Changes of Liver Enzymes in Coronary Heart Disease

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Abstract

Background: Coronary heart disease is one of the leading causes of morbidity and mortality elsewhere in the world. An association between liver enzymes and coronary heart disease is suggested.

Objective: To evaluate the changes in liver enzymes, Alanine aminotransferases and aspartate aminotransferases in patients with coronary heart disease.

Methods: The study included 60 patients with coronary heart disease (41 males and 19 females), and 40 control subjects (25 males and 15 females) from Basrah, Iraq. Alanine aminotransferase, aspartate aminotransferase, lipid profile and fasting blood glucose levels were determined.

Results: Alanine aminotransferase, aspartate aminotransferase, fasting blood glucose, total cholesterol, triglycerides, and low density lipoprotein-cholesterol levels were significantly higher among coronary heart disease patients compared to controls (P<0.001), while high density lipoprotein-cholesterol level was significantly lower among patients with coronary heart disease in comparison to controls (P<0.001). Alanine aminotransferases revealed a significant positive correlation with triglycerides (P=0.060), and significant negative correlation with high density lipoprotein-cholesterol (P=0.031) and no significant correlations with body mass index, blood pressure, and other biochemical parameters (P>0.05). On the other hand, aspartate aminotransferases showed significant positive correlations with total cholesterol (P=0.009), triglycerides (P=0.025) and low density lipoprotein-cholesterol (P=0.042), and no significant correlations with other physiological and biochemical parameters (P>0.05).

Conclusions: A strong association exists between changes in liver enzymes, alanine aminotransferase and aspartate aminotransferase and coronary heart disease. These enzymes could be included within the increasing list of coronary heart disease risk factors. Also, they might have prognostic significance and a predictive value in coronary heart disease complications.

Key words: Coronary heart disease, liver enzymes, lipid profile.

ملخص

القلب، يعد مرض القلب الناجي أحد أهم أسباب الأمراضية والوفاة في العالم. قد توجد علاقة متوقعة بين إنزيمات الكبد ومرض القلب الناجي.

الطريقة: دراسة التحالات المصاحبة في إنزيمات الكبد في مرضى القلب الناجي. تم إجراء دراسة شاملة على 60 مصابًا من مرضى القلب الناجي (41 من الذكور و 19 من الإناث) و 40 من الأشخاص السالمين، بتقييم مستويات إنزيمات الكبد ثلاثية بويون، وإيفونتسترزنير، وإيمينونتستيرزير، بالإضافة إلى تحليلات سكر الدم ودهون الدم.

النتائج: كانت مستويات إنزيمات ألانين بويونتستيرزير، وإيمينونتستيرزير، وكولسترول الدهني، وكولسترول البروتينات الدهنية، ومستويات الكبد، مرتفعة بشكل معنوي بين المرضى، بينما كانت مستويات الكولسترول الدهني، والكولسترول الدهني الثلاثي، والكولسترول الدهني، منخفضة بشكل معنوي بين المرضى، ومتوازنة مع إنزيمات الكبد. ورغم ذلك، لم تظهر أي تباين معين بين إنزيمات بويونتستيرزير، وإيمينونتستيرزير، ومستويات الكولسترول الدهني، ومستويات الكولسترول الدهني الثلاثي. هذه النتائج تدعم البحثات السابقة. 

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Introduction

Coronary heart disease (CHD) is one of the leading causes of morbidity and mortality in the developed as well as the developing world.1-3 The risk factors for CHD have been remarkably revolutionized, where a diversity of new risk factors were included in the CHD risk along with the well known conventional risk factors, notably the inflammatory and haemostatic variables such as high plasma fibrinogen (PF), C-reactive protein (CRP)6-11 and homocysteine levels.12,13 Several studies reported an association between changes of liver enzymes and the risk of CHD.14,15 It has been proposed that liver enzymes particularly alanine aminotransferase (ALT), and gamma-glutamyl transferase (γ-GT) are markers of liver dysfunction and non-alcoholic fatty liver disease (NAFLD), and are considered part of the metabolic syndrome (MS). Persistently elevated ALT and γ-GT even within the reference range are associated with clinically adverse cardiovascular disease (CVD) risk.16 In addition, aspartate aminotransferase (AST), ALT and γ-GT are considered as independent CHD risk factors, and may serve as predictors of atherosclerotic CVD and type 2 diabetes (T2D).17-20

The aim of this study: was to evaluate the alterations in ALT and AST in patients with CHD in Basrah.

Patients and Methods

In this prospective study, conducted from October, 1st, 2008, throughout September, 30th, 2009, 60 patients with CHD admitted to the Medical Ward in AL-Sadr Teaching Hospital, Basrah, Iraq were included. They were 41 men and 19 women, 35-85 years of age. All patients were diagnosed by consultant physicians depending on detailed history, physical examination and investigations such as resting electrocardiography (ECG), exercise ECG, stress echocardiography or others in accordance with the diagnostic needs in each patient. In addition, 40 apparently healthy individuals were included. They were 25 men and 15 women, 33-78 years of age, with no history of CHD, hypertension or diabetes mellitus.

Blood specimens were collected in a fasting state. ALT, AST, total cholesterol (TC), triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C) concentrations were determined enzymatically using diagnostic kits from bioMerieux, France. Fasting blood glucose (FBG) was estimated enzymatically using diagnostic kit from Randox, U.K. All procedures were followed in accordance with the instructions of the manufacturer. Low-density lipoprotein-cholesterol (LDL-C) level was calculated using the following equation:21

\[
LDL-C = TC - (HDL-C + TG/5)
\]

Statistical analysis was carried out using Chi-square and t-tests. Correlation and regression analysis was performed by SPSS programme. P<0.05 was considered statistically significant.
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Results

Characteristics of patients with CHD and control subjects are shown in Table 1. Body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly higher in CHD patients compared to controls (P<0.001). Also, as shown in Table 1, the frequency of cigarette smokers was significantly higher among patients with CHD than controls (P<0.05).

Table 1. Characteristics of CHD patients and control subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients (n=60)</th>
<th>Controls (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.2 (11.3)</td>
<td>53.9 (10.2)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.1 (4.9)**</td>
<td>26.3 (4.6)</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>147.6 (13.7)***</td>
<td>126.3 (8.9)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>92.4 (8.4)***</td>
<td>86.1 (8.2)</td>
</tr>
<tr>
<td>Cigarette smokers, n (%)</td>
<td>25 (41.7)%#</td>
<td>9 (22.5%)</td>
</tr>
</tbody>
</table>

Data are expressed as mean (SD)

** : P<0.01
*** : P<0.001
# : χ² = 3.93, P<0.05

ALT, AST, FBG, TC, TG, and LDL-C serum concentrations were significantly higher among patients with CHD compared to controls (P<0.001). On the other hand, HDL-C level was significantly lower among CHD patients in comparison to controls (P<0.001), as shown in Table 2.

Table 2. Aminotransferases, FBG and and lipid profile among CHD patients and control subjects.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients (n=60)</th>
<th>Controls (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (IU/L)</td>
<td>74.7 (21.1)***</td>
<td>18.0 (5.8)</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>58.3 (15.2)***</td>
<td>13.2 (3.9)</td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>240.9 (39.1)***</td>
<td>190.6 (17.8)</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>236.7 (58.5)***</td>
<td>163.8 (14.5)</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>155.8 (39.9)***</td>
<td>113.2 (18.2)</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>37.8 (4.7)***</td>
<td>44.7 (5.6)</td>
</tr>
<tr>
<td>FBG (mg/dL)</td>
<td>117.6 (26.6)***</td>
<td>96.6 (7.8)</td>
</tr>
</tbody>
</table>

Data are expressed as mean (SD)

*** : P<0.001

Table 3 presents the results of correlation and regression analysis of ALT and AST with conventional cardiovascular (CV) risk factors in patients with CHD, and revealed a significant positive correlation of ALT with TG (r=0.352, P=0.006), and significant negative correlation with HDL-C (r=-0.279, P=0.031), Fig. 1, and no significant correlations with BMI, SBP, DBP, FBG, TC and LDL-C (P>0.05). On the other hand, AST showed significant positive correlations with TC (r=0.334, P=0.009), TG (r=0.289, P=0.025) and LDL-C (r=0.263, P=0.042), Fig.2, and no significant correlations with BMI, SBP, DBP, FBG, and HDL-C (P>0.05).

Discussion

The evidence that suggest a relationship between liver enzymes and the risk of CHD is accumulating. ALT and AST are markers of NASH which is emerging as a hepatic component of MS, and markers of NAFLD (ALT and AST) predict MS. Abnormal levels of ALT and AST have been found in MS. In addition, ALT was associated with insulin resistance (IR) independent of
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conventional metabolic parameters.\textsuperscript{26} IR is considered as is the major pathogenetic mechanism in the development of MS which is also termed as “insulin resistance syndrome”.\textsuperscript{27,28} MS, a cluster of disorders including abdominal obesity, atherogenic dyslipidaemia (low HDL-C and elevated TG), hypertension, impaired glucose tolerance as well as proinflammatory and thrombotic state,\textsuperscript{29,30} is in turn associated with an increased risk of development of T2D atherosclerotic CVD, and CV events.\textsuperscript{31,32}

The present study clearly demonstrated strong association between liver enzymes, ALT and AST with CHD. This finding is similar to the observation of other studies.\textsuperscript{15,18,21} A strong relationship has been observed between ALT levels and MS in NAFLD, and the cluster of MS components might be the predictor for the elevations of ALT\textsuperscript{33}.

Subjects with NAFLD and elevated ALT levels are at an increased risk of developing MS, and also at a high risk of developing T2D and CVS.\textsuperscript{24,34,36} This may be because of the presence of associated metabolic risk factors.\textsuperscript{34} In addition, AST and ALT independently predict T2D. Baseline elevations of these enzymes may reflect NAFLD or related diseases.\textsuperscript{30}

Unfortunately, ultrasonographic diagnosis of NAFLD of CHD patients and controls participated in this study was not feasible because of technical difficulties. A number of metabolic syndrome components, notably, obesity, IR, and high sensitivity C-reactive protein (hs-CRP), are considered as strong predictors of elevated ALT activity in patients with NAFLD. Central obesity, elevated TG, reduced HDL-C, and elevated FBG are MS components that contributed to increased ALT activity.\textsuperscript{37}

Table 3. Correlations of ALT and AST with Conventional CV risk factors in CHD patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ALT (IU/L)</th>
<th>AST (IU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m(^2))</td>
<td>(r=0.242, P=0.062)</td>
<td>(r=0.166, P=0.204)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>(r=0.117, P=0.375)</td>
<td>(r=0.050, P=0.703)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>(r=0.075, P=0.569)</td>
<td>(r=0.126, P=0.338)</td>
</tr>
<tr>
<td>FBG (mg/dL)</td>
<td>(r=0.038, P=0.658)</td>
<td>(r=0.022, P=0.866)</td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>(r=0.243, P=0.062)</td>
<td>(r=0.334, P=0.009)***</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>(r=0.352, P=0.006)**</td>
<td>(r=0.289, P=0.025)*</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>(r=0.167, P=0.202)</td>
<td>(r=0.263, P=0.042)*</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>(r=0.279, P=0.031)**</td>
<td>(r=0.179, P=0.170)</td>
</tr>
</tbody>
</table>

*: P<0.05  
**: P<0.01

Fig. 1. Significant correlations of ALT with TG and HDL-C
The significant correlations that we found between aminotransferases and lipid parameters particularly with TG and HDL-C, which are important components of MS, support the existence of a strong relationship between MS and abnormal ALT and AST levels. Furthermore, it has been proposed that a strong association exists between ALT level and MS as well as its components independent of IR.  

ALT is a marker of NAFLD and predicts incident T2D. It has been proposed that liver enzymes particularly γ-GT signals oxidative stress, and the association with T2D may indicates both hepatic steatosis and the increased oxidative asst. On the other hand, ALT was shown to be also associated with endothelial dysfunction and carotid atherosclerosis. In addition, Elevated concentrations of HDL-C may lose their protective effect against coronary events in patients with hepatic damage and raised liver enzyme activity. Furthermore, in middle-age non-diabetic persons subjects, carotid atherosclerosis, CHD risk, and reduced insulin sensitivity are associated with high values of fatty liver index. Moreover, the simultaneous measurements of ALT and hs-CRP have been shown to correlated with CV risk factors, and should be considered together as a screening test.
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for MS and CVD risk factors in young persons with overweight or obesity. It has been suggested that statin therapy is safe and can improve abnormal liver tests and reduce CV morbidity in patients with mild-to-moderately adverse liver tests that might be associated with NAFLD.

Finding a raised ALT and/or AST levels in asymptomatic should not be regarded as an innocent and incidental finding. Instead, it may give a clue to the presence of NAFLD which is now linked to the MS, and this necessitates additional evaluation and investigations including hepatic ultrasoundography. Furthermore, detection of abnormal ALT and/or AST levels in a patient with established CHD should raise the degree of the clinical suspicion about the existence of MS, and this merits further investigations.

In conclusion, a strong relationship exists between changes in liver enzymes, ALT and AST and CHD. These enzymes could be used to list risk factors which dynamically increased. Also, ALT and AST might serve valuable diagnostic as well as predictive value in CHD.

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