Risk assessment of alcohol and obesity on liver enzymes (transaminases, cholestatic)

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Received 30 March 2012; revised 14 April 2012; accepted 27 April 2012

ABSTRACT

Background: This study was designed to investigate the BMI and alcohol consumption effects on hepatic enzymes. The degree of alteration among moderate drinkers is still unclear. Objective: To determine causes of liver failure due to alcohol and obesity. We observed the association between moderate alcohol consumption, body mass index (BMI; in kg/m2) and transaminase, cholestatic enzymes. Design: Serum alanine aminotransferase (ALT), alkaline phosphate (ALP), aspartate aminotransferase (AST), and gamma-glutamyl-transferase (GGT) were examined in 995 healthy persons. In this study 400 persons were reported as abstainers and 595 participants involved as a moderate drinkers. The study population was further split according to BMI as follows: <19 (underweight), ≥19 and <25 (normal weight), ≥25 and <30 (overweight), and ≥30 (obese). Results: Serum ALT (P < 0.002), GGT (P < 0.001) and ALP (P < 0.001) but not AST (P < 0.883) activities in moderate drinkers were higher than those in abstainers. Mean ALT activity is higher in obese and overweight in alcohol consumers and abstainers as compared to mean AST activity in the same groups. ALP activity was increased with BMI in moderate drinkers. In abstainers activity of ALP shows weak relation in order to BMI. Conclusion: The result of moderate alcohol use raises activity of hepatic enzymes with increasing BMI. Most participants with alcohol consumption have an AST/ALT ratio above 1.

Keywords: Moderate Alcohol; Body Mass Index; Obesity; Liver Enzymes

1. INTRODUCTION

Alcoholic hepatic syndrome is a world extensive health problem [1,2]. There are three most common type of alcoholic liver diseases are fatty liver/steatosis, alcoholic hepatitis and liver cirrhosis. The steatosis has been reported 80% in heavy drinkers, 10% - 35% alcoholic hepatitis, and about 10% liver cirrhosis [3,4]. Alcoholic hepatitis is liver inflammation cause by alcohol intake. The alcoholic hepatitis mostly develops in those people who use alcohol heavily from many years, the correlation between alcoholic hepatitis and drinking is complex. Not all heavy drinkers develop alcoholic hepatitis, this can also occur in moderate drinkers [5,6]. The alcohol in beer, wine and liquor consist of extremely lethal chemicals, like acetaldehyde. These chemicals cause inflammation that devastates liver cells. At this point, web-like scars and small loops of tissue replace with healthy liver tissue, which effects on the ability of liver function. This scarring called cirrhosis, is the last stage of alcoholic liver disease [6]. The swiftly increasing of obesity is a major hazard to modern health care. Overweight or obesity is a major threat in most of the industrialized countries [7]. During the last few decades the ethanol consumption medical disorders have increased quickly [8]. Moderate alcohol consumption with obesity may increase fat accumulation in hepatic tissue and changes in liver enzymes. The serum-liver enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT) are broadly used as indicator to assess the level of liver injury [9].

The aim of the present study was to observe the associations between alcohol consumption, BMI, and different liver enzymes in a healthy abstainers and drinkers.

2. SUBJECTS AND METHODS

2.1. Subjects and Study Protocol

The subjects of this study were residents of Karachi city, Pakistan. The population of healthy volunteers was 995 men and their range of age was (34 ± 17). The participants were classified as abstainers (n = 400, age 34 ±
17) and drinkers (n = 595, age 35 ± 19) and further classified according to BMI as shown in Table 1. The BMI value defined as weight (kg)/height (m²), was used as a weight index. Abstainers were those participants who used no alcohol during since last 3 to 4 months. Those participants who consumed alcohol during past 1 to 2 days before sampling were categorized as smoker. None of the participants had any history of medical disorders. In this study, 65% participants were smokers and 35% participants were nonsmokers. Smoking was not allowed for one hour before sampling. Hepatic enzymes (AST, ALT ALP and GGT) were measured with the help of Micro-Vita-Lab.

A Performa (survey and questionnaire form) was designed to collect the detailed information from the donors indicating their name, age, residence, health status, alcohol intake and smoking habit.

2.2. Collection of Serum

About 10 cc of blood was collected by venepuncture using disposable sterilized syringes. It was collected in dry and clean test tubes and centrifuged at 3000 rpm for ten minutes to separate serum and kept at -70°C. It was further used to study above mentioned parameters.

3. RESULTS

The key features of the participants according to weight status are shown in Table 1. Overweight and obesity were common in study population. The underweight participants were younger (P < 0.01) than participants of other BMI groups. The normal weight participants mean age was (35 ± 7), also younger than other groups of BMI. Mean alanine aminotransferase (ALT or SGPT), aspartate aminotransferase (AST or SGOT), y-glutamyl transferase (GGT) and alkaline phosphatase (ALP) activities in abstainers and moderate drinkers as further divided according to BMI (in kg/m²). Significant main effects of drinking status were observed (P < 0.001 for ALT, ALP and GGT). Significant main effects of BMI (P < 0.05) were noted for all enzymes. BMI < 19 was considered underweight, BMI ≥ 19 and < 25 was considered normal weight, BMI ≥ 25 and < 30 was considered overweight and BMI ≥ 30 was considered obese (Figure 2). The highest activities of hepatic enzymes were reported in those participants who had drinking status with obesity. In the present analyses between BMI and drinking status, liver enzymes effect in population as a dependent variable. Significant effects of BMI showed for all enzymes while drinking status was associated with ALT, GGT and ALP. ALP showed a marked difference among AST, ALT and GGT with regards to alcohol consumption and BMI.

Mean ALT activity is higher in obese and over weight in alcohol consumers and abstainers as compared to mean AST activity in the same groups. ALP activity was increased with BMI in moderate drinkers. ALP activity in abstainers shows weak relation in relation to BMI.

The values of AST: ALT above or below in the total population was also found to vary according to drinking status. Among the BMI subgroups, the distributions showed significant differences according to drinking status in participants with underweight and overweight (P < 0.05) among moderate drinkers and obese (P < 0.001). But no significance difference in participants with normal weight (Figure 3).

The significance correlations between the body mass index and hepatic enzyme in the current study population were observed for ALT, GGT and ALP among moderate drinkers than abstainers (Table 2).

Statistical Methods

Values are expressed as mean ± SD. Comparisons were made with the Kruskal-Wallis test or the Mann-Whitney test when compare two groups. Correlations were calculated with Pearson’s product-moment correla-

Table 1. Key Characteristics of the study participants.

<table>
<thead>
<tr>
<th>BMI &lt; 19 Underweight</th>
<th>BMI ≥ 19 and &lt; 25 Normal</th>
<th>BMI ≥ 25 and &lt; 30 Overweight</th>
<th>BMI ≥ 30 Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Participants</td>
<td>48</td>
<td>581</td>
<td>291</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>30 ± 17&lt;sup&gt;3&lt;/sup&gt;</td>
<td>35 ± 17&lt;sup&gt;2.5&lt;/sup&gt;</td>
<td>40 ± 17&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Abstainers [n (%)]</td>
<td>19 (39.58)</td>
<td>248 (42.68)</td>
<td>108 (37.11)</td>
</tr>
<tr>
<td>Drinkers [n (%)]</td>
<td>29 (60.41)</td>
<td>333 (57.31)</td>
<td>183 (62.8)</td>
</tr>
</tbody>
</table>

<sup>1</sup>Significantly different from the other groups, P < 0.01 (Kruskal Wallis test); <sup>3</sup>Significantly different from the overweight group, P < 0.005 (Kruskal-Wallis test); <sup>2</sup>± SD.
tion coefficients or with Spearman’s rank correlation, as required. The analyses were obtained with the help of SPSS statistical software after transformation of the raw data to obtain symmetrical distributions.

4. DISCUSSION

The present statistics shows that effect of moderate drinking on hepatic enzymes increased with increases of BMI. On the contrary, it may be said that increased drinking increases the effect of adiposity on liver activity. The impacts of alcohol or obesity on liver were re-

Figure 1. Mean values of liver enzymes in abstainers and moderate drinkers.

Figure 2. ALCOHOL, BMI and LIVER ENZYMES.

Figure 3. ALCOHOL, BMI and AST/ALT ratio.
significant difference (was significantly high [21]. In current study ALT shows from normal, whereas in overweight and obese males it mean ALT value did not show any significant change with BMI [20]. Among overweight and obese females zymes, the activities of ALT were found to be related
diseases even advanced cirrhosis [19]. Among liver en-
faintly abnormal LFTs do not rule out abundant liver
directly proportional with weight change. Normal or
observation proposed that hepatic enzymes could be di-
may be momentary and the change in BMI was the
significance of BMI change means that the effects of adiposity
BMI changes [17] same as present findings. The signifi-
correlation between BMI and hepatic en-
zymes in subjects examined during study,
most serious causes of high serum activities of the
sociation of liver but not bone serum ALP levels with
murine preadipocyte cell, 3T3-L1.15 Therefore, the as-
zyme (as are bone and kidney ALP), and it is known that
a tissue non-specific alkaline phosphate (TNALP) isoen-
a result of ALP release from adipose tissue. Liver ALP is
higher level of liver ALP in obese than in lean subjects is
measured in 32,329 subjects [37]. It is possible that the
levels are higher in obese than in lean subjects. In con-
crease with BMI in both groups but significantly higher
AST [35].
In current study observed that ALP is gradually in-
crease with BMI in both groups but significantly higher in
obese moderate alcohol consumers and ALP serum
levels are higher in obese than in lean subjects. In con-
trast to previous study in which serum ALP levels were
measured in 32,329 subjects [37]. It is possible that the
higher level of liver ALP in obese than in lean subjects is
a result of ALP release from adipose tissue. Liver ALP is
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TNALP is present in human preadipocytes16 and in the
murm predipocyte cell, 3T3-L1.15 Therefore, the as-
association of liver but not bone serum ALP levels with
obesity suggests that the TNALP isoform in adipose tis-
side to metabolize extracellular reduced glutathione and GGT
enzyme induction may also be strongly related with the
generation of reactive oxygen species [14-16]. AST and
ALT had no relationship with alcohol consumption al-
though there is association between alcohol consumption
with GGT [17] but in our study AST and GGT showed
association with alcohol consumption. There is signifi-
cant relationship between alcohol and GGT [18]. The
serum GGT level showed a strong correlation between
BMI changes [17] same as present findings. The signifi-
cance of BMI change means that the effects of adiposity
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strongest determinant of change in GGT [18]. Present
observation proposed that hepatic enzymes could be di-
rectly proportional with weight change. Normal or
faintly abnormal LFTs do not rule out abundant liver
diseases even advanced cirrhosis [19]. Among liver en-
zymes, the activities of ALT were found to be related
with BMI [20]. Among overweight and obese females
mean ALT value did not show any significant change
from normal, whereas in overweight and obese males it
was significantly high [21]. In current study ALT shows
significant difference (P < 0.001) in obese male from
normal. This is comparable to prior findings that obese
persons may have higher levels of serum transaminases
than their corresponding person [22].
In present study, most of the participants with alcohol
consumption have an AST/ALT ratio above 1. The cur-
rent study shows that there may be particular changes in
the enzyme ratios also among healthy persons with only
little changes in ALT and AST activities, signifying that
the ratio of AST/ALT may depend on drinking status and
BMI (Figure 2).
In patients with increased serum aminotransferase ac-
tivity, the predominance of AST over ALT in alcoholic
liver disease was first studied by Harinasuta, in 1967
[23]. The investigative significance of a high AST/ALT
ratio for alcohol-related hepatic disease was reported
[24]. The high AST/ALT ratio in alcoholic liver disease:
1) a decrease hepatic ALT activity [25]; 2) pyridoxal 5-
phosphate diminution in the livers of alcoholics [26]; and
3) damage of mitochondrial in patients with high alcohol
consumption may increase activity of mitochondrial as-
partate in serum [27]. In early report high AST/ALT ra-
tio with increased serum aminotransferase activity has
also been correlated with the growth of cirrhosis in Non-
alcoholic Steatohepatitis patients [28]. A high AST/ALT
ratio in patients with increased serum aminotransferases
has been observed in chronic viral hepatitis [29-33].
In current study mean ALT values in overweight and
obese male abstainers and drinkers remained higher than
the mean AST values in the same groups (Figure 3). While the ALT levels are higher than AST levels in most
cases of nonalcoholic steatohepatitis (NASH) [34], the
AST level may sporadically be higher than the ALT level,
particularly in the presence of cirrhosis [35].
Enzyme levels often do not correlate with the severity
of histological abnormalities [36] that varies from alco-
holic hepatitis in which the ALT activity is higher than
AST [35].
In current study observed that ALP is gradually in-
crease with BMI in both groups but significantly higher in
obese moderate alcohol consumers and ALP serum
levels are higher in obese than in lean subjects. In con-
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TNALP is present in human preadipocytes16 and in the
murm predipocyte cell, 3T3-L1.15 Therefore, the as-
association of liver but not bone serum ALP levels with
obesity suggests that the TNALP isoform in adipose tis-
sue may be the liver form.
In conclusion, although alcohol is certainly one of the
most serious causes of high serum activities of the
hepatic enzymes in subjects examined during study,
marked overweight is potentially another important risk
factor in the increase of liver enzymatic activities.

TABLE 2. Spearman’s correlation between BMI and hepatic en-
zymes in abstainers and moderate drinkers.

<table>
<thead>
<tr>
<th></th>
<th>Abstainers</th>
<th>Moderate drinkers</th>
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<tbody>
<tr>
<td>ALP</td>
<td>0.21</td>
<td>0.36</td>
</tr>
<tr>
<td>ALT</td>
<td>0.23</td>
<td>0.34</td>
</tr>
<tr>
<td>AST</td>
<td>0.20</td>
<td>0.21</td>
</tr>
<tr>
<td>GGT</td>
<td>0.24</td>
<td>0.39</td>
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doi:10.1186/1471-2296-6-17

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