Lipid profile among cirrhotic patients with and without hepatocellular carcinoma in Upper Egypt

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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

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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 35–65 mg/dl, and LDL is 60–130 mg/dl.

HBsAg was determined using the Auszyme HBsAg Monoclonal 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.

Statistical analysis

Statistical analysis was performed using the statistical package for the social sciences (version 15, SPSS Inc., Chicago, Illinois, USA). All data was expressed as mean ± SD or frequencies. For statistical evaluation, the Student *t*-test was used. Significance was considered at *P*-value less than 0.05.

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 1 Etiology of liver cirrhosis in patients

	N (%)	
Etiology	Cirrhotic patients (*n*=74)	Cirrhotic patients with HCC (*n*=36)
HCV infection	57 (77.0%)	23 (63.9%)
HBV infection	9 (12.2%)	7 (19.4%)
Combined HCV and HBV infections	4 (5.4%)	6 (16.7%)
Negative HCV-Ab and negative HBsAg	4 (5.4%)	0 (0%)

HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HCV-Ab, hepatitis C antibody.

Table 2 Clinical and laboratory characteristics of cirrhotic patients and cirrhotic patients with hepatocellular carcinoma

Characteristics	Control ($n=65$)	Cirrhotic patients ($n=74$)	Cirrhotics with HCC ($n=36$)
Sex (male/female)	35/30	41/33	27/9[b,c]
Age (years)	48.1 ± 9.2	47.3 ± 7.9	54.8 ± 6.5[b,c]
BMI	24.6 ± 3.9	23.0 ± 2.4[a]	24.8 ± 4.1[c]
Ascites [*N* (%)]	0 (0.0%)	60 (81.1%)[a]	35 (97.2%)[b,c]
Hepatic encephalopathy [*N* (%)]	0 (0.0%)	13 (17.6%)[a]	17 (47.2%)[b,c]
Total bilirubin (mg/dl)	0.9 ± 0.1	3.6 ± 0.8[a]	3.7 ± 0.9[b]
Direct bilirubin (mg/dl)	0.3 ± 0.0	2.5 ± 0.7[a]	2.6 ± 0.8[b]
Serum albumin (gm/dl)	4.0 ± 0.2	2.4 ± 0.5[a]	2.5 ± 0.5[b]
ALP (IU/l)	100.4 ± 9.1	143.5 ± 16.9[a]	180.5 ± 33.4[b,c]
GGT (IU/l)	88.1 ± 5.4	91.3 ± 6.6[a]	99.2 ± 14.9[b,c]
ALT (IU/l)	21.0 ± 5.3	53.8 ± 11.2[a]	58.7 ± 12.5[b,c]
AST (IU/l)	21.7 ± 3.5	71.7 ± 13.0[a]	77.6 ± 14.1[b,c]
Prothrombin time (s)	13 ± 0.5	16.9 ± 2.2[a]	18.1 ± 2.2[b,c]

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, γ glutamyl transpeptidase; HCC, hepatocellular carcinoma.
[a]Statistically significant difference between cirrhotic patients and controls.
[b]Statistically significant difference between cirrhotic patients with HCC and controls.
[c]Statistically significant difference between cirrhotic patients and cirrhotics with HCC.

Table 3 Lipid profile and lipid abnormalities in cirrhotic patients and cirrhotic patients with hepatocellular carcinoma vs. the controls

	Cirrhotic patients ($n=74$)	Cirrhotics with HCC ($n=36$)	Control ($n=65$)
Lipid profile			
Total cholesterol (mg/dl)	69.8 ± 49.0[a]	75.2 ± 50.3[b]	129.9 ± 58.0
Triglycerides (mg/dl)	54.8 ± 54.1[a]	59.9 ± 30.2[b]	131.4 ± 60.0
HDL (mg/dl)	32.3 ± 16.8[a]	16.6 ± 10.3[b]	52.3 ± 7.5
LDL (mg/dl)	49.2 ± 21.9[a]	43.6 ± 23.2[b]	96.9 ± 22.7
Lipid abnormality			
Hypercholesterolemia	5 (6.8%)	1 (2.8%)	11 (16.9%)
Hypertriglyceridemia	5 (6.8%)	1 (2.8%)	10 (15.4%)
Low HDL	42 (56.8%)[a]	35 (97.2%)[b]	1 (1.5%)
High LDL	4 (5.4%)	0 (0.0%)	2 (3.1%)

Lipid profile is expressed as mean ± SD.
Lipid abnormality is expressed as number (percentage).
HCC, hepatocellular carcinoma; HDL, high-density lipoprotein; LDL, low-density lipoprotein.
[a]Statistically significant difference between cirrhotic patients and control.
[b]Statistically significant difference between cirrhotic patients with HCC and control.

Table 4 Lipid profile and lipid abnormalities in cirrhotic patients in relation to Child grades

	Child grade			
	Child A ($n=17$)	Child B ($n=24$)	Child C ($n=33$)	*P*-value
Lipid profile				
Total cholesterol (mg/dl)	136.76 ± 63.53	62.92 ± 10.87	40.25 ± 6.91	0.000*
Triglycerides (mg/dl)	125.55 ± 78.31	41.08 ± 6.63	28.23 ± 6.53	0.000*
HDL (mg/dl)	39.17 ± 11.82	33.25 ± 12.60	28.12 ± 20.42	0.082
LDL (mg/dl)	67.85 ± 18.71	56.21 ± 15.40	34.45 ± 17.34	0.000*
Lipid abnormality				
Hypercholesterolemia	5 (29.4%)	0 (0.0%)	0 (0.0%)	0.000*
Hypertriglyceridemia	5 (29.4%)	0 (0.0%)	0 (0.0%)	0.000*
Low HDL	7 (41.2%)	18 (75.0%)	17 (51.5%)	0.070
High LDL	3 (17.6%)	1 (4.2%)	0 (0.0%)	0.369

Lipid profile is expressed by mean ± SD.
Lipid abnormality is expressed by number (percentage).
HDL, high-density lipoprotein; LDL, low-density lipoprotein.
*Statistically significant at a $P<0.05$ using the Pearson correlation.

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)

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

	Cirrhotic patients ($n=74$)	Cirrhotics with HCC ($n=36$)
Lipid profile		
Total cholesterol (mg/dl)	69.8±49.0	75.2±50.3
Triglycerides (mg/dl)	54.8±54.1	59.9±30.2
HDL (mg/dl)	32.3±16.8	16.6±10.3*
LDL (mg/dl)	49.2±21.9	43.6±23.2
Lipid abnormality		
Hypercholesterolemia	5 (6.8%)	1 (2.8%)
Hypertriglyceridemia	5 (6.8%)	1 (2.8%)
Low HDL	42 (56.8%)	35 (97.2%)*
High LDL	4 (5.4%)	0 (0.0%)

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 $P<0.05$.

decreased significantly in cirrhotic patients with and 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.

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, and LDL but not HDL levels and our study has some similarities to previous reports by Ghadir *et al*. [16], who reported that total cholesterol, HDL, and LDL but not TG levels correlated with the severity of liver damage.

However, a study carried out by Okeke *et al*. in Nigeria [18] documented that the LDL levels were normal in cirrhotic patients when compared with the controls. This finding may be because of the role of alcohol in those patients. Alcoholic cirrhosis has been associated with increased TC and LDL levels [19]. It is possible that this may have contributed to normal levels of LDL 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.

Hepatocellular injury or chronic liver diseases including 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].

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].

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.

Motta *et al*. [11] studied 40 patients with HCC, and evaluated the LDL-C, HDL C. In patients with HCC, the LDL-C level was significantly lower than those in the controls. Kanel *et al*. [25] reported that patients with primary or metastatic liver cancer had markedly decreased HDL-C. Ooi *et al*. [5] suggested that HDL-C may be clinically useful to indicate pathologic conditions, and can be used to evaluate the severity of liver diseases. Low HDL has long been known to be a strong and independent risk factor for coronary artery disease even when the LDL level is low [26]. The low HDL levels observed in these patients may further predispose them to vascular events, a subset of patients already at risk of cardiac disease [27]. Lipid abnormalities in chronic liver disease may then require treatment.

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.

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Conflicts of interest

There are no conflicts of interest.

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