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ASSOCIATION BETWEEN HIGHER LEVELS OF ALANINE TRANSAMINASE (ALT) AND CORONARY ARTERY DISEASE (CAD)

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Abstract:

Background*: Coronary artery disease (CAD) is the most common form of heart disease with multifactorial etiology and atherosclerosis. Recently it is considered that ALT associated with endothelial dysfunction and carotid atherosclerosis. The predictive value of ALT for coronary events seems independent of traditional risk factors and the features of the metabolic syndrome.*

Aim: *To find out association of elevated ALT with coronary artery disease*

Methods: *This cross sectional study was carried out on 100 patients presented with clinically suspected CAD. Serum ALT was measured. Patients underwent angiography and images of coronary arteries were obtained and presence of CAD was noted. Relative risk was calculated to measure association between raised ALT and CAD.*

Results: *The mean age range of patients was 49.16±10.15 years. There were 78 male and 22 female patients. The male to female ratio was 3.54:1. The mean ALT was 41.58±16.18U/L. Coronary angiography findings showed that 29% patients had normal coronaries, 4% had mild CAD, 49% had moderate CAD and 18% had severe CAD. There were 1.8 times high risk of CAD in patients with raised ALT.*

Conclusion: *It is concluded that although difference in CAD and raised ALT is insignificant but the risk of CAD is 1.8 times high in patients with raised ALT.*

Keywords: *Coronary Artery Diseases, Serum Alanine Transaminase.*

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INTRODUCTION:

Coronary Artery Disease (CAD) is the most common form of heart disease with multifactorial etiology and atherosclerosis is its most common cause. Atherosclerosis is caused by obstruction of the coronary arteries by atheromatous plaque. It is the commonest cause of cardiovascular disability and death and includes chronic (stable) angina, unstable angina, Prinzm et al (variant) angina, micro vascular angina and acute myocardial infarction. Syndromes of CAD also occur in the form of asymptomatic (silent) myocardial ischemia, congestive heart failure, cardiac arrhythmias and sudden death [1]. Eighty percent of the deaths due to these diseases and 86% of the global burden of cardiac disease are in the developing countries including Pakistan. [2] In Pakistan the prevalence of ACS is increasing rapidly with definite diagnosis in men than in women (6.1% vs 4.0%; p=0.009) [3,4] . The World Health Organization (WHO) has estimated that by 2020, the global number of deaths from CAD will have risen from 7.2 million in 2002 to 11.1 million [5,6] . It is now well known that development of insulin resistance results in increased hepatic gluconeogenesis and overproduction of triglyceride-rich lipoproteins and consequently nonalcoholic fatty liver disease (NAFLD) and is associated with central obesity, type 2 diabetes and dyslipidemia [7] . The correlation of liver transaminases with blood pressure, dyslipidaemia, blood glucose and waist circumference as components of the metabolic syndrome have been suggested in several studies8 . Besides prior reports, recent evidence of the association between hepatic steatosis or its marker alanine aminotransferase (ALT) and endothelial dysfunction, carotid atherosclerosis and coronary events substantiates the probable predictive value of liver enzymes for CAD; however, this has not been directly and quantitatively investigated before, specially here in Pakistan [9,10,11] . The objective of the study was to find out association of elevated ALT with coronary artery disease.

MATERIAL AND METHODS:

This cross-sectional study was conducted in the Department of Cardiology, Jinnah Hospital Lahore for a period of two years. Sample size: 100 patients presenting with clinically suspected CAD. Inclusion criteria: Age 18-70 years of either gender presenting with clinically suspected CAD Exclusion criteria: Excessive alcohol intake, cancer, rheumatoid arthritis, chronic kidney disease, hepatotoxic drugs, inflammatory bowel disease, acute myocardial infarction, already known CAD. Data collecting procedure: All patients who were clinically suspected CAD were enrolled from OPD and from cath lab after an informed consent. Baseline demographic information such as age, sex, weight, height, education and address were noted. History of chest pain and shortness of breath with his/her functional class were noted along with examination. Routine laboratory tests were done. Serum ALT were measured on fresh samples according to the methods of the International Federation of Clinical Chemistry. Then angiographic assessments were performed according to Judkin's method with a digital angiographic system. Stenosis score (0-3 points; number and severity of coronary stenosis or lesions; 0 for Normal, 1 for coronary lesion with diameter stenosis 75% diameter stenosis was noted.

Statistical analysis: Data entry and analysis was done by using SPSS 15.0 Quantitative variables were presented with mean±SD. Qualitative variables were presented by using frequency, percentage and appropriate graphs. Relative risk was calculated to measure association between CAD and raised ALT. RR>1 was considered as risk of association with p-value≤0.05 was considered as significant.

RESULTS:

Table 1: Baseline characteristics of patients (n=100)

Characteristic	No. of Patients
Age	49.16±10.15years
Gender (Male / Female)	78 / 22
BMI (kg/m^2)	26.51±2.32
ALT (U/L)	41.58±16.18

Table 2: Distribution of raised ALT

ALT (10-40)	81 (81%)
ALT (>40)	19 (19%)
Total	100 (100%)

Table 3: Association of raised ALT with CAD

AAS SCORE	ALT Level		Total
	10-40	>40	
AAS score 0= Non CAD	27	2	29
AAS score 1-9 = CAD	62	9	71
AAS score 1-3 = Mild CAD	4	0	4
AAS score 4-6= Moderate CAD	43	6	49
AAS score 7-9= Severe CAD	15	3	18
Total	**89**	**11**	**100**

Chi-Square test= 6.629, p-value= 0.356 (Insignificant) Relative risk = 1.838 (95% CI; 0.4226, 7.994)

The mean age of patients was 49.16±10.15years. Out of total 100 patients, 78 males and 22 female with male to female ratio 3.54:1. The mean BMI was 26.51±2.32kg/m2 . The mean ALT was 41.58±16.18 U/L. (Table 1) There were 81 patients with normal ALT while 19 patients had raised ALT. (Table 2) On angiography, CAD was found in 71% patients while CAD was absent in 29% cases (Fig 1). Among 100 patients 29 had no CAD (AAS score 0) but 71 had CAD (AAS score 1-9). Among patients with CAD, 4 had AAS score 1-3 (Mild CAD), 49 had AAS score4-6 (Moderate CAD) and 18 had AAS score 7-9 (Severe CAD) (Table 3).

DISCUSSION:

Associations between elevated serum levels of liver enzymes and increased cardiovascular risk have attracted much interest. In fact, serum ALT have shown to predict cardiovascular events in prospective studies independently from conventional cardiovascular risk factors. [11-14] The most frequent cause of elevated liver enzymes in current clinical practice is non-alcoholic fatty liver disease, which affects as much as 15–20% of the general population and up to 90% of patients with type 2 diabetes [15,16] . Pathophysiologically, NAFLD is strongly related to insulin resistance and to the metabolic syndrome, the cluster of cardiovascular risk factors associated with insulin resistance. [17] Indeed, elevated GGT is a predictor of incident of metabolic syndrome. 18 Both insulin resistance and the clinical entity of the metabolic syndrome predict vascular events; it is a matter of debate in as far elevated liver enzymes are associated with cardiovascular events independent of the clinical diagnosis of the metabolic syndrome. [19] Myocardial infarction, a frequently applied endpoint in clinical studies, does not optimally reflect the atherogenicity of metabolic parameters. It is the last step in the development of atherothrombotic CAD, and thrombogenic factors ultimately determine whether or not infarction occurs [20]. Hardly any data on the association between liver enzymes and angiographically determined coronary artery disease is available from the literature. A single small study from Iran, while failing to show an association between liver enzymes and coronary atherosclerosis in the total study population, described an association of liver enzymes with severe CAD in the subgroup of women only; formal interaction analyses were not performed in this study. [21] According to the results of a study in their larger population of angiographically characterized patients, they neither among women nor among men observed an association between liver enzymes and coronary atherosclerosis. Further, interaction analyses in their investigation did not suggest a significant gender difference with respect to the association between liver enzymes and coronary atherosclerosis22 . The association of elevated liver enzymes with the angiographically determined coronary artery state is uncertain in literature. In the present study we therefore aimed at investigating the associations of ALT with angiographically determined CAD. The correlation of liver transaminases with blood pressure, dyslipidaemia, blood glucose and waist circumference as components of the metabolic syndrome have been suggested in several studies. [23-25] Besides prior reports, recent evidence of the association between hepatic steatosis or its marker ALT and endothelial dysfunction, carotid atherosclerosis and coronary events substantiates the probable predictive value of liver enzymes for CAD; however, this has not been directly and quantitatively investigated before [24,25] . More recently, Schindhelm et al[11] in a prospective study suggested that ALT predicts coronary events. It is noteworthy that prior studies have shown that the association between the metabolic syndrome and nonfatal CAD is somewhat stronger in women than in men. Conversely, cardiovascular events more often have a fatal outcome in men. [26] Given that European guidelines for risk stratification are merely based on risk of fatal CVD [27], further prospective studies are needed to elucidate the actual role of liver transaminases in predicting cardiovascular morbidity and mortality. There is a growing body of evidence in support of the association of elevated ALT with

insulin resistance and various components of the metabolic syndrome, namely type 2 diabetes, which is considered to be a major risk factor for atherosclerosis [24,25].

CONCLUSION:

It is concluded that although difference in CAD and raised ALT is insignificant but the risk of CAD is 1.8 times high in patients with raised ALT. But further studies are required to confirm the evidence with large sample size and proper case control or cohort studies are required to confirm the association.

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