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Original Research Article

# Liver enzyme Gamma Glutamyl Transferase (GGT) level in patients with and without coronary artery disease (CAD): A cross sectional study

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ABSTRACT

**Background:** Globally, Coronary Artery Disease (CAD) is the key cause of morbidity and mortality. Gamma Glutamyl Transferase (GGT) levels are related to cardiovascular issue of chronic heart failure, and an increased level of GGT has been revealed to be an independent predictive maker for cardiac death.
**Aims and Objective:** To determine and compare the serum GGT levels in patients with and without CAD.
**Materials and Methods**: A total of 156 subjects, 78 participants with CAD and 78 participants without CAD were considered in the cross-sectional study done during January 2020 to October 2022 at the Department of Biochemistry and Department of Medicine, RIMS, Imphal. In all the subjects, the concentration of serum GGT, ALT, AST, Total Cholesterol, LDL and HDL assayed.
**Results:** Results showed that there is a significant rise in mean serum GGT level in cases compared to control and total cholesterol was also significantly higher in cases compared to control. Similarly, GGT levels and total cholesterol level were positively correlated in CAD patients (r=0.564 and p-value <0.05). In majority of cases serum GGT was above 36U/L (94.9%).
**Conclusion:** Serum GGT may be used as potential biomarker for assessing cardiovascular risk. GGT is positively associated with traditional risk factors for CAD. It can be used as inexpensive screening tool for early intervention in major cardiac events.



## 1. Introduction

Coronary artery disease (CAD) is a condition that typically occurs when there is imbalance between myocardial oxygen supply and demand.[1] Patients with CAD fall largely in 2 groups a) Patients with chronic CAD who most commonly are composed with stable angina b) patients with Acute Coronary Syndrome (ACS) which is comprised of patients with ST-segment elevation on electrocardiogram (STEMI) and those with uneven angina and non-ST segment elevation MI (UA/NSTEMI). ACS is a unifying term representing a common end result, acute myocardial ischemia.[2] About one-third of patients suffering from coronary artery disease progress to acute coronary and every year, about 10% of patients who came to emergency department with complaint of chest pain were diagnosed to have heart attack.[3]

GGT enzyme is available on the surface of various cells and it plays a role in the catabolism of glutathione; one of the major antioxidants. This catabolic process causes oxidative events such as increased production of reactive oxygen species and Low-Density Lipoprotein (LDL) oxidation; known to be major factors playing a central role in the pathogenesis of atherosclerosis.[4] Catalytically active GGT has been present within atherosclerotic coronary

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plaques. GGT is a significant biomarker of oxidative stress and cardiovascular risk assessment. Data related to GGT in Indian population is very limited.[5] Increased GGT activity has been found to be related with the development of hypertension and type 2 diabetes mellitus. Recent studies pointed out that high GGT is positively associated with enhanced mortality or incidence of cardiovascular disease.[6]

The study has been taken up to determine the serum GGT levels in patients with and without CAD and to compare serum GGT between patients with and without CAD.

## 2. Materials and Methods

It is a cross sectional study. The study was carried out in a tertiary care teaching hospital, Imphal. This hospital is located in centre part of Imphal, Manipur. It not only deals with OPD, IPD services to critical care including 24x7 emergency services but also involves in teaching both undergraduate and post graduate students. The hospital has separate cardiac care facilities like cardiology OPD, IPD, Echocardiography, Catheter Laboratory and ICCU.

### *2.1. Duration of the study*

The study was carried out for 21 months with effect from January 2021 to October 2022.

### *2.2. Study population*

Cases: Diagnosed cases of coronary artery disease who attended medicine/cardiology OPD or admitted in medicine ward.

### *2.3. Controls*

Age matched individuals without coronary artery disease attending RIMS hospital.

### *2.4. Inclusion criteria*

Individuals whose age is 18 years and above. Exclusion criteria: Presence of chronic renal, liver diseases, malignancy, chronic inflammatory disease, patients who refused to give consent.

### *2.5. Laboratory test analysed*

Estimation of serum GGT by colorimetric method. This is an optimized method according to European Committee for Clinical Laboratory Standards (ECCLS).

### *2.6. Statistical analysis*

The collected data was analysed using IBM SPSS version 21.0 for windows. Descriptive statistics like mean, SD, frequency and proportion was used to summarise the findings. Age of the participants and serum gamma glutamyl transferase level were expressed in mean and standard deviation and gender, religion, education, occupation, smoking history and any other co-morbidity were expressed in frequency and proportion. To compare the mean levels serum gamma glutamyl transferase level between patients with CAD and the individuals without CAD, student's t-test was used. p value <0.05 was taken as significant.

## 3. Results

It is evident from table 1 that maximum no. of cases is in age group above 60 years with 48 (61.5%) followed by 24 (30.5%) in age group 40-60 years and 6 (7.7%) in the age group below 39 years.

**Table 1:** Age wise distribution of study participants

| Age in years | Cases (n=78) | Control (n=78) |
|---|---|---|
| <39 years | 6 (7.7%) | 6 (7.7%) |
| 40-60 years | 24 (30.8%) | 24 (30.8%) |
| >60 years | 48 (61.5%) | 48 (61.5%) |
| Total | 78 (100%) | 78 (100%) |

From Figure 1, more case is found in the male population with 44 (56.4%) compared to female population with 34 (43.6%).

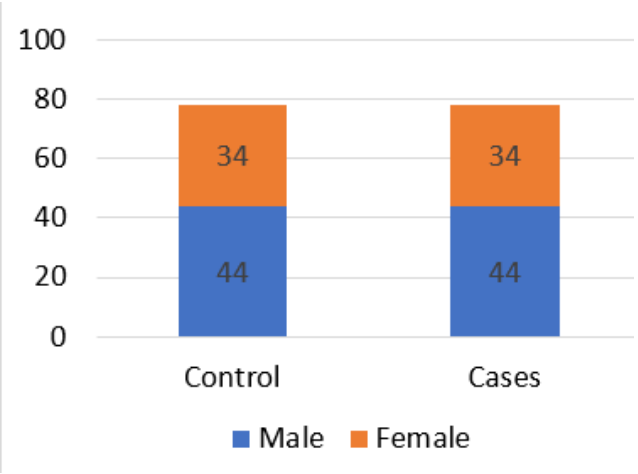


**Figure 1:** Distributions of participants by sex (N=156)

Table 2 shows that more cases found in urban population with 47 (60.3%) compared to 46 (59.0%).

**Table 2:** Distribution of participants by area/address (N=156)

| Address | Cases (n=78) | Control (n=78) |
|---|---|---|
| Rural | 31 (39.7%) | 32 (41.0%) |
| Urban | 47 (60.3%) | 46 (59.0%) |

Table 3 shows distribution of cases and controls based on religion. Maximum number of participants were Hindus (cases=46, control 52) followed by Muslims (cases=17,

control 16) followed by Christians (cases=15, controls=10) respectively.

**Table 3:** Distribution of participants based on religion

| Religion | Case (n=78) | Control (n=78) |
|---|---|---|
| Hindu | 46 (59.0%) | 52 (66.7%) |
| Muslim | 17 (21.8%) | 16 (20.0%) |
| Christian | 15 (19.2%) | 10 (13.3%) |

Chi square test

Table 4 shows distribution of participants based on smoking history. It is evident that history of smoking is higher in cases with 32 (41.0%)vs 15 (19.2) in control. Statistical analysis shows there is significant association between history of smoking and development of cardiovascular diseases) p-value <0.05).

**Table 4:** Distribution of participants based on smoking history

| Smoking history | Cases n (%) | Controls n (%) | p- value |
|---|---|---|---|
| No | 46 (59.0%) | 63 (80.0%) | 0.005 |
| yes | 32 (41.0%) | 15 (19.2%) | |

Chi square test

Table 5 shows mean SBP among cases were 138.21 ± 6.7 mmHg while in controls were 82.0±5.9 mmHg. Diastolic blood in cases and control were 132 .0 ± 6.3 mmHg and 83.4 ± 3.4 mmHg. The difference in systolic BP among cases and control was found to be statistically significant (p-value<0.05).

Table 6 illustrates the comparison of mean serum GGT, total cholesterol, LDL, HDL between cases and control. Mean GGT concentration was found to be significantly higher in cases (67.1±25.7 U/L) when compared to control (34.1±8.8 U/L). Similarly mean total cholesterol was found to be higher in cases (206.1±14.8 mg/dl) when compared to controls (168.9 ±11.6 mg/dl). While there was no statistically significant difference between cases and control when means of LDL & HDL were compared.

Table 7 shows distribution of cases and controls based on serum GGT levels. Majority of cases were found to be more than or equal to 36 U/L with 74 (94.9%) when compared to controls only 38 (48.7%) were more than or equal to 36 U/L. While in controls majority reported serum GGT level below 36 U/L with 40 (51.3%) when compared to cases with 4 (5.1%). The difference in GGT levels in both groups were statistically significant (p-value <0.05).

Table 8 shows correlationbetween GGT levels with various parameters in among the cases in the study Total cholesterol and LDL showed positive correlation (r=0.564 and 0.124 respectively) with GGT levels. HDL levels showed negative correlation (r= -0.105). Total cholesterol showed statistically significant correlation with GGT (p-value<0.05).

## 4. Discussion

This study was conducted on 156 subjects, 78 participants with CAD and 78 participants without CAD.

In the present study it was evident from Table 1 that majority of cases was found in age group above 60 years followed by age groups 40-60 years and in age group less than 39 years. This study confirms the observation made by Tanna NA et al.[7] which included 208 CAD patients, among which majority were above 60 years with 77. This may be due to the functional fluctuations in aging adults' hearts, which include both diastolic and systolic dysfunction.[8] Aging has been related to a number of factors, including increased oxidative stress overall myocardial deterioration, inflammation, degeneration and apoptosis.

Concerning the participants by area/address in Table 2 more cases are reported from urban area with 60.3% compared to rural area with 59.0%. Ahmed N et al.[9] also reported similar findings among CAD patients in their systemic review study bases on ECG defined coronary heart disease. This may be due to better availability of healthcare, better clinical diagnosis and greater survival in urban population compared to rural.

Majority of cases are Hindus (59.0%) followed by Muslims (21.8%), followed by Christians (19.2%) which is shown in Table 3. This variation may be because the study was conducted in a Hindu dominated area.

From Table 4 the history of smoking is higher in cases with 41.0% compared to control 19.2%. Statistical analysis shows there is significant association between history of smoking and development of cardiovascular diseases (p-value <0.05). These findings are confirmed by study done by Filion K B et al.[10] which states that smoking as an independent risk factor for development of cardiovascular risk.

Table 5 it is evident that SBP is higher in cases (138.21±6.7mmHg) compared to controls (132.0±6.3mmHg) and the difference in systolic BP among cases and control was found to be statistically significant (p-value<0.05). DBP was found to be slightly more in controls (83.4±3.4mmHg) compared to cases (82.0±5.9mmHg), however this difference was not statistically significant (p-value<0.07). The variation in blood pressure may be due to intake of antihypertensive medications among the cases compared to control.

Table 6 Data from our study showed that the mean serum GGT concentration was found to be significantly (p-value<0.05) higher in cases (67.1 ± 25.7 U/l) when compared to control (34.1 ± 8.8 U/L). Likewise, mean serum total cholesterol was found to be significantly (p-value<0.05) higher in cases (206.1±14.8 mg/dl) when compared to controls (168.9±11.6mg/dl). Whereas there was no statistically significant difference between cases and control when means of AST, LDL & HDL were compared. In a recent study done by Demircan S et al.[11] stated higher

**Table 5:** Mean blood pressure among cases and controls

| Blood pressure | Case (n=78) | Control (n=76) | p-value |
|---|---|---|---|
| SBP (mmHg) | 138.21±± 6.7 | 132 ± 6.3 | 0.00 |
| DBP (mmHg) | 82.0 ± 5.9 | 83.4 ± 3.4 | 0.07 |

Independent t test

**Table 6:** Mean serum concentration of AST, ALT, GGT, Total cholesterol, LDL and HDL

| Variable | Case (n=78) Mean ± SD | Control (n=78) Mean ±SD | P-value |
|---|---|---|---|
| AST (U/L) | 37.4±6.6 | 39.3±5.9 | 0.07 |
| ALT (U/L) | 44.4±6.4 | 42.3±6.3 | 0.05 |
| GGT (U/L) | 67.1±25.7 | 34.1±8.8 | 0.00 |
| Total cholesterol (mg/dl) | 206.1±14.8 | 168.9±11.6 | 0.00 |
| LDL (mg/dl) | 114.7±12.3 | 112.5±7.7 | 0.18 |
| HDL (mg/dl) | 39.7±3.6 | 40.9±2.5 | 0.17 |

Independent t test

**Table 7:** Distribution of cases and controls by serum GGT concentration

| Serum GGT (U/L) | Case (n=78) n (%) | Control (n=78) n (%) | p-value |
|---|---|---|---|
| <36 U/L | 4 (5.1%) | 40 (51.3%) | 0.00 |
| ≥ 36 U/L | 74 (94.9%) | 38 (48.7%) | |

Chi-square test

**Table 8:** Correlation of GGT with various parameters in cases (n=78)

| Parameters | Pearson's "r" value | P value |
|---|---|---|
| Total cholesterol | 0.564 | 0.00 |
| LDL | 0.124 | 0.12 |
| HDL | -0.105 | 0.19 |
| AST | -0.285 | 0.00 |
| ALT | -0.008 | 0.96 |

Pearson correlation test

GGT among CAD patients (38.7 ± 30.9 U/L) compared to controls (27.5±17.5U/L).

Our results illustrate that patients with CAD have relatively higher serum GGT activity than the control group. This is in line with the recent epidemiology and pathology studies which have suggested the independent role of GGT in the pathogenesis and clinical evolution of cardiovascular diseases caused by atherosclerosis.[12] GGT is a plasma membrane enzyme and also associated with glutathione catabolism.[13] Increased serum GGT activity may be a reflection of systemic level of oxidative stress especially oxidation of lipoprotein. Hence, CAD prognosis may be predicted by measuring serum GGT levels.[14]

Furthermore, it has been shown that in table 7 the maximum number of cases observed serum GGT concentration more or equal to 36 U/L with 94% of case when compared to controls with 48.7%. This difference between cases and controls was statistically significant (p<0.00). In a recent study done by Aksakal et al.[15] it was found out that long-term all-cause death rate was higher in the GGT level of ≥ 36 U/L group. The association of GGT with CAD in our patients advocates that it can be used as an adjuvant marker for assessing risk of premature CAD as well as screening tool for selecting in economically underdeveloped countries in making effective decision to whether to perform costly angiography or not.

Correlation of GGT with various parameters in cases are shown in table 8. GGT and total cholesterol shows significantly positive correlation (r=0.5). LDL also show positive correlation (r=0.1) which was not statistically significant (p=0.12). While HDL, AST, ALT were found to be negatively correlated with GGT. In another study published by Nagasawa SY et al[16] was found that significant positive relation between serum total cholesterol and CAD in both middle-aged men and women who were 40-69 years of age. The results from the previous study are consistent with our findings. This positive association may be due to their combined role in pathogenesis of atherosclerosis and increased oxidative stress. GGT shows negative correlation with HDL because of its well-established role to protect against the development of atherosclerotic cardiovascular disease.

## 5. Conclusion

This is the first study of serum GGT in patients with and without coronary artery disease in North East Indian Meitei (Manipur) Population. Majority of CAD patients were found in the age groups above 60 years. Most of the cases were male. Cases were more prevalent in Urban population.

The value of serum level of GGT is associated with the risk of CAD in young Meitei patients. Therefore, it can be used as an adjuvant biomarker and screening tool for risk assessment of premature CAD.

## 6. Limitations

The study considered only a small number of cases and the period was relatively short. Thus, the observation obtained may not reflect the true relationship between GGT, AST, ALT, Total cholesterol, LDL, HDL and prevalence of CAD in population.

## 7. Future Directions

A study with serum GGT values and associated variables will subsidize to a detailed understanding of the pathogenesis of cardiovascular disease.

## 8. Ethical Approval

The study was proceeded after the due clearance of protocol from Research Ethics Board, RIMS, Imphal (Ref no.A/206/REB-Comm(SP)/RIMS/2015/677/18/2020. Informed consent was taken from all the participants.

## 9. Source of Funding

None.

## 10. Conflict of Interest

None.

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