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ORIGINAL RESEARCH

Evaluation of association between serum liver enzymes and cardiovascular diseases at a tertiary care centre:A Cross-Sectional Study

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ABSTRACT

Background: Cardiovascular diseases (CVDs) refer to a group of disorders affecting the heart and blood vessels. The present study was conducted to evaluate association between serum liver enzymes and cardiovascular diseases.

Materials & Methods: 58 patients with incident CVDs of both genders were put in group I and 58 healthy subjects in group II. Parameters such as smoking and drinking habits, WHR, BMI, AST, ALT, ALP, CK-MB, glucose, TC, TG, and HDL-C were measured.

Results: Group I had 30 males and 28 females and group II had 29 males and 29 females. In group I and group II, the mean BMI (kg/m2) was 25.6 and 24.1, waist-hip ratio was 0.99 and 0.92, SBP (mmHg) was 128.4 and 114.6, DBP (mmHg) was 76.4 and 78.8, CK-MB (U/L) was 86.4 and 18.2, Troponin-I (µg/L) was 11.4 and 0.92, AST (U/L) was 126.2 and 26.1, ALT (U/L) was 54.2 and 20.6, ALP (U/L) was 102.5 and 76.2, FBS (mg/dL) was 114.7 and 89.4, HbA1C (%) was 6.2 and 5.3, TC (mg/dL) was 154.8 and 142.6, TG (mg/dL) was 146.2 and 103.5 and HDL-C (mg/dL) was 35.7 and 43.2 respectively. The difference was significant ($P< 0.05$).

Conclusion: There was high liver enzymes level in patients with CVDs. Elevated serum aminotransferease, in particular AST, was found to be the strongest predictor of incident CVDs.

Keywords: Cardiovascular diseases(CVDs), cholesterol, liver enzymes

Introduction

Cardiovascular diseases (CVDs) refer to a group of disorders affecting the heart and blood vessels. These conditions are among the leading causes of death globally and encompass a range of problems, from coronary artery disease to stroke and heart failure.[1] CAD occurs when the blood vessels supplying the heart (coronary arteries) become narrowed or blocked by a build-up of plaque (atherosclerosis). This can lead to angina (chest pain) or a heart attack (myocardial infarction). Risk factors are high blood pressure, high cholesterol, diabetes, smoking, a sedentary lifestyle, physical inactivity, obesity, elevated blood lipids, and family history.[2]Since South Asia is thought to be the world's epicentre for CVDs, and the region suffers significant economic losses and must spend a sizable portion of its national GDP on healthcare. As a result, policies that promote CVD prevention, early diagnosis, and appropriate treatment both protect the national economy and lengthen life expectancy. The overall death rate related to CVDs is rising despite early detection, treatment, and prevention of this risk factors.[3]

The metabolism and equilibrium of multiple biomolecules, including fatty acids, proteins, carbohydrates, lipids, amino acids, and lipoproteins, are significantly affected by the liver.[4] The liver utilises a myriad of enzyme systems, such as AST, ALT, and ALP, for this purpose. In clinical

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settings, the serum levels of liver enzymes, specifically AST, ALT, and ALP, have been utilised as indicators of hepatic dysfunction due to their demonstrated elevation during different liver diseases. These enzymes' plasma levels have been linked to incident CVDs in many searches, and as a result, they may be used as potential CVD risk markers.[5]

However, previous study has shown that the incidence of CVDs is not correlated with an individual liver enzyme.[6]

Baseline levels of ALP and GGT are both log-linearly positively correlated with the risk of CVD. The relationships between ALT and cause-specific cardiovascular outcomes could vary and revealed a positive correlation between ALT and stroke but a negative association with coronary heart disease.[7]While a different study found that elevated levels of ALT and AST were linked to CVD mortality[8].

Aim and objectives

The present study was conducted to evaluate the association between serum liver enzymes and cardiovascular diseases.

Materials and Methods

The present case-control observational study was conducted on 58 patients with incident cardiovascular diseases (CVDs) of both genders in the Department of Cardiology, Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar, India. The duration of the study was from August 2016 to July 2017. All were informed regarding the study, and their written consent was obtained. The Institutional Ethics Committee gave the study its approval. Data such as name, age, gender, etc. was recorded. A total of 116 participants were enrolled, of which 58 had incident CVDs and the remaining 58 were healthy controls.

Inclusion criteria

The patients included in the present research were those who complained of chest pain and had a history of cardiac problems when they were brought to the emergency department and cardiology unit.The treating cardiologists determined that these hospitalised patients had CVDs based on their medical histories, symptoms, serum creatine kinase MB (CK-MB), troponin I (TpI), and ECG results.

Exclusion criteria

The study excluded patients with CVDs who also had musculoskeletal disorders such as muscular dys trophies, myopathies, and celiac disease, as well as acute or chronic liver diseases such as liver damag e, jaundice, hepatitis, and cirrhosis of the liver.

Sampling Size Determination and Sampling Technique

In the present study, the prevalence for sample size calculation, i.e., the prevalence of 5.7%, was taken.[9]

The following simple formula would be used for calculating the adequate sample size in prevalence study

$N = Z^2 P (1-P)/d^2$

N = sample size, Z = level of confidence, P = prevalence, and d = absolute error or precision.

Z = Is standard normal variate (at 5% type 1 error (P< 0.05) it is 1.96 and at 1% type 1 error (P<0.01) it is 2.58). As in majority of studies P values are considered significant below 0.05 hence 1.96 is used in formula. p = Expected proportion in population based on previous studies or pilot studies.

The sample size was calculated using a single population proportion formula by considering a 95% confidence level, a 5% margin of error, and a 5.7% estimated proportion of overall prevalence.

Sample size = $1.96^2 \times 0.057 (1-0.057)/0.05^2$

=73

Considering a 10% non-response rate, the total minimum sample size for the study was 80 patients. We included 116 participants (more than the minimum required number of cases) in Patients were put in group I, and healthy subjects in group II. Parameters such as smoking and drinking habits, WHR,

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and BMI were calculated. The blood pressures of all patients were measured using a sphygmomanometer in a sitting position. About 5 mL of venous blood samples were collected in a plain gel tube. The collected blood samples were then allowed to clot at room temperature, centrifuged at 4000 rpm for about 10 minutes, and the serum was collected in clean, dry serum tubes. The sera obtained were analysed immediately, whenever possible, or stored at -20 °C in case of delay. The serum levels of AST, ALT, ALP, CK-MB, glucose, TC, TG, and HDL-C were measured using a fully automated dry chemistry-based analyzer.

Statistical analysis

The data was entered using Microsoft Windows Excel, and the statistical analysis was done using the Statistical Package for Social Sciences (SPSS) version 21.0. In order to investigate the distribution of a number of quantitative and categorical variables, an SPSS descriptive statistical analysis was done. We used frequency (%) and mean ± standard deviation to summarise categorical data. The Student's t test was used to evaluate the statistical differences in mean values of continuous variables between participants with CVD and healthy controls.The difference in categorical variable frequencies between the two groups of study participants was compared using the chi-square test. A P value < 0.05 was considered significant.

Results

Table 1: Demographic distribution of participants (n=116)

Gender	Group I(n=58)	Group II(n=58)
M:F	30:28	29:29
Mean age (year)	52.09±8.05	56.25±10.50

Table 1, figure 1 shows that group I had 30 males and 28 females, and group II had 29 males and 29 females. The mean age of participants in cases group (group I) was 52.09±8.05 years and in healthy subjects (group II) was 56.25±10.50 years.

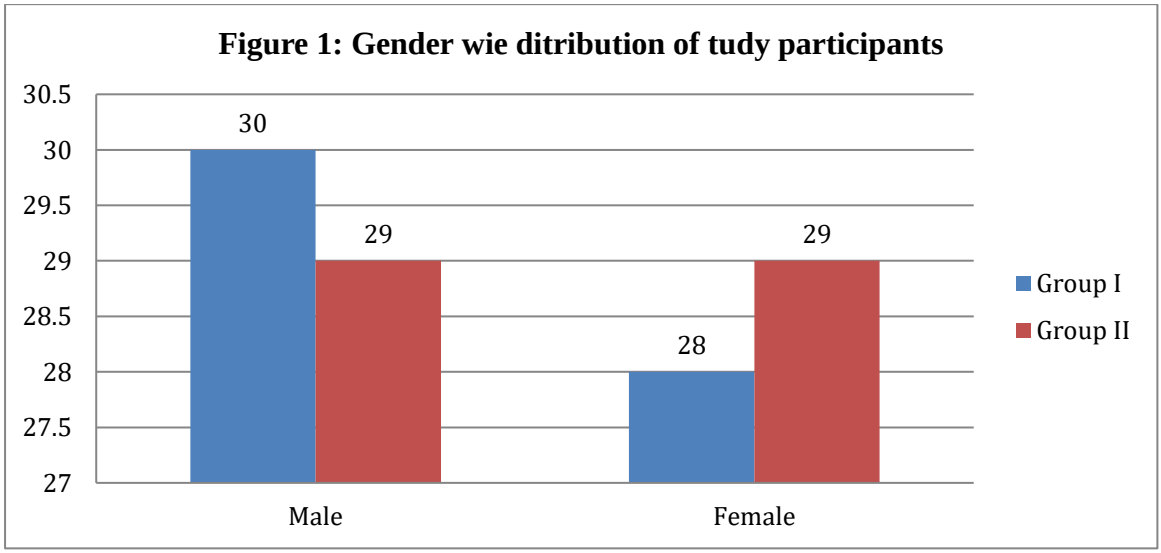

Table 2: Assessment of baseline characteristics of study participants (n = 116)

Parameters	Group I(n=58)	Group II(n=58)	P value
BMI (kg/m2)	25.6±3.05	24.1±2.65	0.001
Waist-Hip ratio	0.99±0.75	0.92±062	0.04
SBP (mmHg)	128.4±10.41	116.6±8.03	0.02

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DBP (mmHg)	78.8±10.03	76.4±8.75	0.05
CK-MB (U/L)	86.4±75.01	18.2±8.90	0.01
Troponin-I (µg/L)	11.4± 18.98	0.92± 0.45	0.01
AST (U/L)	126.2±140.50	26.1± 3.41	0.01
ALT (U/L)	54.2±65.49	20.6±5.82	0.03
ALP (U/L)	102.5± 62.98	76.2±16.70	0.04
FBS (mg/dL)	114.7±52.69	89.4± 7.56	0.03
HbA1C (%)	6.2±1.98	5.3±0.20	0.04
TC (mg/dL)	154.8± 42.85	142.6±18.70	0.01
TG (mg/dL)	146.2±82.05	103.5±24.72	0.02
HDL-C (mg/dL)	35.7±12.90	43.2±10.05	0.03

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; CK-MB: Creatine kinase-MB; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; FBS: Fasting blood sugar; CK-MB: Creatine kinase-MB; CI: Confidence interval; TC: Total cholesterol; TG: Triglycerides; *p value<0.05(Significant)

Table 2, shows that in group I and group II, the mean BMI (kg/m2) was 25.6 and 24.1, waist-hip ratio was 0.99 and 0.92, SBP (mmHg) was 128.4 and 114.6, DBP (mmHg) was 76.4 and 78.8, CK-MB (U/L) was 86.4 and 18.2, Troponin-I (µg/L) was 11.4 and 0.92, AST (U/L) was 126.2 and 26.1, ALT (U/L) was 54.2 and 20.6, ALP (U/L) was 102.5 and 76.2, FBS (mg/dL) was 114.7 and 89.4, HbA1C (%) was 6.2 and 5.3, TC (mg/dL) was 154.8 and 142.6, TG (mg/dL) was 146.2 and 103.5 and HDL-C (mg/dL) was 35.7 and 43.2 respectively. The difference was significant (P< 0.05).

Table 3: Smoking and drinking status of the study participants

Parameters		**Group I(N=58)**	**Group Ii(N=58)**	**P Value**
Smoking status	Yes	26 (44.83%)	6 (10.34%)	0.01
	No	32 (55.17%)	52 (89.65%)	
Drinking habit	Yes	35 (60.34%)	25 (43.10%)	0.01
	No	23 (39.65%)	33 (56.89%)	

Discussion

These enzymes' plasma levels have been linked to incident CVDs in numerous studies, suggesting that they may be employed as potential CVD risk markers.[10,11] Nevertheless, prior research has demonstrated that the risk of CVD is not correlated with any particular liver enzyme.[12]

The prevalence of CHD in the study population was 5.7% (95% confidence interval: 4.26–7.13). The significant associated risk factors included tobacco use, a history of hypertension, family history, and age. While one study found that raised levels of ALT and AST were linked to a higher risk of dying from cardiovascular disease (CVD), another stratified analysis found a positive correlation between ALT and stroke and a negative correlation with coronary heart disease.[13]

The present study was conducted to evaluate the association between serum liver enzymes and cardiovascular diseases. In the present study, elevated liver enzymes were statistically higher ($p<0.05$) in patients with CVDs. The serum levels of AST, ALT, and ALP were higher in patients with CVDs than in healthy controls, respectively. Higher levels of liver enzymes (AST, ALT, and ALP) were found in male than female patients with CVDs. The present study findings showed that AST was significantly associated with CVDs and showed a positive correlation with age, BMI, CK-MB, troponin-I, FBS, and HbA1C.

A study by Rehman H et al.[14] showed that there was a higher prevalence of a positive correlation between AST and CVDs in the Asian population. The fundamental process behind the link between

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AST and CVD is mostly speculative. Liver diseases are frequently the cause of elevated AST, and non-alcoholic fatty liver disease (NAFLD) is mostly associated with cardiovascular problems.[15]Diabetes mellitus, metabolic syndrome, and obesity are further cardiovascular risk factors associated with increased AST.[16]

We found that group I had 30 males and 28 females, and group II had 29 males and 29 females. Yadavet al.[18] explored the association between liver enzymes and CVDs. The frequency of smoking ($p<0.001$) and drinking habits ($p<0.001$), and mean values of body mass index (BMI) ($p<0.001$) and systolic blood pressure (SBP) ($p=0.006$), waist hip ratio (WHR), aspartate aminotransferases (AST), alanine aminotransferases (ALT), alkaline phosphatase (ALP), fasting blood sugar (FBS), glycated haemoglobin (HbA1c), creatine kinase-MB (CK-MB), Troponin I (TpI), total cholesterol (TC), and triglyceride (TG) were significantly higher ($p<0.001$) in CVD patients than in healthy controls. The high-density lipoprotein cholesterol (HDL-C), on the other hand, was significantly lower in CVD patients. Only the AST showed a significant correlation with the cardiac markers CK-MB and TpI. Logistic regression analysis revealed that aminotransferases were the best predictor (due to differences in odd's ratio) than ALP for incident CVDs in the adult population.

We found that in group I and group II, the mean BMI (kg/m2) was 25.6 and 24.1, waist-hip ratio was 0.99 and 0.92, SBP (mmHg) was 128.4 and 114.6, DBP (mmHg) was 76.4 and 78.8, CK-MB (U/L) was 86.4 and 18.2, Troponin-I (µg/L) was 11.4 and 0.92, AST (U/L) was 126.2 and 26.1, ALT (U/L) was 54.2 and 20.6, ALP (U/L) was 102.5 and 76.2, FBS (mg/dL) was 114.7 and 89.4, HbA1C (%) was 6.2 and 5.3, TC (mg/dL) was 154.8 and 142.6, TG (mg/dL) was 146.2 and 103.5, and HDL-C (mg/dL) was 35.7 and 43.2, respectively.

Park et al.[19] assessed the compounding relationship between liver enzymes and cardiovascular risk factors in subjects with mild dyslipidemia. Significant linearly increasing trends were observed in blood pressure level and other cardiovascular risk factors across quartiles of serum γ-glutamyltransferase (GGT) or alanine aminotransferase (ALT), with the increment in hypertension prevalence occurring across the quartiles of GGT and ALT. On multivariate logistic regression analyses, the odds ratios for hypertension, adjusted for smoking, drinking, and obesity, in the highest quartiles of GGT, ALT, aspartate aminotransferase, and alkaline phosphatase were 3.688, 1.617, 1.372, and 1.166, respectively.

ALP was shown to be significantly correlated with age, but also correlated with a number of CVD risk variables, according to Kunutsor SK et al.[17] Several studies have found a correlation between increased ALP and CVDs in various demographic groups.[18,19]

The increased correlations between ALP and CVD explain various underlying mechanisms. A common association between increased ALP and CVDs is inflammation. Liver disease (NAFLD) may be associated with a high ALP level.[20] ALP's catalysis of the hydrolysis of inorganic pyrophosphate, an inhibitor of vascular calcification that results in vascular hardening and speeds up the progression of atherosclerosis, is another possible mechanism.[19,21]

Study Limitations: The shortcoming of the study is the small sample size.

Conclusion

The authors found that there was a high liver enzyme level in patients with cardiovascular diseases (CVDs). Elevated serum aminotransferase, in particular AST, was found to be the strongest predictor of incident CVDs.

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Reference

1. Motamed N, Rabiee B, Poustchi H, Dehestani B, Hemasi GR, Khonsari MR, et al. Non-alcoholic Fatty Liver Disease (NAFLD) and 10-year risk of cardiovascular diseases. Clin Res HepatolGastroenterol. 2017;41(1):31-38.
2. Kim HC, Nam CM, Jee SH, Han KH, Oh DK, Suh I. Normal serum aminotransferase concentration and risk of mortality from liver diseases: Prospective cohort study. BMJ. 2004; 328:983.
3. Arndt V, Brenner H, Rothenbacher D, Zschenderlein B, Fraisse E, Fliedner TM. Elevated liver enzyme activity in construction workers: Prevalence and impact on early retirement and all-cause mortality. Int Arch Occup Environ Health. 1998;71(6):405-12.
4. Cox M, Nelson DL. Lehninger Principles of Biochemistry, 4th ed; New York, NY, USA: W.H. Freeman; 2005. ISBN 0716743396
5. Henrion J. Hypoxic hepatitis. Liver International. 2012;32(7):1039-52.
6. Choi KM, Han K, Park S, Chung HS, Kim NH, Yoo HJ, et al. Implication of liver enzymes on incident cardiovascular diseases and mortality: A nationwide population-based cohort study. Sci Rep. 2018;8(1):01-09.
7. Kunutsor SK, Apekey TA, Khan H. Liver enzymes and risk of cardiovascular disease in the general population: A meta-analysis of prospective cohort studies. Atherosclerosis. 2014;236(1):07-17.
8. Lee H, Shin DW, Lee TH, Yang HK, Ahn E, Yoon JM, et al. Association between change in serum aminotransferase and mortality: A nationwide cohort study in Korea. Medicine (Baltimore). 2016;95(12):e3158.
9. Vaidya A, Pokharel PK, Nagesh S, Karki P, Kumar S, Majhi S. Prevalence of coronary heart disease in the urban adult males of eastern Nepal: A populationbased analytical cross-sectional study. Indian Heart J. 2009;61(4):341-47.
10. Kim HC, Kang DR, Nam CM, Hur NW, Shim JS, Jee SH, et al. Elevated serum aminotransferase level as a predictor of intracerebralhemorrhage: Korea medical insurance corporation study. Stroke. 2005;36(8):1642-47.
11. Goessling W, Massaro JM, Vasan RS, D'AgostinoSr RB, Ellison RC, Fox CS. Aminotransferase levels and 20-year risk of metabolic syndrome, diabetes, and cardiovascular disease. Gastroenterology. 2008;135(6):1935-44.
12. Schindhelm RK, Dekker JM, Nijpels G, Bouter LM, Stehouwer CD, Heine RJ, et al. Alanine aminotransferase predicts coronary heart disease events: A 10-year follow-up of the Hoorn Study. Atherosclerosis. 2007;191(2):391-96.
13. Vaidya A, Pokharel PK, Nagesh S, Karki P, Kumar S, Majhi S. Prevalence of coronary heart disease in the urban adult males of eastern Nepal: A population based analytical cross-sectional study. Indian Heart J. 2009;61(4):341-47.
14. Rehman H, Samad Z, Mishra SR, Merchant AT, Narula JP, Mishra S, et al. Epidemiologic studies targeting primary cardiovascular disease prevention in South Asia. Indian Heart J. 2018;70(5):721-30.
15. Adams LA, Anstee QM, Tilg H, Targher G. Non-alcoholic fatty liver disease and its relationship with cardiovascular disease and other extrahepatic diseases. Gut. 2017;66(6):1138-53.
16. Porter SA, Pedley A, Massaro JM, Vasan RS, Hoffmann U, Fox CS. Aminotransferase levels are associated with cardiometabolic risk above and beyond visceral fat and insulin resistance: The Framingham Heart Study. ArteriosclerThrombVasc Biol. 2013;33(1):139-46.
17. Kunutsor SK, Bakker SJ, Kootstra-Ros JE, Gansevoort RT, Gregson J, Dullaart RP. Serum alkaline phosphatase and risk of incident cardiovascular disease: Interrelationship with high sensitivity c-reactive protein. PloS One. 2015;10(7):e0132822.
18. Tonelli M, Curhan G, Pfeffer M, Sacks F, Thadhani R, Melamed ML, et al. Relation between alkaline phosphatase, serum phosphate, and all-cause or cardiovascular mortality. Circulation. 2009;120(18):1784-92.

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19. Wannamethee SG, Sattar N, Papcosta O, Lennon L, Whincup PH. Alkaline phosphatase, serum phosphate, and incident cardiovascular disease and total mortality in older men. ArteriosclerThrombVasc Biol. 2013;33(5):1070-76.
20. Targher G, Bertolini L, Padovani R, Rodella S, Tessari R, Zenari L, et al. Prevalence of nonalcoholic fatty liver disease and its association with cardiovascular disease among type 2 diabetic patients. Diabetes Care. 2007;30(5):1212-18.
21. Abramowitz M, Muntner P, Coco M, Southern W, Lotwin I, Hostetter TH, et al. Serum alkaline phosphatase and phosphate and risk of mortality and hospitalization. Clin J Am SocNephrol. 2010;5(6):1064-71.