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SERUM GGT AND AST AS BIOMARKERS FOR CORONARY ARTERY DISEASE: AN ASSOCIATIVE STUDY

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Abstract
Coronary Artery Disease (CAD) remains a leading cause of morbidity and mortality globally, with early detection and risk stratification critical for effective management. Serum markers such as Gamma-Glutamyl Transferase (GGT) and Aspartate Aminotransferase (AST) have been linked to systemic inflammation and oxidative stress, key contributors to CAD. This research aims to explore the association between elevated GGT and AST levels with CAD, potentially offering new biomarkers for early detection and risk assessment.

Methods: *This comparative cross-sectional study involved 240 participants selected through stratified random sampling to include both coronary artery disease (CAD) and non-CAD patients. The research was conducted at Adil Diagnostic Center, Rawalpindi, from September to December 2024, following ethical approval.*

Results: *The results of the study show that a family history of Coronary Artery Disease (CAD) significantly correlates with higher prevalence rates of CAD in the study population. Patients with a positive family history and other risk factors exhibited elevated levels of Aspartate Aminotransferase (AST), Gamma-Glutamyl Transferase (GGT), and other liver parametrs such as Alkaline Phosphatase (ALP), Alanine Aminotransferase (ALT), and Total Bilirubin in CAD group as compared to Control group.*

Conclusion: *This study demonstrates the substantial correlation between coronary artery disease (CAD) and risk factors, including high blood pressure, diabetes, smoking, high cholesterol. It also demonstrates the obvious link between CAD and liver enzyme levels, particularly GGT and AST. Elevated GGT levels have been associated with the severity of CAD and have been identified as an independent risk factor for the condition. This emphasises how crucial it is to diagnose and treat CAD while taking into account both conventional risk factors and liver health.*

INTRODUCTION

Coronary artery disease (CAD) remains a leading cause of death globally, resulting from complex interactions of metabolic, inflammatory, and oxidative stress pathways that promote atherosclerosis. [1] Accurate and early identification of individuals at elevated risk is crucial for effective prevention and management. While traditional markers focus on lipid profiles and inflammatory parameters, emerging evidence points to the potential of enzymes such as serum gamma-glutamyl transferase (GGT) and aspartate aminotransferase (AST) as informative biomarkers in CAD risk assessment. [2]

Gamma-glutamyl transferase, an enzyme involved in glutathione metabolism and antioxidant defense, has been increasingly recognized beyond its conventional use as a liver function marker.

Elevations in serum GGT are linked with oxidative stress and the promotion of low-density lipoprotein (LDL) oxidation, which are important drivers of endothelial dysfunction and plaque formation in coronary vessels. [3] Meta-analyses have shown that higher serum GGT levels associate independently with increased cardiovascular mortality and all-cause mortality among CAD patients, reflecting its involvement in atherogenesis and systemic oxidative processes [4].

Similarly, aspartate aminotransferase, present in the liver, heart, and other tissues, has been studied in relation to cardiovascular injury and metabolic dysfunction. [5] Serum AST elevations may indicate myocardial damage or subclinical cardiomyocyte stress, correlating with adverse cardiovascular outcomes and severity of coronary atherosclerosis. Together, serum GGT and AST levels provide insights into the overlap between metabolic, inflammatory, and oxidative mechanisms that underlie CAD pathology. [6]

Understanding the associations of serum GGT and AST with coronary artery disease offers an opportunity to enhance diagnostic precision and to identify individuals at higher risk who may benefit from intensified therapeutic interventions. This study aims to explore these associations in a defined patient population, contributing to the body of evidence supporting the integration of these biomarkers in cardiovascular risk stratification.

Methodology

This comparative cross-sectional study involved 240 participants selected through stratified random sampling to include both coronary artery disease (CAD) and non-CAD patients. The research was conducted at Adil Diagnostic Center, Rawalpindi, from September to December 2024, following ethical approval. Inclusion criteria comprised confirmed CAD and non-CAD patients, while those with liver or kidney diseases, hepatitis infections, or cardiac conditions other than CAD were excluded. Diagnosis of CAD was based on ECG, angiography, and cardiac markers per 2019 ESC guidelines.

Blood samples were collected via standard phlebotomy procedures into serum separator tubes for analysis of liver enzymes—ALT, AST, GGT, ALP, and total bilirubin. Samples were processed using the Cobas C311 automated analyzer, with strict quality control measures in place. Enzyme levels were compared against standard reference ranges, and abnormal results were correlated with CAD presence and severity. All data and test results were carefully documented to ensure accuracy and confidentiality.

Results

The study was carried out at Adil Diagnostic Center. The data from 229 study subjects (n=229) was collected in which 135 were CAD patients and 94 were Normal Control group as shown in figure.

Figure 4.1: Total participants of study

The study was carried out at Premium Diagnostic Center. The data from 229 study subjects (n=229) was collected in which 135 were CAD patients and 94 were Normal Control group. The data from both males and females were collected in our study. Among all study subjects 74 male (n=74) and 61 females (n=61) were CAD patients. While 42 males (n=42) and 52 females (n=52) were control group as shown in figure.

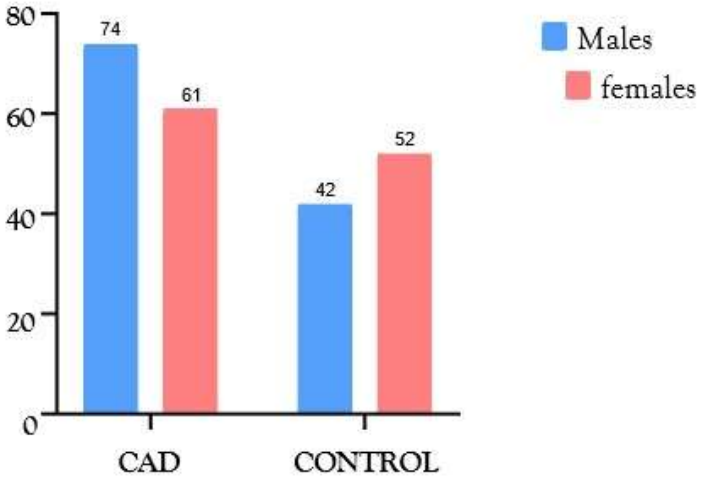


Figure 4.2: Gender Distribution in CAD patients and Control group

Patients of all age groups were included in our study. According to our data most of the CAD population was falling at the mean value of 60.563 ± 14.5472 and normal control population was falling at mean value of 47.6383 ± 17.12249 as shown in figure.

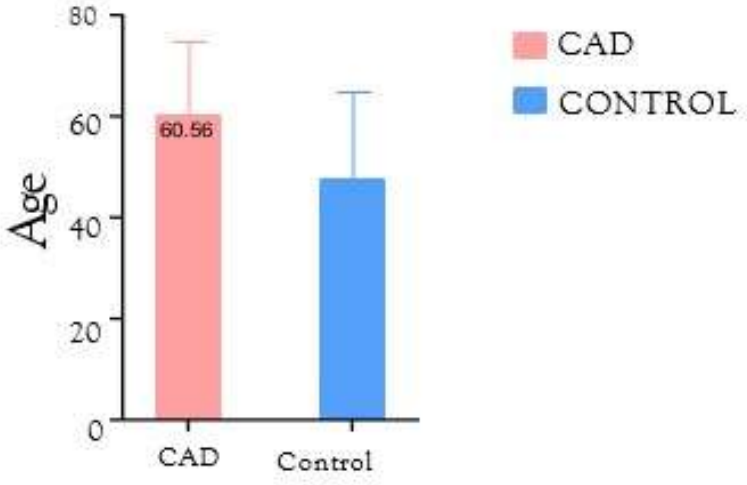


Figure 4.3: Age distribution between CAD patients and Control group

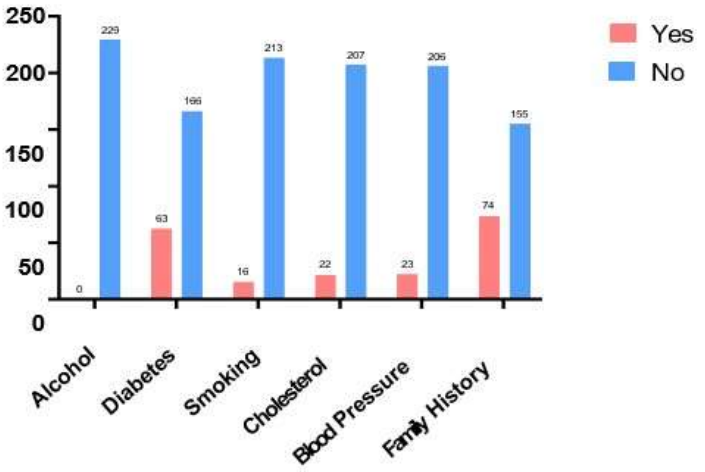


Figure 4.4: Prevalence of Risk Factors and Conditions

The graph 4.4 illustrates the prevalence of various risk factors and conditions such as alcohol consumption, diabetes, smoking, cholesterol, blood pressure and family history among CAD patients and control group.

Table 4.1 Presents an analysis of the relationship between CAD and various risk factors such as sex, alcohol use, diabetes, cholesterol, blood pressure, family history and smoking. The table shows the distribution of these factors in CAD and control groups, along with the p-values and Phi Cramer's V values to assess statistical significance and the strength of associations.

Table 4.1: Association of risk factors among CAD Patients and Control group:

Risk Factors		CAD	Control	p Value	Phi Cramer
Sex	Male	74(63.8%)	42(36.2%)	.085	0.13
	Female	61(54.0%)	52(46.0%)		
Alcohol	Yes	0	0		
	No	135(59.0 %)	94(41.0 %)		
Diabetes	Yes	63(100.0 %)	0	< .001***	0.7
	No	72(43.4%)	94(41.0%)		
Smoking	Yes	16(100 %)	0	< .001***	0.6
	No	119(55.9%)	94(44.1%)		
Cholesterol	Yes	22(100%)	0	< .001***	0.65
	No	113(54.6%)	94(45.4%)		
Blood pressure	Yes	23(100%)	0	< .001***	0.65
	No	112(54.4 %)	94(45.6%)		
Family History	Yes	74(100%)	0	< .001***	0.7
	No	61(39.4%)	94(60.6 %)		

The graph 4.5 shows the BMI (Body Mass Index) among the CAD patients and Control group. The CAD patients has mean and standard deviation of 23.94 ± 3.76 while Control group has 25.27 ± 2.96 p value:0.004*

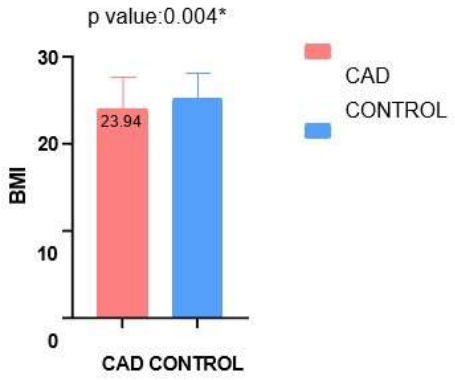


Figure 4.5: BMI among CAD patients and Control group

The graph 4.6 compares the serum ALT, AST, ALP, and GGT levels between CAD patients and control groups. The mean and standard deviation of ALT in the control group are 23.61 ± 8.82, respectively, while in the CAD group, they are 41.95 ± 28.02. For AST, the control group has a mean and standard deviation of 24.65 ± 6.76, while CAD group has 47.89 ± 39.73. ALP in the control group has a mean and standard deviation of 77.19 ± 19.56, compared to a mean and standard deviation of 88.66 ± 21.75 in the CAD group. And GGT has a mean and standard deviation 37.78 ± 15.45 in the control group and a mean and standard deviation of 62.27 ± 37.43 in the CAD group. While the graph 4.7 illustrates the Bilirubin level among CAD patients and Control group.Serum levels of ALT, AST, ALP, GGT, and bilirubin were categorized based on their reference ranges as normal, abnormal, low, and high. The table presents P-values and Phi Cramer's statistics to indicate the significance of these comparisons. Table 4.2 displays the ALT, AST, ALP, GGT, and bilirubin levels among CAD patients and controls, highlighting the distribution of normal and abnormal values.

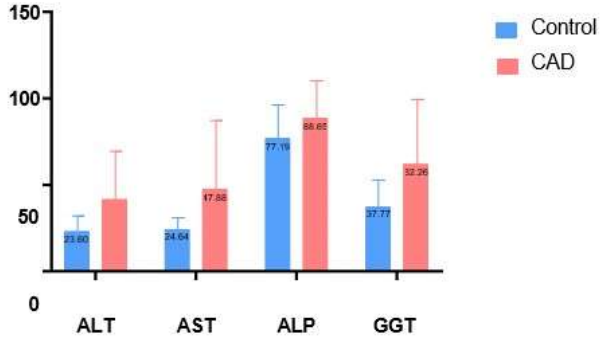


Figure 4.6: Comparison of Liver enzymes among CAD Patients and Control Group

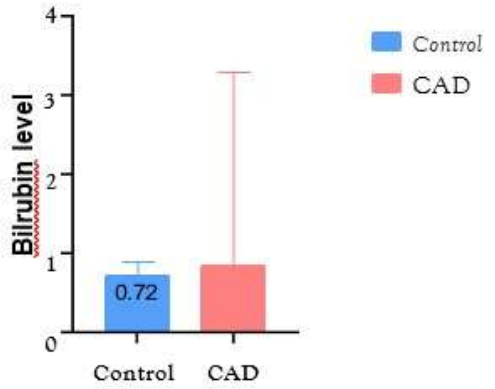


Figure 4.7: Bilirubin level among CAD patients and Control group

Table 4.2: Association of liver parameters among CAD patients and Control groups:

Parameter		CAD	Control	p Value	Phi Cramer
ALT (U/L)	Normal (10–40 U/L)	93(50.0%)	93(50.0 %)	< .001***	0.45
	Abnormal (> 40 U/L)	42(97.4%)	1(2.3 %)		
AST (U/L)	Normal (10–32 U/L)	73(46.2%)	85(53.8 %)	< .001***	0.65
	Abnormal (> 32 U/L)	62(87.3 %)	9(12.7%)		
ALP (U/L)	Low (< 35 U/L)	1(20.0%)	4(80.0%)	0.003**	0.40
	Normal (35–105 U/L)	122(57.5 %)	90(42.5%)		
	High (> 105 U/L)	12(100.0 %)	0		
GGT (U/L)	Normal Males: > 36 U/L Females: ≤ 36 U/L	105(52.8%)	94(47.2%)	< .001***	0.7
	High Males: ≤ 64 U/L Females: > 64 U /L	30(100%)	0		

The pie graph illustrates the proportion of CAD with 47% of patients having SVD, 34% with DVD, and 19% with TVD.

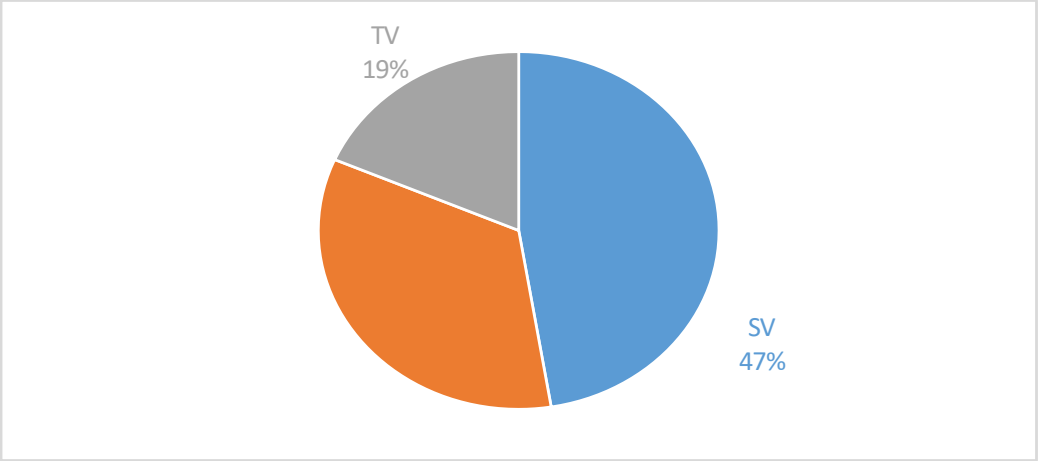


Figure 4.8: Proportion of Coronary Artery Disease (CAD).

The table 4.3 presents the serum (ALT, AST, ALP, GGT) across control, SVD, DVD and TVD CAD groups. It shows the distribution of normal and abnormal values for each parameter, with significant differences noted through P values and Phi Cramer's statistics.

Table 4.3 Association of Liver enzymes across Control, SVD, DVD and TVD in CAD patients:

Parameter		Control	SV	DV	TV	p value	Phi Cramer
ALT (U/L)	Normal (10–40 U/L)	93(50.0%)	61(32.8 %)	28(15.1%)	4(2.2%)	< .001***	0.45
	Abnormal (> 40 U/L)	1(2.3%)	3(7.0%)	18(41.9%)	21(48.8 %)		
AST (U/L)	Normal (10–32 U/L)	85(53.8%)	53(33.5%)	18(11.4 %)	2(1.3%)	< .001***	0.60
	Abnormal (> 32 U/L)	9(12.7 %)	11(15.5 %)	28(39.4%)	23(32.4 %)		
ALP (U/L)	Low (< 35 U/L)	4(80.0 %)	1(20.0 %)	0	0	< .001***	0.40
	Normal (35–105 U/L)	90(42.5%)	63(29.7%)	45(21.2 %)	14(6.6%)		

	High (> 105 U/L)	0	0	1(8.3%)	11(91.7%)		
GGT (U/L)	Normal Males: > 36 U/L Females: ≤ 36 U/L	94(47.2%)	63(31.7%)	38(19.1%)	4(2.0%)	< .001***	0.75
	High Males: ≤ 64 U/L Females: > 64 U/L	0	1(3.3 %)	8(26.7%)	21(70.0%)		

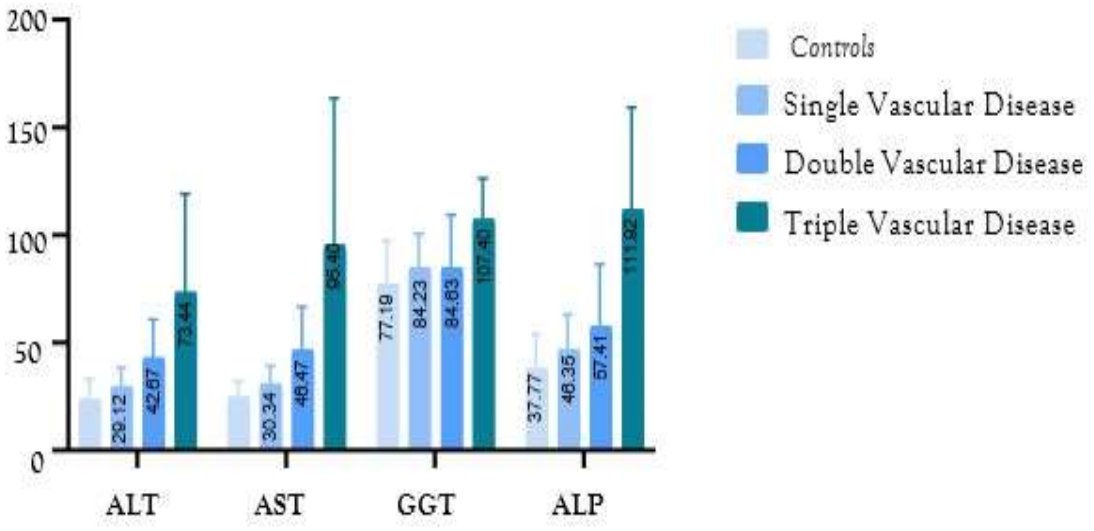
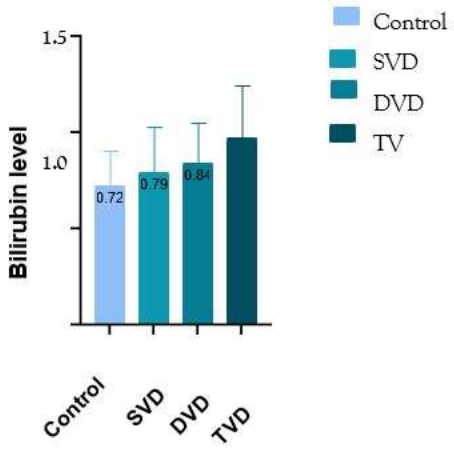


Figure 4.9: ALP, AST, GGT and ALP among Control, SVD, DVD and TVD.

The graph illustrates the comparison of liver parameters ALT, AST, ALP, GGT and Total Bilirubin level across Control, SVD, DVD, and TVD in CAD patients.

Figure 4.10: Bilirubin level among Control, SVD, DVD and TVD



Discussion

In this study, we thoroughly examined the association between serum gamma-glutamyl transferase (GGT) and aspartate aminotransferase (AST) levels and coronary artery disease (CAD). Our findings revealed that (1) patients with CAD had significantly higher serum GGT levels compared to controls, (2) elevated GGT levels were independently linked to an increased risk of CAD, (3) there was a modest yet significant correlation between serum GGT levels and disease severity, and (4) GGT levels were influenced by factors such as gender, smoking and alcohol use, body mass index, diabetes mellitus, hypertension, as well as blood glucose and lipid profiles.

GGT is an enzyme widely distributed in organs including the kidneys, liver, pancreas, spleen, and vascular endothelium. Its elevation often reflects liver or biliary tract diseases, alcohol consumption, or medication effects. Because of this, GGT is commonly measured alongside other liver enzymes like ALT and AST to assess liver function and detect hepatic disorders.

The link between liver dysfunction and dyslipidemia has gained considerable interest, suggesting the liver's significant role in cardiovascular disease (CVD). Evidence indicates an increased CVD risk among individuals with liver disease. Hepatic enzymes, including GGT, serve as reliable markers of liver function, and elevated GGT may indicate greater hepatic impairment, contributing to CVD through disrupted lipid metabolism, including cholesterol transport. Furthermore, microRNAs in macrophages influence cholesterol balance and atherosclerosis progression, with specific microRNAs affecting plasma cholesterol and plaque development.

Glutathione (GSH), a vital antioxidant, depends on GGT activity to maintain intracellular levels by providing cysteine through GGT-mediated degradation. This process can generate reactive oxygen species (ROS) and promote oxidative

stress, a key factor in endothelial dysfunction and CAD development.

Analysis of data from 229 participants (135 CAD patients and 94 controls) showed significantly elevated GGT levels in CAD patients (62.27 ± 37.43 U/L) compared to controls (37.78 ± 15.45 U/L; $p < 0.001$). Similar elevations were observed for ALT and AST. Moreover, comorbid conditions such as diabetes and smoking were significantly more prevalent in CAD patients. These results underscore the strong association between higher GGT levels and CAD risk.

Our previous research also demonstrated significant increases in liver enzymes among CAD subgroups, with the highest levels in patients with triple-vessel disease compared to those with single- or double-vessel disease or no significant stenosis. Despite these trends, the correlation between GGT levels and Gensini scores was weaker than expected, possibly due to sample characteristics or methodological limitations.

Conclusion

This study highlights a significant association between coronary artery disease (CAD) and risk factors such as hypertension, diabetes, smoking, and high cholesterol. It also reveals a clear link between CAD and elevated liver enzymes, especially GGT and AST. Higher GGT levels correlate with CAD severity and serve as an independent risk factor. These findings suggest liver enzymes could be valuable markers for assessing CAD severity, underscoring the importance of considering both traditional risk factors and liver health in CAD diagnosis and management.

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