

# ELEVATED ALANINE AMINOTRANSFERASE (ALT) LEVELS AS PREDICTORS OF CORONARY HEART DISEASE: A CROSS-SECTIONAL STUDY ON RISK FACTORS AND EARLY DIAGNOSIS

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### Abstract

**Objective:** This study aimed to determine the levels of Alanine Aminotransferase (ALT) in patients with Coronary Heart Disease (CHD) and examine the relationship between ALT levels and the presence and severity of CHD. **Study Design, Place, and Duration:** A cross-sectional study was conducted by the Institute of Medical Lab Technology, Isra University Islamabad, in collaboration with DHQ Hospital, Jhelum, and Premium Diagnostic Lab, Rawalpindi, from October 1, 2023, to December 31, 2023. **Methodology:** We collected 3ml blood samples from 100 CHD patients and 100 healthy controls. Samples were analyzed using the Roche Cobas Model C311. Demographic and clinical data (age, gender, diabetes, smoking, family history) were recorded. Data analysis was performed using SPSS version 25. **Results:** The mean ALT level was 36 U/L in the control group and 196 U/L in the CHD group. The standard deviation was 23.7 for the control group and 544.8 for the CHD group. **Conclusion:** The study confirmed that CHD is associated with factors like type 2 diabetes, dyslipidemia, smoking, and family history. Elevated AST and ALT levels are significant risk factors for CHD. Lifestyle changes, such as a balanced diet and smoking cessation, can help prevent CHD. ALT and AST may serve as independent predictors for early CHD diagnosis and prevention.

**Keywords:** Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Coronary Heart Disease (CHD), Statistical Package for the Social Sciences (SPSS), Type 2 Diabetes, Dyslipidemia.

## 1. INTRODUCTION

A medical condition called coronary atherosclerotic heart disease causes the coronary arteries to constrict, which reduces the blood flow and oxygen delivery to the heart muscle. This pathological state, commonly referred to as coronary heart disease (CHD), can also be influenced by functional changes in the coronary arteries such as spasms.<sup>1</sup> Several risk factors, including dyslipidaemia, type 2 diabetes, and smoking, act at various phases of the disease pathway and have an impact on the development of CHD.<sup>2</sup> In CAD patients, type 2 diabetes has been found to exacerbate coronary lesions and impede the formation of collateral circulation, significantly increasing the mortality rate of CAD patients.<sup>3</sup> CAD is a crucial public health issue and a leading global cause of death (World Health Organization, 2021).<sup>4</sup>

Ischemic Heart Disease (IHD) caused a substantial number of deaths in 2008, resulting in 7,249,000 fatalities worldwide, which accounted for 12.7% of all global deaths.<sup>5</sup> IHD accounted for 11.8% of fatalities in low and middle income countries in 2001 and 17.3% of fatalities in high-income countries.<sup>6</sup> This condition was shown to be the leading cause of death in most regions, with the exception of Sub-Saharan Africa and East Asia and the Pacific.<sup>7</sup> IHD was responsible for 29.7% of all fatalities in Europe and Central Asia.<sup>8</sup> IHD, on the other hand, only accounted for 3.2% of all fatalities in Sub-Saharan Africa, where it was the eighth most common cause of death, after HIV/AIDS, malaria, lower respiratory tract infections, diarrhea sickness, newborn illnesses, and measles.<sup>9</sup> IHD accounted for 8.8% of all fatalities in East Asia and the Pacific, making it the third most common cause of death.<sup>10</sup> These findings underscore the worldwide burden of IHD and the urgent need for focused treatments to reduce the disease's incidence.

Cardiovascular disorders, especially coronary heart disease, have emerged as a serious public health problem around the world. According to the World Health Organization (2017).<sup>11</sup> CVD caused 17.9 million deaths in 2016, or 31% of all deaths worldwide.<sup>12</sup> Developing countries are disproportionately affected, accounting for more than 75% of CVD-related fatalities.<sup>13</sup> The increasing prevalence of CHD in developing countries is attributed to the impact of social and economic changes that accompany industrialization and urbanization.<sup>14</sup>

Nearly 17 million people die from cardiovascular disease (CVD) each year, making it the second largest cause of death worldwide.<sup>15</sup> According to a recent study, there was a 7% rise in worldwide cardiovascular fatalities from 1990 to 2013, with an increase in the death rate from ischemic heart disease (IHD) of up to 40% over this time period.<sup>16</sup> LMICs bear the greatest burden of CVD, contributing for about 80% of CVD fatalities (WHO, 2021).<sup>17</sup> CVD in LMICs exhibits unique patterns when compared to HICs, with the bulk of CVD fatalities occurring in younger age groups and IHD mortality on the rise.<sup>18</sup> To address this rising public health problem, specific methods for CVD prevention and treatment in LMICs are required, as resources and prioritization for CVD prevention and management are frequently weak.<sup>19</sup> Numerous prior scientific investigations have revealed a strong link between obesity and coronary artery disease (CAD) risk factors.<sup>20</sup> Obesity, type2 diabetes, hypertension, and dyslipidemia are pathological conditions linked to

nonalcoholic fatty liver disease (NAFLD). The prevalence of this condition ranges from 14 to 23% in the general population and from 70 to 90 percent in individuals with obesity and type 2 diabetes mellitus.<sup>21</sup>

The pyridoxal-5'-phosphate-dependent enzyme alanine aminotransferase (ALT) catalyses the conversion of alanine to pyruvate and glutamate in transamination reactions.<sup>22</sup>

This study aims to explore the potential links between liver enzyme and cardiovascular health. Elevated AST and ALT level suggest a connection between liver health and cardiovascular risk factors investigating this correlation could provide insight into complex interplay between liver function and CHD.

## **2. OBJECTIVES**

The objectives of this study are

- Determination of the association of serum ALT and CAD to determine its level in CAD patients.
- Determination of the association of serum AST and CAD to determine its level in CAD patients.

## **3. MATERIALS AND METHODS**

### **3.1 Ethical Approval:**

The ethical committee of Al-Nafees Medical College, Isra University Islamabad, approved the study (Letter No F.3/Ethical Letter/MLT/IU2023/001, dated September 25, 2023). Informed consent was obtained from all subjects.

### **3.2 Study Settings:**

The study was conducted at the Institute of Medical Lab Technology, in collaboration with the Cardiology Department of DHQ Hospital, Jhelum, and Premium Diagnostic Lab, Rawalpindi.

### **3.3 Study Design:**

This was a cross-sectional study with a prospective design.

### **3.4 Study Duration:**

The study was conducted from October 1, 2023, to December 31, 2023.

### **3.5 Sample Population and Size:**

200 subjects were enrolled: 100 CHD patients (confirmed by ECG) and 100 controls from Premium Diagnostic Lab. The sample included 96 males and 104 females.

### 3.6 Sampling Technique:

Non-probability convenient sampling was used, including all reporting patients at DHQ who met the inclusion criteria.

### 3.7 Inclusion Criteria:

Subjects with CAD were included in the study.

### 3.8 Exclusion Criteria:

Subjects with chronic liver diseases, Hepatitis B, and Hepatitis C were excluded.

### 3.9 Patient Information:

A standardized questionnaire collected sociodemographic data, including age, height, weight, residence, smoking, exercise, family history of CAD, diabetes, and dyslipidemia.

### 3.10 Data and Blood Sample Collection:

Data were collected from the Cardiology Department of DHQ Jhelum. Blood samples were taken from control subjects at Premium Diagnostic Lab. Venous blood (3ml) was drawn, allowed to clot, and centrifuged to isolate serum. Samples were stored at 2-8°C until testing.

### 3.11 Laboratory Tests:

The serum levels of ALT and AST were measured using the Roche Cobas Model C311.

Statistics:

ANOVA was performed using SPSS version 25. A significant result ( $p < 0.05$ ) indicated a close relationship between high serum ALT and AST levels in CAD patients compared to the control group.

## 4. RESULTS

We collected 200 samples: 100 CHD patients and 100 controls. The mean ALT level was 36 U/L in controls and 196 U/L in CHD patients, with standard deviations of 23.7 and 544.8, respectively.

**Table 1: Descriptive statistics of study**

Parameters	Number	Minimum	Maximum	Mean	Std. Deviation (SD±)
Age in Diseased	100	25	87	57.40	14.062
Serum ALT in Diseased Group	100	8	3377	196.09	544.843
Age in Control Group	100	21	60	42.91	9.637
Serum ALT in Control	100	9	158	36.97	23.705
Serum AST in Diseased group	100	10	2215	167.6	502.8
Serum AST in control group	100	11	142	32.9	20.70

#### 4.2 Age distribution in control and diseased group:

In this study minimum age of subjects for control group was 21 years and maximum age were 60 years, mean of control group for age was 42.91 and their standard deviation was 9.63 whereas, minimum age for disease group were 25 years and maximum age were 87 years and their mean is 57.4 and standard deviation was 14.06 as listed in table 4.1. The study subjects were further divided into three age groups with minimum age of subject for control group was 21 years and maximum age was 65 years. Disease group subjects were divided into four groups with minimum age of subjects for diseased group are 21 years and maximum age was > 80 years as listed in figure 1.

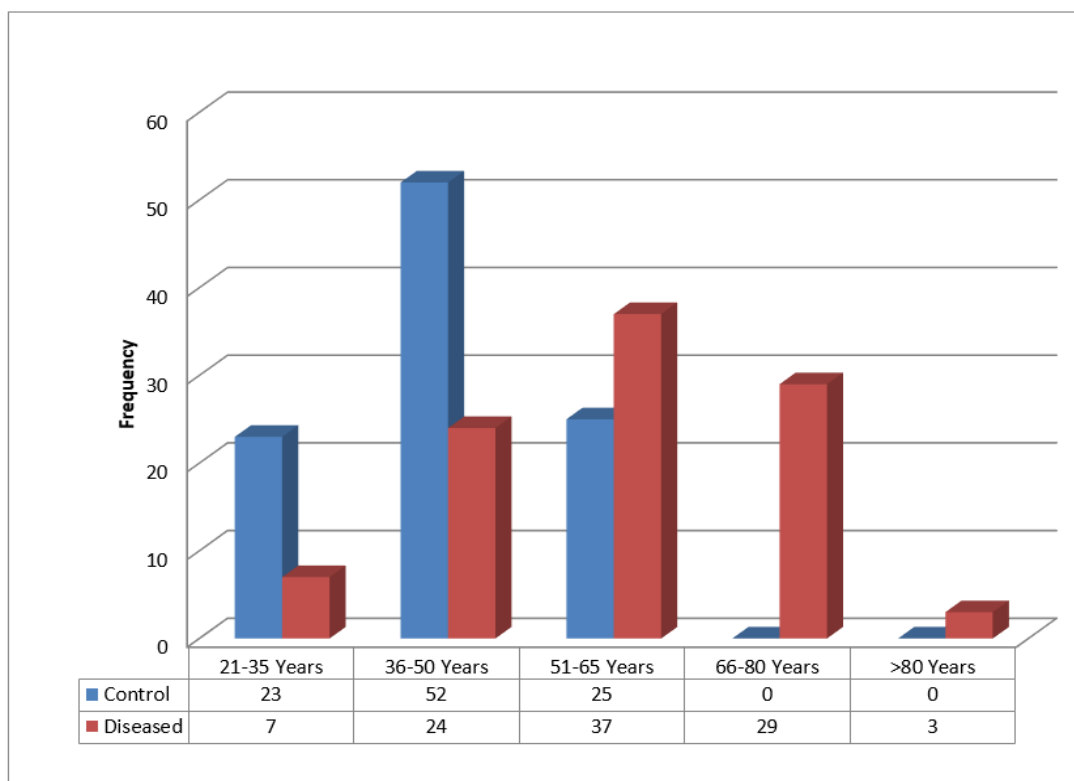


Figure 1: Age group distribution

#### 4.3 Gender distribution in control and diseased group

The study includes 54 male and 46 females in diseased group. Whereas, there are 58 male and 42 females in control group as in table 4.3.

Table 4.3.1 Gender distribution in diseased group:

Gender	Frequency	Percent
Male	54	54.0
Female	46	46.0
Total	100	100.0

**Table 4.3.2 Gender distribution in control group:**

Gender	Frequency	Percent
Male	58	58.0
Female	42	42.0
Total	100	100.0

#### 4.4 Smoker distribution in control and diseased group

In this study population, 28 subjects were Smoker whereas, 72 subjects were non-smokers in control group, while in Diseased group 44 subjects were smokers and 56 subjects were non-smokers as listed in table 4.4.

**Table 4.4.1 Smoker in Control**

Smoker	Frequency	Percent
Yes	28	28.0
No	72	72.0
Total	100	100.0

**Table 4.4.2 Smoker in Diseased**

Smoker	Frequency	Percent
Yes	44	44.0
No	56	56.0
Total	100	100.0

#### 4.5 Family history in control and diseased group

In control group, 36 subjects were presented with positive family history whereas 65 were without positive family history. Whereas, in disease group 30 subjects were with positive family history and 70 subjects were without positive family history as in table 4.5.

**Table 4.5.1 Family history in control group**

Family history	Frequency	Percent
Yes	36	36.0
No	64	64.0
Total	100.0	100.0

**Table 4.5.2 Family history in disease group**

Family history	Frequency	Percent
Yes	30	30.0
No	70	70.0
Total	100	100.0

#### 4.6 Diabetic distribution

In Control group there were 31 diabetic study subjects and 69 were non-Diabetic whereas, in diseased groups 70 subjects were Diabetics and 30 subjects were non-diabetic as listed in graph below fig 2.

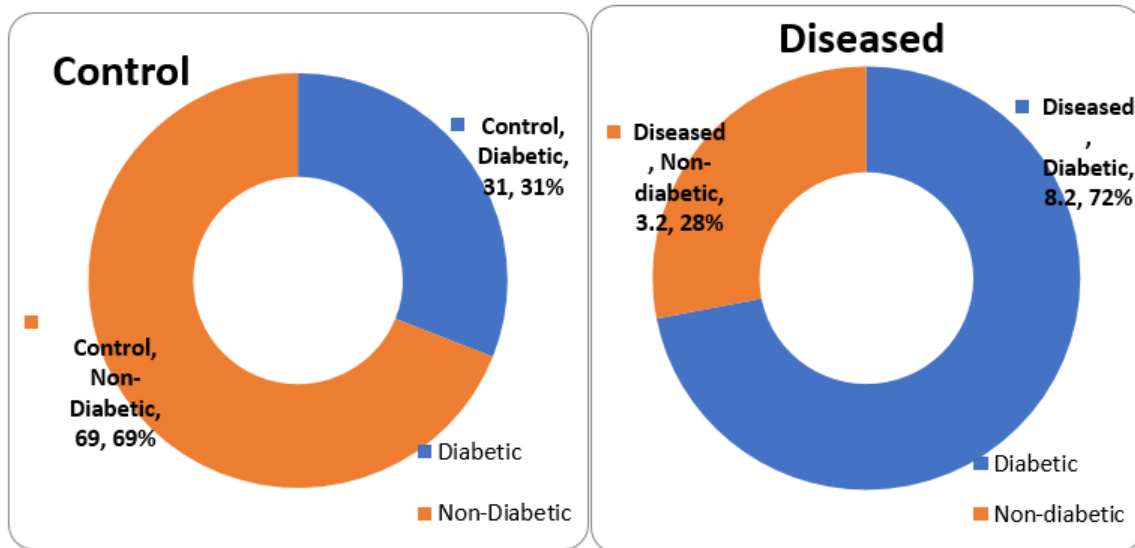


Figure: 2 Diabetic association

#### 4.7 Stastical Analysis

ANOVA was performed using the statistical package for social sciences 25 (SPSS).

ANOVA					
Diagnosis	Sum of Squares	Df	Mean Square	F	p value
Between Groups	498.446	89	5.601	1.438	.035
Within Groups	428.274	110	3.893		
Total	926.720	199			

### 5. DISCUSSION

This study was conducted at DHQ Jhelum Hospital Cardiology department and premium diagnostic lab Rawalpindi, we have collected data from 100 patient's reports and 100 blood samples. 100 were without disease (control group) and 100 with Cardiac disease (disease group). The demographic data (Age, gender, diabetes, smoking, family history) was taken through structured questionnaire from both diseased and control group. The Serum ALT, AST were measured from all blood samples. Statistical analysis was done for the measurement of mean value, standard deviation, frequency and correlation by SPSS.

The current study results show that the mean value of ALT in the control group is 36 (<42U/l) and mean value of ALT in diseased group is 196 (>42U/l). Standard deviation of ALT for control group is 23.7 and for disease group is 544.8.

Similarly, East Asian studies have reported that ALT elevation or liver dysfunction is associated with cardiovascular risk factors and subclinical atherosclerosis.<sup>23</sup> These findings suggest that elevated serum ALT activity in the absence of viral hepatitis or excessive alcohol consumption is associated with increased cardiovascular risk and the association

is mostly due to nonalcoholic fatty liver disease (NAFLD). Elevated ALT level is also closely related to major cardiovascular risk factors and the metabolic syndrome.<sup>24</sup>

In this study subject minimum age of subjects for control group was 21 years and maximum age were 60 years, as listed in table 4.1. The study subjects were further divided into three age groups with minimum age of subject for control group was 21 years and maximum age was 65 years. Disease group subjects were divided into four groups with minimum age of subjects for diseased group are 21 years and maximum age was > 80 years as listed in table 4.2.

The number of people affected by heart disease increases with age in both men and women.<sup>25</sup> About four out of five people who die of coronary heart disease are 65 or older.<sup>26</sup> In older age with the age blood vessels become less flexible, making it harder for blood to move through them easily. These things, along with poor nutrition and exercise habits, can increase your risk of heart disease.<sup>27</sup> Add other risk factors — such as high blood pressure, smoking, and diabetes — and it's likely that you will have a greater risk for a heart attack.

Study that was conducted in USA, indicate that in early age, premenopausal women ( $\leq 40$  yrs) run significantly lower risks in developing CHD than postmenopausal women.<sup>28</sup> Middle-aged men and women (between 40-65 years) show greater risks for developing CHD than younger ones, along with incidences of co-morbidities such as hypertension and diabetes. Though in general the risk for CHD doubles for every 10mm Hg rise in blood pressure for individuals between 40-70 years, isolated systolic hypertension is steeper for women  $\geq 55$  years, tilting the risk towards women.<sup>29</sup> Older age, Elderly people ( $\geq 65$  years) are normally associated with high incidences of CHD, resulting in the steep mortality rates of CHD. The risks for hypertension are the greatest along with the hazards of diabetes mellitus, evident by the fact that most diabetic patients die of CHD.<sup>30</sup>

Similarly, a study conducted in an Indian hospital, the prevalence of CAD in hospital admissions was found to be 29.6%<sup>31</sup>. Highest incidence of CAD was seen in the age group of 51 to 60 years.

In control group, there were 54 Males and 46 Females, while in diseased group, there were 58 males and 42 females as listed in Table 4.3.

Males are more affected with CHD than females due to unhealthy behaviors that include cigarette smoking, heavy alcohol use, eating more red meat, and exposure to physical hazards.<sup>32</sup> Females are less effected with CHD then males because in female's exposure to endogenous estrogens during the fertile period of life delays the manifestation of atherosclerotic disease. Estrogens have cardio protective role as they promote a direct vasodilatory effect through alpha and beta receptors in the vessel walls.<sup>33</sup>

The sex differences in the measured cardiovascular risk factors explained nearly half of the observed sex difference in CHD incidence and mortality<sup>34</sup>. In both sexes, the risk of CHD increased markedly with age. In most populations, serum total cholesterol increases as age increases. In men, this increase usually levels off around the age of 45 to 50 years, whereas in women, the increase continues sharply until the age of 60 to 65 years<sup>35</sup>. Like



serum cholesterol, blood pressure also tends to increase with age, and more prominently in women than in men<sup>36</sup>. In Control group there were 31 diabetic study subjects and 69 were non-Diabetic whereas, in Disease groups 70 subjects were Diabetics and 30 subjects were non-diabetic as listed in graph 4.6. Diabetes is caused by different risk factors such as hypertension; stress, obesity, low socio-economic status, sedentary lifestyles. All these risk factors lead to insulin resistance. Due to lack of physical activity obesity chances increases that is an independent risk factors of CHD.

In the Framingham study, the incidence of cardiovascular disease among diabetic men was twice that among non-diabetic men, and similarly was three times more elevated in diabetic women compared to non-diabetic women.<sup>37</sup> In the Copenhagen City Heart Study, the relative risk of incident myocardial infarction was 2 to 3-fold increase in diabetics compared to non-diabetics, independent of the presence of other known cardiovascular risk factors (such as hypertension).<sup>38</sup>The burden of diabetes is rapidly increasing due to the increasing prevalence of unhealthy diet, sedentary lifestyle, population aging, and smoking. According to a recent survey, 5.1% of Pakistanis have been newly diagnosed with DM: 5.1% men and 6.8% women in urban areas and 5.0% men and 4.8% women in rural areas.<sup>39</sup>

In this study 44 subjects are smoker whereas, 56 subjects are non-smokers. Similarly, family history cases are also low in this study population.30 subjects are with positive family history and 70 subjects are without family history of CHD as listed in table 4.5. Low levels in our study as compared to other studies because the information is taken by structured questionnaire which might be wrong. Smoking is a major cause of CVD and causes one of every three deaths from CVD. Smoking can: Raise triglycerides (a type of fat in your blood) lower “good” cholesterol (HDL) Make blood sticky and more likely to clot, which can block blood flow to the heart and brain.

The relationship between smoking and CVD is unequivocal; it is the major health risk in today's world. According to the 2015 World Health Organization (WHO) report, 22.2% of men and 2.1% of women smoke in Pakistan.<sup>40</sup> In the 20th century, 100 million people died the world over due to diseases caused using excess tobacco, and it is projected that by 2030, one of every six individuals will die due to the deadly effects of smoking.<sup>41</sup> Individuals who smoke 40 or more cigarettes per day have a nine times higher risk of heart problems than those who have never smoked.

## 6. CONCLUSION

The results reveal that the occurrence and development of CHD are related to multiple factors and caused via multiple steps. Classic risk factors of CHD including type 2 diabetes, dyslipidemia, history of smoking, and family history of CHD are confirmed in the present study. Moreover, results also indicate that AST and ALT are also a risk factors of CHD. Thus, rational diet, controlling of intake of cholesterol and fat, intake of more fruits and vegetables, smoking cessation, drinking cessation and reduction in passive smoking are helpful to prevent CHD. In addition, serum AST and ALT may serve as independent predictors of CHD and be used for the early diagnosis and prevention of CHD.

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