Lipid profile among cirrhotic patients with and without hepatocellular carcinoma in Upper Egypt
Khairy H. Morsya, Mohamed A.A. Ghaliony a and Mohammad A. Kobeisy b

Departments of Tropical Medicine and Gastroenterology and Internal Medicine, Faculty of Medicine, Assiut University, Assiut, Egypt

Correspondence to Khairy H. Morsy, Departments of Tropical Medicine and Gastroenterology, Faculty of Medicine, Assiut University, 71111, Assiut, Egypt
Tel: + 20882413611; fax: + 20882333327; e-mail: khairy.morsy@yahoo.com

Received 26 February 2012
Accepted 15 March 2012

Background/aim
An impaired lipid metabolism is often observed in patients with chronic liver diseases. This study was carried out to determine the lipid profile in cirrhotic patients with and without hepatocellular carcinoma (HCC) and to determine whether it relates to the severity of cirrhosis in Upper Egypt.

Patients and methods
In an analytical cross-sectional study, 74 patients with cirrhosis and 36 patients with cirrhosis and HCC (cases) and 65 age-matched and sex-matched healthy individuals (control) were studied from the Tropical Medicine and Gastroenterology Department and Internal Medicine Department, Assiut University Hospital. For all the participants, the following was carried out: clinical evaluation, abdominal ultrasound (US) examination, and laboratory investigations including the lipid profile [total cholesterol, triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein (HDL)].

Results
In cirrhotic patients with and without HCC, there was a significant decrease in serum total cholesterol, triglycerides, LDL, and HDL levels compared with the control group. Comparison of the lipid profile with the severity of cirrhosis indicated that serum cholesterol, triglyceride, and LDL but not HDL levels decreased linearly with progression of liver damage (Child C vs. Child A). The HDL level was significantly lower in cirrhotic patients with HCC than in cirrhotic patients without HCC.

Conclusion
The lipid profile (total cholesterol, triglycerides, HDL, and LDL levels) is impaired in cirrhotic patients with and without HCC. The lipid profile (but not HDL) is inversely correlated with the severity of cirrhosis. The HDL level is significantly lower in cirrhotic patients with HCC than in cirrhotic patients without HCC.

Keywords:
cirrhosis, hepatocellular carcinoma, lipid profile

Introduction
The liver plays a key role in several metabolic pathways. The most important among these is the metabolism of plasma lipids and lipoproteins. Therefore, it is reasonable to expect an abnormal lipid profile in patients with severe liver dysfunction. There is a marked decline in plasma cholesterol and triglyceride (TG) levels in patients with severe hepatitis and hepatic failure because of a reduction in lipoprotein biosynthesis. For reduced liver biosynthesis capacity, low levels of TG and cholesterol are usually observed in chronic liver diseases [1].

Cirrhotic patients require frequent visits and multiple hospitalizations for the management of cirrhosis or its complications. However, the choice of the proper treatment plan depends on the severity, type of liver damage, and the possibility of assessing its extent. To evaluate cirrhosis, the Child–Turcotte–Pugh criteria can be used [2].

Under normal physiological conditions, the liver maintains homeostasis of lipid and lipoprotein metabolism. It has been shown that the plasma lipid profiles may be altered in hepatocellular carcinoma (HCC) patients [3]. In the majority of the reports, plasma levels of TG, cholesterol, free fatty acids, high-density lipoprotein (HDL), low-density lipoproteins (LDL), lipoprotein (a) (Lp(a)), apolipoprotein AI (apoAI), and apoB were slightly to significantly decreased in HCC patients; however, in certain cases, the plasma levels of TG and Lp(a) might even increase [4–6]. It has been suggested that analysis of the plasma levels of lipids, lipoproteins, and apolipoproteins in HCC patients may reflect the status of hepatic cellular impairments [5], and decreased serum levels of cholesterol and apoAI may indicate a poor prognosis [4–6].

HCC is the fifth most malignant tumor in the world [7]. HCC is frequently accompanied by chronic hepatitis B virus (HBV) infection and hepatic cirrhosis; therefore, liver function is clearly impaired in HCC because of chronic hepatocellular damage [3,8,9]. Studies [5,10–12] have shown that severe chronic liver diseases are associated with a disordered lipoprotein metabolism and altered plasma patterns of lipid and lipoprotein.
Because of the high prevalence of chronic liver disease in our country, we carried out this study to determine the lipid profile in patients with cirrhosis with and without HCC and to assess whether it relates to the severity of cirrhosis.

Patients and methods

Patients

In an analytical cross-sectional study, out of 550 consecutive cirrhotic patients admitted during the period from July 2011 to December 2011 in the Tropical Medicine and Gastroenterology Department and Internal Medicine Department, Assiut University Hospital, 74 patients without HCC and 36 patients with HCC were included in our study, after excluding those with diabetes mellitus, cancer other than HCC, renal failure, acute gastrointestinal bleeding, and patients with a history of hyperlipidemia and those taking lipid-lowering drugs.

For all the participants, the following was carried out: clinical evaluation (medical history and physical examination), abdominal ultrasound examination, testing of hepatitis B surface antigen (HBsAg) and hepatitis C antibody (HCV-Ab), estimation of fasting serum level of glucose, lipid profile (fasting serum levels of cholesterol, LDL cholesterol, HDL cholesterol, and TG), liver profile (serum levels of bilirubin, albumin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and γ-glutamyl transpeptidase), and prothrombin time.

The diagnostic criteria for liver cirrhosis included:

1. Clinical criteria of liver cirrhosis.
2. Ultrasonographic confirmation of liver cirrhosis (coarse liver, irregular surface ± reduced size) [13].
3. Biochemical confirmation of liver cirrhosis.

The diagnostic criteria of HCC were a mass lesion of more than 2 cm in size with arterial hypervascularity on triphasic computed tomography and serum α-fetoprotein level of more than 200 ng/ml [14,15]. Finally, the Child–Turcotte–Pugh scores were calculated for each patient as an index for the extent of liver damage.

Furthermore, 65 age-matched and sex-matched apparently healthy individuals were selected as our control group.

Serum levels of total cholesterol, TG level, HDL, and LDL were measured using the enzymatic method after 12-h fasting. The normal serum level of total cholesterol is 50–200 mg/dl, the TG level is 50–200 mg/dl, HDL is 50–200 mg/dl, and LDL is 60–130 mg/dl.

HBsAg was determined using the Auszyme HBsAg Monochonal Assay, which is a qualitative third-generation enzyme immunoassay (Abbott Laboratories, Chicago, USA).

An anti-HCV antibodies test was carried out using anti-HCV ELA third generation, which is a qualitative third-generation enzyme immunoassay (Abbott Laboratories HCV EIA 3.0 # B 7A160 # 67-6443/R5).

Ethical considerations

Before enrollment, all participants signed a consent certificate. Before signing, they were informed in detail about the certificate and the aim of the study. Participants were clearly informed that refusal to participate would not affect the medical service and treatment available to them. Data were collected through personal interviews with participants taking into consideration data confidentiality.

Results

The most common causes of cirrhosis were HCV infection (77% of patients in the cirrhotic group and 63.9% in the group of cirrhotic patients with HCC), followed by HBV infection (12.2% of patients in the cirrhotic group and 19.4% in the group of cirrhotic patients with HCC). Combined HCV and HBV infections were found in 5.4% of cirrhotic patients and 16.7% of cirrhotic patients with HCC as shown in Table 1.

Table 2 shows the clinical and laboratory characteristics of cirrhotic patients, cirrhotic patients with HCC, and the control group. Alkaline phosphatase, γ-glutamyl transpeptidase, alanine aminotransferase, and aspartate aminotransferase were significantly higher in cirrhotic patients with and without HCC than the control group.

Prothrombin time was significantly impaired in cirrhotic patients with and without HCC compared with the control group.

Total cholesterol, TG, HDL, and LDL were significantly lower in group of cirrhotic patients and in the group of cirrhotic patients with HCC patients compared with the control group. The only significant lipid abnormality was low HDL among cirrhotic patients (56.8%) and cirrhotic patients with HCC (97.2%) versus the control group (1.5%) as shown in Table 3.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Cirrhotic patients (n=74)</th>
<th>Cirrhotic patients with HCC (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV infection</td>
<td>57 (77.0%)</td>
<td>23 (63.9%)</td>
</tr>
<tr>
<td>HBV infection</td>
<td>9 (12.2%)</td>
<td>7 (19.4%)</td>
</tr>
<tr>
<td>Combined HCV and HBV infections</td>
<td>4 (5.4%)</td>
<td>6 (16.7%)</td>
</tr>
<tr>
<td>Negative HCV/Ab and negative HBsAg</td>
<td>4 (5.4%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HCV-Ab, hepatitis C antibody.
Total cholesterol, TG, and LDL but not HDL were inversely correlated with the severity of cirrhosis. They were significantly lower in Child C than A and B. Hypercholesterolemia and hypertriglyceridemia were present only in Child grade A (Table 4).

HDL was significantly lower in cirrhotics with HCC than cirrhotic patients without HCC. A low level of HDL was present in 56.8% of cirrhotic patients versus 97.2% in cirrhotic patients with HCC (Table 5).

**Discussion**

Our study made some important observations. First, the lipid profile (total cholesterol, TG, HDL, and LDL)
HCC may result in a distinctly abnormal pattern of cirrhosis in our study. Chronic hepatitis (C) is the most common cause of liver disease [20] but this is not true in our environment as an important cause of cirrhosis in that environment. In this study, because alcohol has been identified as an important cause of cirrhosis in that environment [20] but this is not true in our environment as chronic hepatitis (C) is the most common cause of liver cirrhosis in our study.

Lipid abnormality is expressed by number (percentage).

Our present study has some similarities to previous reports by Selimoglu et al. [17] in Turkey, who found low levels of LDL and HDL and normal levels of total cholesterol and TG among cirrhotic patients. In the present study, the final results also showed that the severity of liver damage was correlated with total cholesterol, TG, HDL, and LDL but not HDL levels in cirrhotic patients were lower than those in the control group.

Our study showed that the serum level of HDL was significantly lower in HCC patients than in cirrhotic patients without HCC. Second, total cholesterol, TG, and LDL levels in cirrhotic patients were inversely correlated with the severity of cirrhosis. Third, the HDL level was significantly lower in cirrhotic patients with HCC than cirrhotic patients without HCC.

The results of this study are similar to those of a previous study by Ghadir et al. [16]. They reported that all four of the variables studied (total cholesterol, TG, HDL, and LDL) were significantly lower in cirrhotic patients than those in the control group, which is reasonably expected as liver biosynthesis has been reduced. Also, the present study obtained results similar to those from the west [12–14], which have documented that all the lipid fragments in cirrhotic patients were lower than those in the control group.

In HCC and chronic liver diseases, the synthesis and metabolism of cholesterol are impaired. It leads to a decrease in plasma cholesterol levels [5,11,12,24]. In a study carried out by Jiang et al. [10], it was found that total cholesterol, apoB, and HDL cholesterol were decreased in HCC patients and there were no obvious changes in serum LDL cholesterol in HCC patients compared with the controls.

Our present study has some similarities to previous reports by Selimoglu et al. [17] in Turkey, who found low levels of LDL and HDL and normal levels of total cholesterol and TG among cirrhotic patients. Our study showed that the serum level of HDL was significantly lower in HCC patients than in patients without HCC and this is in agreement with many studies. Ahaneku et al. [24] analyzed HDL fraction levels including HDL-C, HDL-phospholipids (HDL-PL) and the ratio of HDL-C/HDL-PL in HCC patients and compared these with the controls. They found that plasma HDL-C, HDL-PL, and HDL-C/HDL-PL were significantly lower in HCC patients than those in the controls.

In HCC and chronic liver diseases, the synthesis and metabolism of cholesterol are impaired. It leads to a decrease in plasma cholesterol levels [5,11,12,24]. In a study carried out by Jiang et al. [10], it was found that total cholesterol, apoB, and HDL cholesterol were decreased in HCC patients and there were no obvious changes in serum LDL cholesterol in HCC patients compared with the controls.

Our study showed that the serum level of HDL was significantly lower in HCC patients than in patients without HCC and this is in agreement with many studies. Ahaneku et al. [24] analyzed HDL fraction levels including HDL-C, HDL-phospholipids (HDL-PL) and the ratio of HDL-C/HDL-PL in HCC patients and compared these with the controls. They found that plasma HDL-C, HDL-PL, and HDL-C/HDL-PL were significantly lower in HCC patients than those in the controls.

Patients with HCC frequently have other liver diseases such as chronic hepatitis and/or cirrhosis. All these conditions (hepatitis and cirrhosis of the liver) are often associated with plasma lipid and lipoprotein aberrations [11]. In the present study, we found that serum total cholesterol, TG, LDL, and HDL levels were significantly decreased in HCC patients than in the normal individuals, similar to the data reported that plasma TG decreased by 20–30% in the patients with HCC [11]. However, Alsabti [21] reported that serum TG in HCC patients was even increased when compared with those with cirrhosis.

Ooi et al. [5] have reported that plasma TG levels in HCC patients were not significantly different compared with the controls. These results emphasize the fact that changes in the plasma lipid profile may not always imply the presence of HCC and these results should be interpreted with caution. Approximately 80% of endogenous cholesterol is synthesized in the hepatocellular microsomes that contain cholesterol synthesis enzymes [22,23].

Table 5 Lipid profile and lipid abnormalities in cirrhotic patients vs. cirrhotics with hepatocellular carcinoma

<table>
<thead>
<tr>
<th>Lipid profile</th>
<th>Cirrhotic patients (n=74)</th>
<th>Cirrhotics with HCC (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>69.8 ± 49.0</td>
<td>75.2 ± 50.3</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>54.8 ± 54.1</td>
<td>59.9 ± 30.2</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>32.3 ± 16.8</td>
<td>16.6 ± 10.3*</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>49.2 ± 21.9</td>
<td>43.6 ± 23.2</td>
</tr>
<tr>
<td>Lipid abnormality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>5 (6.8%)</td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>5 (6.8%)</td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td>Low HDL</td>
<td>42 (56.8%)</td>
<td>38 (97.2%)*</td>
</tr>
<tr>
<td>High LDL</td>
<td>4 (5.4%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

Lipid profile is expressed by mean ± SD.
Lipid abnormality is expressed by number (percentage).
HCC, hepatocellular carcinoma; HDL, high-density lipoprotein; LDL, low-density lipoprotein.
*Significant difference compared with the cirrhotic group at P<0.05.

Patients with HCC may result in a distinctly abnormal pattern of plasma lipids, apolipoproteins, and lipoproteins, which may be related to or regulated by various cytokines and/or metabolic cellular substances, or tumor factors, although the detailed mechanisms are not fully understood [3].

Our study showed that the serum level of HDL was significantly lower in HCC patients than in patients without HCC and this is in agreement with many studies.

Hepatocellular injury or chronic liver diseases including HCC may result in a distinctly abnormal pattern of lipid abnormalities in chronic liver disease may then require treatment.
References

Conclusion
Lipid abnormalities exist in cirrhotic patients with and without HCC. The serum lipid profile (total cholesterol, TG, HDL, and LDL) is significantly reduced in these patients. Patients with liver cirrhosis should thus be routinely screened for such abnormalities. The extent of decrease (except HDL) is related to the progress in cirrhosis. Further studies are required to determine the predictive values of determining lipid profiles as a means to estimate the extent of liver damage in cirrhotic patients. Analysis of serum levels of lipids in patients with HCC may reflect the extent of hepatic cellular impairment, and may also be used as an indicator to evaluate a patient’s prognosis.

Acknowledgements
The authors wish to acknowledge the resident doctors in the Departments of Tropical Medicine and Gastroenterology and Internal Medicine, Assiut University Hospital, who helped with patient recruitment and the laboratory technologists who helped with biochemical analysis.

Conflicts of interest
There are no conflicts of interest.

Lipid profile among cirrhotic patients Morsy et al. 37