutamyl transferase levels were significantly elevated above normal in cases of acute coronary syndrome. GGT levels were independently correlated with STEMI and NSTEMI but it did not correlate with unstable angina. There is a significant correlation between GGT levels and the incidence of left ventricular systolic LV dysfunction. The mean value of GGT was significantly higher in patients who suffered from major cardiovascular complications.

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

Introduction

Acute coronary syndrome (ACS) means a spectrum of clinical presentations ranging from ST-segment elevation myocardial infarction (STEMI) to presentations found in non-ST-elevation-MI and Non-ST-elevation-MI patients but not in unstable angina patients. The patients who suffered complications has a mean GGT Value of 90.22. (IU/L) (SI units). The mean value for patients without MACE is significantly less than 46.44 (IU/L) (SI units).
almost similar but with certain unique features based on the type of acute coronary syndrome. Numerous recent advances have shown better accuracy and efficacy in the workup of cases with acute chest pain, mainly owing to better biomarkers of cardiac injury. GGT shows promise as a new tool in the risk stratification of various types of acute myocardial infarction.[51] In some cases, the cells do not die, but damage due to an inadequate supply of oxygen results in heart muscles that do not work correctly or efficiently. The problem may be temporary or permanent. Unstable angina is the term used to describe the condition when acute coronary syndrome does not lead to cell death. The location of the blockage, the length of time that the blood flow is blocked and the amount of damage that occurs determine the type of acute coronary syndrome.[6, 7].

Materials and Methods
This is a cross-sectional study conducted at Rajah Muthiah Medical College and Hospital. After obtaining clearance from institutional research and ethical committee, informed consent was obtained and cases of Acute Coronary Syndrome in our CCU were selected. Using a standardized method serum levels of GGT were measured and all the cases were followed for five days in the hospital for any cardiac complications. This study was done for some time between November 2019 to October 2021 and 75 patients with diagnosed ACS were included. All patients presenting with the acute coronary syndrome were included in the study excluding alcoholics and hepatobiliary disease patients. Gamma-glutamyltransferase levels were measured in all cases using a standardized photometric method with normal value ranging from 0-45 IU/L. Blood samples are collected in a similar manner since 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 observed for five days in the coronary care unit for in-hospital outcome. Major adverse cardiovascular events were recorded in the form of re-infarct, cardiogenic shock requiring ionotropes, ventricular tachyarrhythmias requiring cardioversion, pulmonary edema, and cardiac death. Changes in the serum levels of GGT in ACS and its prognostic value on MACE were also observed in this study. Blood sampling and laboratory methods: A venous blood sample of 3 ml size, was drawn from the patient at the date of admission to CCU, collected into gel tube, serum then separated by centrifugation and GGT calculated manually by enzymatic method using the Abbott Architect C16000 auto analyzer.

Statistical Analysis
Data was analyzed with help of SPSS. Baseline information about modifiable and non-modifiable risk factors was collected through a predefined and pretested questionnaire. Modifiable risk factors included addiction details such as smoking, tobacco usages. Non-modifiable risk factors included gender, age, family history, etc. The clinical profile of all these patients were documented. Complications were classified as re-infarct, pulmonary edema, arrhythmia, cardiogenic shock and the treatment modalities and outcome of admission were documented for all patients.

Results

Table 1: Correlation between GGT and gender

| Sex      | GGT       | Total | P-value |
|----------|-----------|-------|---------|
|          | Positive  | Negative |       |
| Male     | Count     | 20     | 26      | 46      | 0.201   |
|          | % within sex | 43.5% | 56.5%   | 100.0%  |
| Female   | Count     | 17     | 12      | 29      |
|          | % within sex | 58.6% | 41.4%   | 100.0%  |
| Total    | Count     | 37     | 38      | 75      |
|          | % within sex | 49.3% | 50.7%   | 100.0%  |

Table 1: 20 out of 46 males had a positive value for GGT (43.5%). 17 out of 29 females were positive or GGT (54.1%). The p-value was 0.201. There was no significant correlation between gender and GGT in this study.

Table 2: Distribution Of Study Subjects Based On Type Of Acute Coronary Syndrome And Correlation With Ggt Values

| Type of ACS | GGT       | Total | P-value |
|-------------|-----------|-------|---------|
|             | Positive  | Negative |       |
| STEM        | Count     | 23     | 7       | 30      | <0.001  |
|             | % within type of ACS | 76.7% | 23.3%   | 100.0%  |
| NSTEMI      | Count     | 14     | 10      | 24      |
|             | % within type of ACS | 58.3% | 41.7%   | 100.0%  |
|             | % within GGT | 37.8% | 26.3%   | 32.0%   |
| UA          | Count     | 0      | 21      | 21      |
|             | % within type of ACS | 0%    | 100.0%  | 100.0%  |
| Total       | Count     | 37     | 38      | 75      |
|             | % within type of ACS | 49.3% | 50.7%   | 100.0%  |

Table 2: In our study of 75 patients, 30 had ST elevation in their ECGs, 24 were NSTEMI and 21 patients suffered from unstable angina.23 out of 30 cases with STEMI were positive for GGT. 14 out of 24 cases were positive for GGT while no one of unstable angina subsets had a positive GGT value. P-value is 0.001. Therefore there is a highly significant correlation between the type of ACS and GGT levels with STEMI and NSTEMI showing positive values compared to unstable angina.
Graph 1: Out of the study population of 75, 18 subjects suffering from major adverse cardiovascular events (MACE) within their five-day in-hospital period in the form of one of the following; reinfarction, ventricular tachycardia or fibrillation requiring defibrillation, cardiogenic shock requiring inotropic support, death. All 18 patients had significantly positive GGT values. P-value is <0.001. There is a significant correlation between the incidence of MACE and GGT levels.

Table 3: Correlation Of Ggt Values In Three Types Of Acs By Anova Test

| Subsets  | N  | Mean  | Std. Deviation | P value |
|----------|----|-------|----------------|---------|
| STEMI    | 30 | 74.03 | 23.348         | <0.001**|
| NSTEMI   | 24 | 54.88 | 23.058         | <0.001  |
| UA       | 21 | 34.90 | 7.609          |         |

Discussion

In this cross sectional study, serum levels of gamma glutamyl transferase were measured in ACS patients and we observed higher values of GGT above normal among these patients. Several studies have shown that circulating concentrations of GGT were higher in patients with ACS than in those with healthy control subjects [8]. One of the first studies that support this relation, where GGT levels were first associated with cardiovascular disease. A lesser correlation was seen between blood pressure, heart rate, and cigarette smoking. This goes against the finding of our study in that (There was no correlation with acute cardiac events) Another study that showed no correlation to acute vascular events against what our current study shows, is the cross-sectional and longitudinal study reported by Hannon TS et al. [9] The enzymatically active GGT identification in the plaque was done by an azo-coupling reaction using gamma-glutamyl-4-methoxy-2-naphthylamide as a substrate for GGT activity, stained with fast garnet GBC as the chromogen. They felt the pathogenic mechanism proposed for the role of GGT should be considered independent, complementary, and synergistic to conventional determinates. There is also evidence that atherosclerotic plaques contain GGT activity, revealed by many studies [10]. Where they evaluated the clinical utility of GGT activity in predicting high troponin levels in patients with the acute coronary syndrome (ACS) admitted to the emergency department with chest pain. A total of 200 troponin-positive and 203 troponin-negative patients were classified 1 and 2, respectively. γ-Glutamyl transferase activity was significantly higher in group 1 (44 ± 34 U/L) compared with group 2 (31 ± 26 U/L, P = 0.001). GGT activity cutoff >25.5
significant [12]. The mean GGT value of the MACE subset of one subset with each of the other subsets. This once again p-value was highly significant while comparing GGT levels predicting different types of acute coronary syndromes. The ACS [15].

and GGT with a p-value of 0.004 [11]. Two patients suffered of the 36 hypertensives in our study were positive for GGT. playing an important role in LDL oxidation, which in turn is higher LDL values were prone to GGT positivity. This is MACE had an elevated GGT and the p-value was highly significant [12]. The mean GGT value of the MACE subset was 90.22+7.818 and the mean GGT of the non-MACE group was 46.44+19.363. Comparing the two groups too, the p-value was highly significant. Hence our study shows that an elevated GGT level at presentation can anticipate adverse cardiovascular outcomes in ACS patients. GGT therefore can be an important tool in prognosticating MI patients based on risk. Comparing LDL and GGT, the p-value was <0.001 [13]. Therefore in our study, cases with higher LDL values were prone to GGT positivity. This is compatible with the recent studies which reveal GGT as playing an important role in LDL oxidation, which in turn is a hallmark of atherosclerotic heart disease [10]. A post hoc test was calculated to determine the strength of GGT in predicting different types of acute coronary syndromes. The p-value was highly significant while comparing GGT levels of one subset with each of the other subsets. This once again proves the utility of GGT in differentiating different types of ACS [15].

Conclusion
Gamma-glutamyltransferase levels are significantly elevated above normal in cases of acute coronary syndrome. GGT levels were independently correlated with STEMI and NSTEMI but doesn’t correlate with unstable angina. The correlation between serum GGT levels and the incidence of left ventricular systolic LV dysfunction is well established with significant p value. 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 Percutaneous coronary intervention/Coronary artery bypass graft. As a conclusion in ischemic heart disease, the GGT assay seems to have the elements of a good prognostic marker with optimal sensitivity of the diagnostic assay and it helps to 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.

Limitations of the study
There was no control group in the study. Even though the Unstable Angina subset acted as a control group given its almost normal GGT distribution, a subset containing people with nonanginal chest pain would have given a clearer picture of the discriminatory power of GGT. There is no way to know whether some subjects already had elevated GGT values or if the rise was linked to the ischemic event. Only further long term prospective studies will elucidate this cause-and-effect dilemma.

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Conflict of Interest-NONE

Ethical Committee Clearance Obtained From Institution

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