Study of Serum Lipid Profile in Patients of Alcoholic Cirrhosis

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Abstract

Introduction: Alcoholic cirrhosis is the end spectrum of alcoholic liver disease (ALD), which includes fatty liver or simple steatosis, alcoholic hepatitis, fibrosis, cirrhosis and super-imposed hepatocellular carcinoma. Although several studies have been conducted on dyslipidemia in cirrhotics in developed countries, there is a paucity of data in this regard in India. As there is a high prevalence of chronic liver disease in our country, we conducted this study to determine lipid levels in patients with cirrhosis and to assess if it relates to the severity of cirrhosis according to pugh criteria.

Materials and Methods: This is a cross sectional case-control study conducted on alcoholic cirrhotic patients and 50 healthy individuals (controls) without history of alcohol consumption. All the cases were investigated for fasting lipid profile and ultrasonographic evidence of cirrhosis. Biochemical tests including liver function tests were performed, which assisted in the diagnosis of alcoholic cirrhosis. These include serum bilirubin, total serum protein, serum albumin, serum globulin, aspartateaminotransferase (AST), alanineaminotransferase (ALT) and alkaline phosphatase (ALP). The data was collected systematically and analysed statistically according to the standard statistical methods.

Results: Serum total, LDL, HDL, VLDL, cholesterol and triglyceride level in patients with cirrhosis is inversely correlate with severity of cirrhosis.

Keywords: Child pugh criteria, Cirrhosis, Lipid profile.

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INTRODUCTION

Cirrhosis is an increasing cause of morbidity and mortality in more developed countries. Being the 14th most common cause of death worldwide. In an effort to solve the major health problems of developing countries, the importance of liver has been well recognized since a long time. The liver plays an essential role in lipid metabolism, several stages of lipid synthesis and transportation [2-4].

Dyslipidemia seen in chronic liver disease differs from that found in most of the other causes of secondary dyslipidemias because circulating lipoproteins are not only present in abnormal amount but they also frequently have abnormal composition, electrophoretic mobility and appearance. Pre beta and alpha bands can be absent on electrophoreses in all types of liver disease. In acute hepatocellular disease such as alcoholic or viral hepatitis, there is a cholestatic phase and similar changes may be seen e.g. increased cholesterol and phospholipid levels [5].

Severe metabolic impairment in cirrhosis can produce a worsening of the serum lipoprotein pattern. High-density lipoprotein (HDL) cholesterol and its major apolipoproteins have been shown to be reduced in cirrhosis, as also the serum levels of low-density lipoprotein (LDL) cholesterol [6].

Prognostic evaluation of patients with liver cirrhosis is an important topic often challenging clinicians. Correct The Child-Pugh score is an important component of the prognostic evaluation of cirrhotic patients [7-10].

Prognostic scores also represent a quantitative estimation of the ‘reserve’ in terms of liver function and the capacity to stand up surgery or other aggressive therapeutic interventions [11].

Although several studies have been conducted on dyslipidemia in cirrhotics in developed countries, there is a paucity of data in this regard in India. As there is a high prevalence of chronic liver disease in our country, we conducted this study to determine lipid levels in patients with cirrhosis and to assess if it relates to the severity of cirrhosis according to pughcrieteria.

MATERIALS AND METHODS

The study was conducted on 50 alcoholic cirrhotic subjects (cases) and 50 healthy subjects (controls) without history of alcohol consumption attending outdoor and indoor patient department in
The study was conducted after approval from institutional thesis and ethical committee. Patients were informed about the study procedure and written informed consent will be taken according to the performa attached. Patients with history of alcoholism with clinical, biochemical and ultrasonographic evidence of cirrhosis were included in the study. Random blood sugar and fasting blood sugar were checked for all study participants. All the cases were investigated for fasting lipid profile and ultrasonographic evidence of cirrhosis. Biochemical tests including liver function tests were performed, which assisted in the diagnosis of alcoholic cirrhosis.

These include serum bilirubin, total serum protein, serum albumin, serum globulin, aspartateaminotransferase (AST), alanineaminotransferase (ALT) and alkaline phosphatase (ALP). The data was collected systematically and analysed statistically according to the standard statistical methods. Data were analyzed by SPSS. χ2, one-way analysis of variance (ANOVA) and Student's t test were used. A p value <0.05 was considered statistically significant.

RESULTS

Table-1: Mean Age

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (N=50)</th>
<th>Group II (N=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (in years) ±SD</td>
<td>49.04 ± 10.81</td>
<td>51.24 ± 11.15</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Table-2: Sex Distribution

<table>
<thead>
<tr>
<th>Sex</th>
<th>Group I (N=50)</th>
<th>Group II (N=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>47</td>
<td>46</td>
<td>0.69</td>
</tr>
<tr>
<td>Females</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
</tbody>
</table>

Table-3: Level of FBS, RBS, S.BILIRUBIN, AST, ALT, TSP, DSP, ALP in Both the Groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I</th>
<th>Group II</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS</td>
<td>86.26</td>
<td>91.36</td>
<td>0.006</td>
</tr>
<tr>
<td>RBS</td>
<td>118.04</td>
<td>112.38</td>
<td>0.07</td>
</tr>
<tr>
<td>S. Bilirubin</td>
<td>3.77</td>
<td>0.79</td>
<td>0.0001</td>
</tr>
<tr>
<td>AST</td>
<td>130.15</td>
<td>24.22</td>
<td>0.0001</td>
</tr>
<tr>
<td>ALT</td>
<td>120.56</td>
<td>29.76</td>
<td>0.0008</td>
</tr>
<tr>
<td>TSP</td>
<td>5.98</td>
<td>7.01</td>
<td>0.0001</td>
</tr>
<tr>
<td>DSP</td>
<td>2.99</td>
<td>4.05</td>
<td>0.0001</td>
</tr>
<tr>
<td>ALP</td>
<td>187.07</td>
<td>101.34</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Table-4: Mean Total Cholesterol

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N=50</th>
<th>Mean</th>
<th>S.D</th>
<th>T Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T.Chol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>151.28</td>
<td>22.25</td>
<td>6.2</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>189.74</td>
<td>37.42</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table-5: Mean Triglyceride

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N=50</th>
<th>Mean</th>
<th>S.D</th>
<th>T Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>122.73</td>
<td>18.81</td>
<td>1.83</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>130.1</td>
<td>21.31</td>
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</table>

Table-6: Mean LDL

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N=50</th>
<th>Mean</th>
<th>S.D</th>
<th>T Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>90.28</td>
<td>11.06</td>
<td>8.02</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>112.88</td>
<td>16.56</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In present study in group I mean
in their study reported
which show
ubin, AST, ALT, TSP, DSP and ALP are
are in accordance
retion of ALP in bile will result in
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AST activity is characteristically elevated in
AST is higher than mean ALT. In alcoholic liver injury,
compared to group II. Our result
increase in mean values of AST and ALT in group I as
significantly increased serum bilirubin in cirrhotic
significantly higher in group I as compared to group II.
found that among 50 patients of cirrhosis 47 were men.
that the mean age for alcoholic cirrhosis is 44 years.We
studies done by Douds AC et al. [20, 21].
features of chronicalcoholic liver disease are
progressive hypoalbuminemia [5, 28]. Acute exposure
to alcohol depressed albumin. The decrease in serum
albumin level is attributed to nutritional status of the
subjects. Ethanol consumption slows down the rate of
hepatic protein catabolism [20, 21].
Alkaline phosphatase levels in present study
were significantly higher in group I than group II. Hyder MA et al., [22] and Nargis W et al., [23] in their
studies also reported increased ALP levels in cirrhosis.
Increased in serum ALP is associated with liver disease
is caused by intra or extra hepatic cholestatis and some
increased ALP is associated with liver disease
stimulates
extracted from liver. The increased cholestatis
with disease closely resembles the ALP that can be
sinusoid. The increased ALP present in the patients
regurgitation of enzyme into circulation via the hepatic
that impaired excr
comparison to ALT activity, although mild elevation of
ALT level is common. The reasons for the higher AST
activity in alcoholic hepatitis appear to be multiple: 1) Alcohol increases mitochondrial AST activity in
plasma, while other forms of hepatitis do not [17]; 2) Pyridoxine deficiency common observed in alcoholics,
which is a cofactor for the enzymatic activity of ALT, decreases hepatic ALT activity [18]. 3) Alcohol induces
the release of mitochondrial AST, which has longer
life, from cells without visible cell damage [19].

In present study total serum protein and
differential serum protein are significantly lower in
child I than group II. Das SK and Vasudevan DM [20]
in their study also reported similar results. Common
features of chronicalcoholic liver disease are
progressive hypoalbuminemia [5, 28]. Acute exposure
to alcohol depressed albumin. The decrease in serum
albumin level is attributed to nutritional status of the
subjects. Ethanol consumption slows down the rate of
hepatic protein catabolism [20, 21].

Alkaline phosphatase levels in present study
were significantly higher in group I than group II. Hyder MA et al., [22] and Nargis W et al., [23] in their
studies also reported increased ALP levels in cirrhosis.
Increased in serum ALP is associated with liver disease
is caused by intra or extra hepatic cholestatis and some
destruction of hepatic cell membrane. Any mechanism
that impaired excretion of ALP in bile will result in
regurgitation of enzyme into circulation via the hepatic
sinusoid. The increased ALP present in the patients
with disease closely resembles the ALP that can be
extracted from liver. The increased cholestatis
stimulates the synthesis of ALP by the bile ductules cell

<table>
<thead>
<tr>
<th>Table-8: Mean VLDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td>VLDL</td>
</tr>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table-9: Child Pugh Score in Group I</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Of Patients</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>N=50</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table-10: Comparison of Lipid profile according to Child Pugh Score (n = 50) or Severity Liver Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>T Chol</td>
</tr>
<tr>
<td>TGL</td>
</tr>
<tr>
<td>LDL</td>
</tr>
<tr>
<td>HDL</td>
</tr>
<tr>
<td>VLDL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean±SD</th>
<th>Mean±SD</th>
<th>Mean±SD</th>
<th>F</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T Chol</td>
<td>24.28±6.03</td>
<td>36.85±5.73</td>
<td>145.71±18.84</td>
<td>0.736</td>
<td>0.12</td>
</tr>
<tr>
<td>TGL</td>
<td>3.23</td>
<td>3.84</td>
<td>3.15</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td>3.84</td>
<td>3.15</td>
<td>3.23</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>HDL</td>
<td>3.23</td>
<td>3.15</td>
<td>0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VLDL</td>
<td>0.04</td>
<td>0.05</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

The results of this study showed that the Mean
age for study group that is cirrhotic patients is 49.04
years and for control group (healthy individuals) is
51.24 years. This result corroborates with previous
studies done by Douds AC et al., [12] which showed
that the mean age for alcoholic cirrhosis is 44 years.We
found that among 50 patients of cirrhosis 47 were men.
Bellentani S et al., [13] also reported male
predominance in cirrhosis.

All the individuals included in the study also
underwent biochemical tests for fasting blood sugar,
random blood sugar, serum bilirubin, ALT, ALP, TSP
and DSP.

There was a significant increase in fasting
blood sugar in group II. No significant difference was
found in random blood sugar levels in both the groups.
S. Bilirubin, AST, ALT, TSP, DSP and ALP are
significantly higher in group I as compared to group II.
Kumar W et al., [14] in their study reported
significantly increased serum bilirubin in cirrhotic
group than control group. This is in accordance with
our study. The mean serum bilirubin value in this study
is 3.77 mg/dl and in their study was 4.44 mg/dl which is
similar to some extent.

In the present study there is significant
increase in mean values of AST and ALT in group I as
compared to group II. Our results are in accordance
with the studies done by Meikle PJ et al., [15] and
Ramesh et al., [16]. In present study in group I mean
AST is higher than mean ALT. In alcoholic liver injury,
AST activity is characteristically elevated in
comparison to ALT activity, although mild elevation of
ALT level is common. The reasons for the higher AST
activity in alcoholic hepatitis appear to be multiple: 1) Alcohol increases mitochondrial AST activity in
plasma, while other forms of hepatitis do not [17]; 2) Pyridoxine deficiency common observed in alcoholics,
which is a cofactor for the enzymatic activity of ALT, decreases hepatic ALT activity [18]. 3) Alcohol induces
the release of mitochondrial AST, which has longer
life, from cells without visible cell damage [19].
Further in present study the cirrhotic patients in group I were divided into three subgroups according to child pugh score. Amongst 50 patients in GROUP 1 two patients had child pugh score A, 27 patients had child pugh score B and 21 patients had child pugh score C. Jaiswal P et al., [25] had divided the cirrhotic patients according to child pugh score. In their study Most of 25 (50%) cases were of class B, 20(40%) cases were of class C severity and 5(10.0%) were of class A. Kumar W et al., [14] also divided the cirrhotic patients according to child pugh score. In their study out of 100 patients 18 cases were of class A, 33 cases were of class B severity and 45 were of class C.

The value of serum total cholesterol was significantly lower in patients with cirrhosis when compared to controls in our study. This observation supports the earlier reports. The probable explanation for the reduced serum total cholesterol is due to the decline in synthetic function and altered metabolism. This was confirmed in the study conducted by Phillips et al., [26]. Miller et al., [27] found that in cirrhosis without cholestasis, cholesterol and apo B levels was reduced. LCAT activity and the proportion of plasma cholesterol esterified were also be markedly reduced. D’Arienzo A et al., [28] said in their study that a low serum cholesterol level is associated with a higher mortality rate in patients with liver cirrhosis. Studies done by Ghadir MR et al., [29], Subhan F et al., [30] have similar results according to our study.

Further comparison of the total cholesterol values in different Child Pugh Classes showed reduction in cholesterol level as the disease advances. But the difference in cholesterol level among three child pugh classes in our study was not significant. Andrzej P et al’ also found insignificant difference between three child pugh classes. But studies done by Ghadir MR et al., [29] and Subhan F et al., [30] found significant difference between three child pugh classes. This supported that Cholesterol falls as the disease advances.

In present study serum triglyceride levels were significantly lower in cases of cirrhosis than in control. The difference was statistically significant (p< 0.001). In studies done by Ghadir MR et al., [29] and Subhan F et al., [30] it was found that serum triglycerides in cirrhotic patients was lower than healthy controls, this was in accordance to our study.

In our study, among cirrhotic patients, mean serum total cholesterol was lower in Child B patients than Child A patients and mean serum total cholesterol was lower in Child C patients than Child B patients but this difference was not statistically significant. In study done by Andrzej F et al., [31] mean serum total cholesterol decreased with the progression of liver disease according to child pugh score but the difference was insignificant. In study done by Ghadir MR et al., [29] and Subhan F et al., [30] similar reduction was seen but the difference was statistically significant. The mechanism responsible for reduction of triglyceride level in patient with cirrhosis could be that the metabolism of free fatty acids might be reduced in cirrhotics due to decreased reserve of liver parenchyma. The poor nutrition, altered metabolism and abstinence from alcohol of cirrhosis patients may explain the lower TGL in cirrhosis in them [14].

There was a significant decrease in levels of serum LDL in patients with cirrhosis, when compared to controls in present study. Observations by Ghadir MR et al., [29] and Subhan F et al., [30] were in accordance to our study. LDL metabolism was greatly altered resulting in reduced level of LDL [32]. We found that the reduction in the LDL level was proportionate to the Severity of Liver damage in Cirrhosis as detected by the Child Pugh scoring system. This was supported by Subhan et al., [30]. The amount of decrement in the serum LDL was significant with increasing severity of liver damage.

The level of serum HDL in our study was significantly decreased in cases of Cirrhosis when compared to control are consistent with a large volume of publications on this subject. HDL estimation in patients with cirrhosis is an important marker of hepatic function. The decrease in HDL in patients with cirrhosis can be attributed to decreased hepatic synthesis of HDL. This could be due to LCAT deficiency. Liver is the only source of this enzyme (LCAT) and serum levels of this enzyme are decreased in liver disorders. The decreased LCAT results in impairment of conversion of nascent HDL to matureHDL resulting in an increase in immatureHDL in blood which is more prone for degradation, resulting in decreased levelsof HDL. We also found that the levels of HDL reduction was proportional to the severity of liver damage in cirrhosis. These observations were in accordance with the studies done by Ghadir MR et al., [29] and Subhan F et al., [30].

In our study, we found that mean serum VLDL cholesterol in cirrhotic patients was lower than healthy controls. This difference was statistically significant. This was in accordance with the study done by Sposito AC et al., [33]. Mean serum VLDL levels also decreased with the progression of liver disease. This is in accordance with study done by Bassani L et al., [34]. Presumably these low levels were due to failure of VLDL synthesis and release, either because of malnutrition or because of damage to the parenchymal cells responsible for the manufacture of VLDL [32].
Alcoholism is significantly associated with the Child-Pugh. These results suggested that the lipid profile could be used as an auxiliary tool in evaluating liver disease, given that there were statistically significant differences in these levels using instruments validated for this purpose.

REFERENCES


