Al-Nahrain University
College Of Medicine

Hyperlipidemia in Chronic Liver Diseases

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَمَا تَوْفِيقِي إِلا بِاللَّهِ عَلَيْهِ تَوَكَّلْتُ وَإِلَيْهِ أُنِيبُ

صدق الله العلي العظيم
سورة هود (من الآية 88)

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Low density lipoprotein	**LDL**
High density lipoprotein	**HDL**
Very low density lipoprotein	**VLDL**
Intermediate density lipoprotein	**IDL**
Triglyceride	**TG**
Cardio vascular dise	**CVD**
lecithin-cholesterol acyl transferase	**LCAT**
phospholipid transfer protein	**PLTP**
Non alcoholic steatohepatitis	**NASH**
Hepatitis C virus	**HCV**
World health organization	**WHO**

DEDICATION

To My…

Father & Mother,

For their ever support…

ACKNOWLEDGEMENT

I would like to express my sincere attitude to my supervisor DR. Zaid Mohammed Saeed for his great help, kind and enthusiastic support throughout the period of this study…

Further, I am greatly indebted to Internal Medicine Department team at Al-Nahrain Medical College, whose professional expertise is matched only by their concern to make a researcher task as trouble-free as possible…

ABSTRACT

Background: Liver plays a vital role in lipid metabolism. It contributes both in exogenous and endogenous cycles of lipid metabolism and transport of lipids through plasma. Due to the high prevalence of chronic liver disease in our country, we conducted this study to determine lipid profile in patients with chronic liver disease

Aim: To study lipid profiles in patients with chronic liver disease regardless its etiology.

Patients and methods: The present study was conducted in the internal medicine ward in Al Imamain Al-Kadhimain teaching hospital over a period of five months. All patients with chronic liver disease were included in the study with the exclusion of patients with medical conditions which may cause dyslipidemia and patients taking lipid lowering agents. Fasting lipid profiles including (total cholesterol, LDL, HDL and triglyceride levels) were assessed in the study group.

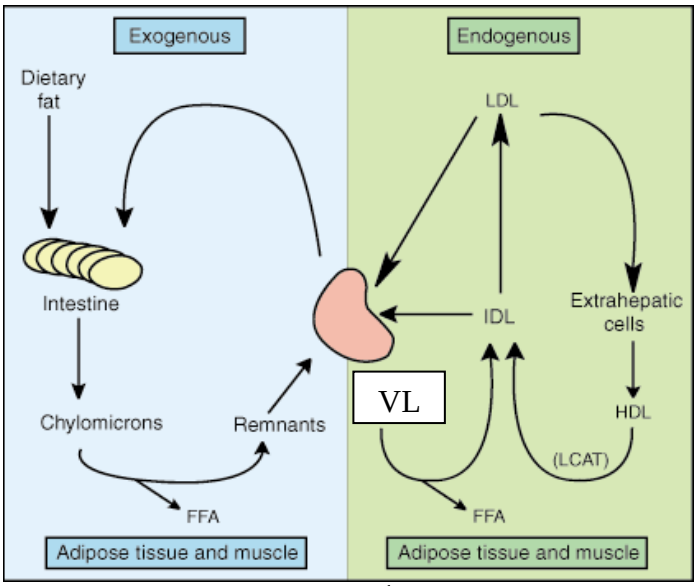
Results: 26 patients were included in the study, there were 15 male patients (57%) and 11 female patients (43%), with age ranging from 40-70 years. There was reduction in the total cholesterol level and in all its components and also there was reduction (to a lesser extent) in the triglyceride level.

Conclusion: In conclusion, dyslipidemia exists in patients with chronic liver disease and screening is important for intervention with appropriate therapy to prevent cardiovascular events.

INTRODUCTION

Lipids are essential component of biological membranes, free molecules and metabolic regulators that control cellular function and homeostasis. (1) Liver plays a vital role in lipid metabolism. It contributes both in exogenous and endogenous cycles of lipid metabolism and transport of lipids through plasma. (2)

Exogenous fat is transported in chylomicrons from the intestine to the liver. After entry in the blood stream the chylomicrons are hydrolyzed by the endothelial-bound lipoprotein lipase. The chylomicron remnants are rapidly taken up into the liver via the LDL receptor and the LDL receptor-related protein. The liver utilizes the exogenous fat and can release surplus lipids via VLDL into the blood. The VLDL are another substrate for lipoprotein lipase. The remaining VLDL remnants (intermediate density lipoprotein (IDL)) can either be taken up into the liver or are hydrolyzed to LDL. LDL delivers cholesterol to all body cells via the LDL receptor. On the other hand, HDL transports the excess lipids from the tissues back to the liver. These processes are shown in figure 1. (3)



Different etiologies of chronic liver diseases produce different abnormalities in lipid profiles,

- NAFLD is associated with insulin resistance which results in atherogenic dyslipidemia characterized by increased LDL and triglyceride levels and decreased HDL levels.(4)
- Alcoholic liver disease can increase plasma HDL cholesterol concentrations and fasting triglyceride concentrations.(5)
- HCV infection decreases serum LDL and total cholesterol levels.(6)
- Cholestatic liver diseases are associated with elevated plasma total cholesterol concentrations which can be attributed to the presence of an abnormal lipoprotein, Lipoprotein-X, but this elevation in plasma cholesterol concentrations doesn't appear to confer excess CVD risk.(7)

Cirrhosis is the common advanced histologic endpoint for chronic liver diseases in which the formation of fibrotic nodules in the liver often obscure the etiology of the responsible disease process.(8)

The changes in lipoprotein metabolism associated with cirrhosis generally reflect the degree of impairment of hepatic function. Plasma concentrations of total cholesterol, HDL cholesterol, LDL cholesterol, and VLDL cholesterol varied in proportion to prothrombin time and albumin, which are measures of hepatic synthetic function. Lipoprotein compositions are also altered in the setting of cirrhosis, with increased LDL particles enriched with triglycerides and deficient in cholesteryl esters, and HDL particles enriched with triglycerides, free cholesterol and phospholipids. These changes are secondary characteristic abnormalities in plasma enzymes that remodel lipoproteins, including lecithin-

cholesterol acyl transferase (LCAT), hepatic lipase and phospholipid transfer protein (PLTP).(9)

Hepatocellular carcinoma can occur in the setting of cirrhosis and may be associated with alterations in plasma lipids. In instances of hypercholesterolemia, the increase may be driven by elevated rates of cholesterol synthesis and cellular levels of 3-hydroxy-3-methylglutarylcoenzyme A. (10, 11)

CVD risk is dependent upon the etiology of cirrhosis, at least in part due to the association of type diabetes. Cirrhosis due to NASH, HCV and alcoholic liver disease increases the risk of type 2 diabetes, which is not observed in cholestatic liver diseases, presumably contributes to CVD risk.(9) In patients with noncholestatic cirrhosis, low HDL cholesterol serves a liver function test that is an indicator of poor prognosis, increasing the risk of cirrhotic death.(12)

The aim of the study is:

To study lipid profiles in patients with chronic liver diseases

PATIENTS AND METHODS

1. **Study setting and design**

   A hospital based cross sectional was conducted over the period of five months from 1st October 2018 till 1st of March 2019. We conducted the study in the internal medicine ward in Al - Imamain Al-Kadhimain Medical City in Baghdad.

2. **Selection of the study sample**

   Inclusion criteria: all patients with chronic liver disease based upon clinical features, liver function tests, prothrombin time, ultrasonography, upper gastrointestinal endoscopy (if performed).

   Exclusion criteria: Patients suffering from conditions which may alter the lipid profile including chronic renal failure, nephrotic syndrome, hypothyroidism.

3. **Baseline Assessment**

   The patients had full history and clinical examination. Basic biochemical investigations including fasting, random blood sugar, lipid profile, blood urea and serum creatinine, urinalysis and TSH were assessed in all patients. Laboratory analyses performed at Laboratory Department of Al-Imamain Al-Kadhimain Medical City.

4. Data collection:

A preformed Questionnaire was used to get information from studied population, which included general information from the patients and duration chronic liver disease.

A venous blood sample of 5 ml obtained (in a plain tube) and the lipid profiles (total cholesterol, LDL, HDL and triglyceride levels) were measured the reference ranges of normal lipid profile were considered as the following :

Total cholesterol (170,-240 mg/dl)

HDL (40 - 60 mg/dl)

LDL(69 - 160 mg/dl)

VLDL(14 - 30 mg/dl)

Triglyceride (0 - 149 mg/dl)

5. Statistical analysis:

The collected data was organized, tabulated, and statistically analyzed using Microsoft Excel 2016 and the results were expressed as percentages.

RESULTS

Total number of 26 patients were included in the study, 15 patients were males (57%) and 11 patients were females (43%). As shown in figure 2

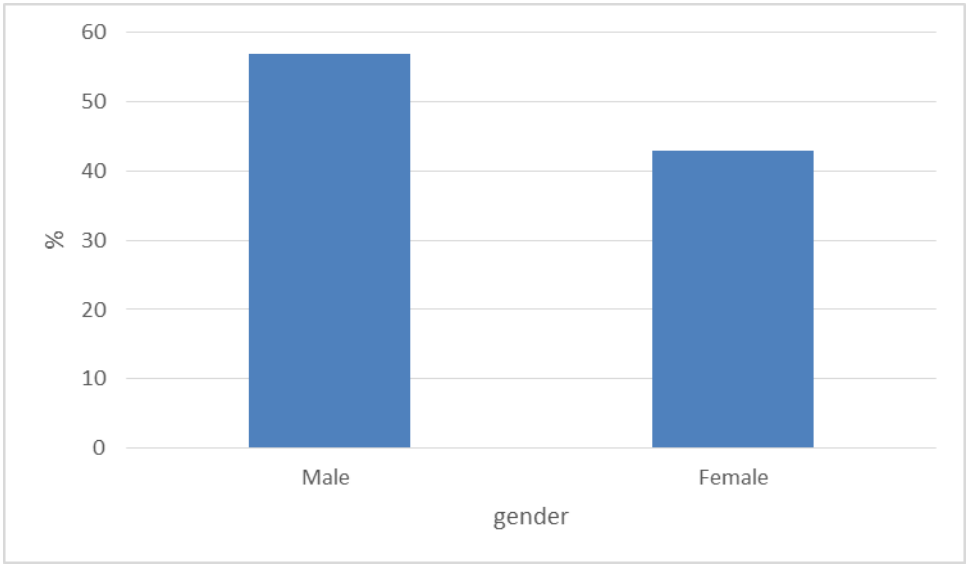


Figure 2. Gender distribution

Age distribution: in the age group 40-50 year there were 10 patients (38%), in the age group 50-60 year there were 7 patients (27%) and in the age group 60-70 there were 9 patients (35%)

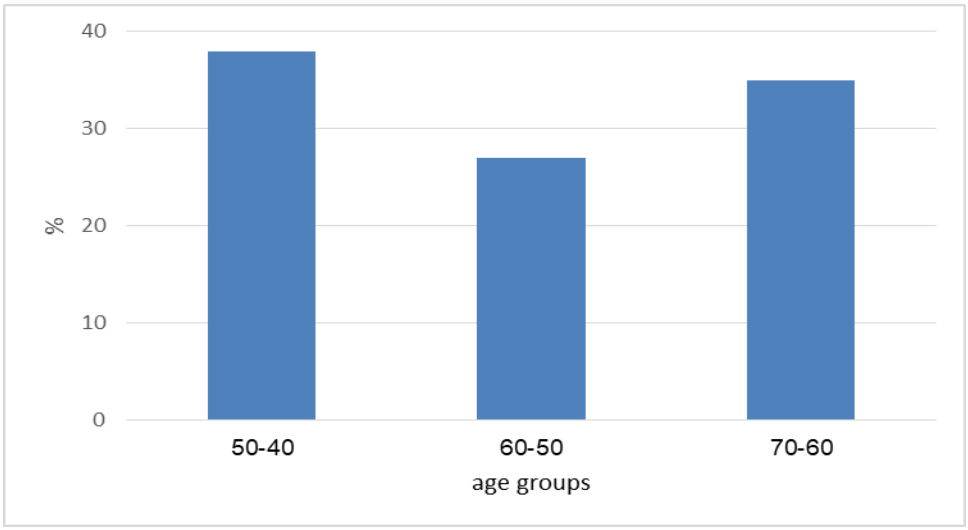


Figure 3. Age distribution

Total cholesterol: 13 patients (50%) had total cholesterol level 50 – 75 mg/dl, 7 patients (27%) had a level 76-100 mg/dl, two patients (7%) had a level 101 – 125 mg/dl and four patients (15%) had a level 126 – 150 mg/dl

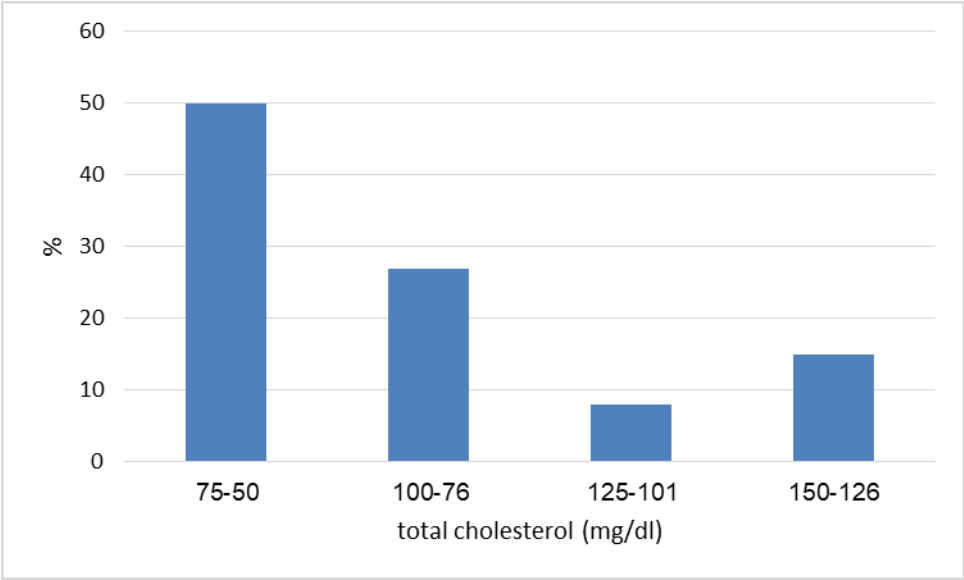


Figure 4: Total cholesterol level in patients with chronic liver disease

LDL: 16 patients (61%) had a LDL level 25-50 mg/dl, 6 patients (23%) had a LDL level 51-75 mg/dl and 4 patients (16%) had a LDL level 76-100 mg/dl.

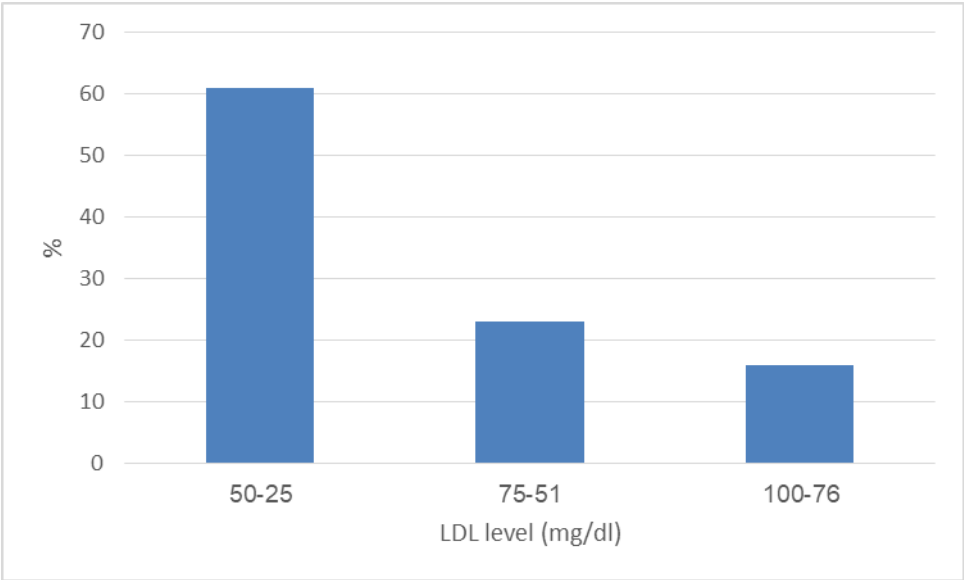


Figure 5: Low density lipoprotein (LDL) level in patients with chronic liver disease

HDL: 4 patients (15%) had a HDL level 1-10 mg/dl, 14 patients (54%) had a HDL level 11-20 mg/dl and 8 patients (31%) had a HDL level 21 – 30 mg/dl

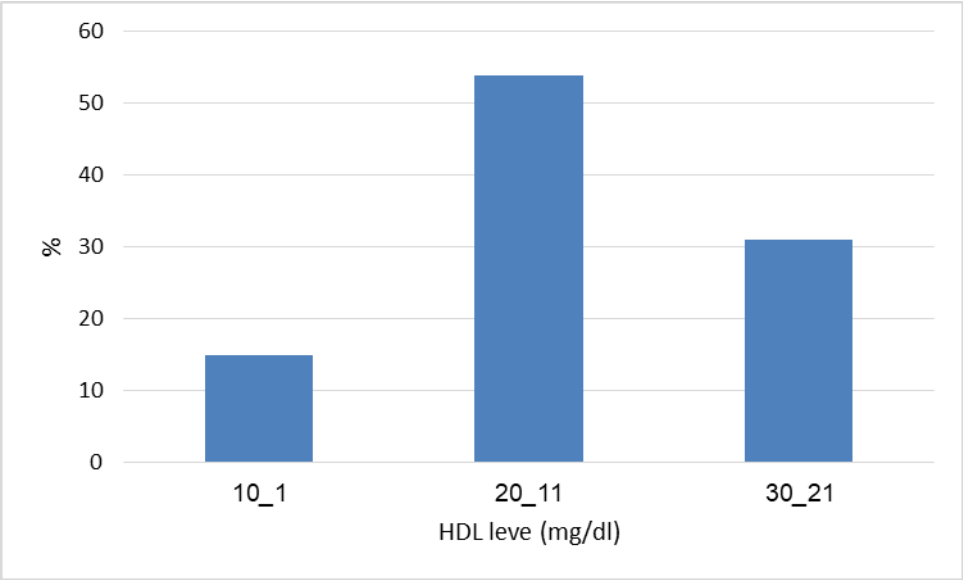


Figure 6: High density lipoprotein (HDL) level in patients with chronic liver disease

Triglycerides: 8 patients (30%) had TG level 1-50 mg/dl, 12 patients (46%) had TG level 51-100 mg/dl, 2 patients had TG level 101-150 mg/dl and 4 patients (16%) had TG level 150-200 mg/dl.

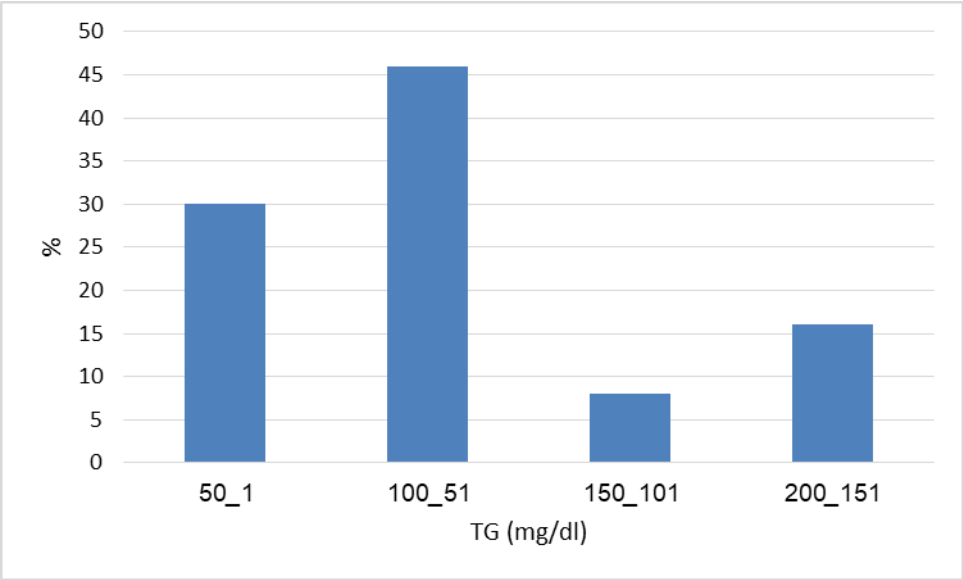


Figure 7: Triglyceride (TG) level in patients with chronic liver disease

Discussion

The results of this study show dramatic reductions in plasma triglyceride and cholesterol level due to reduced lipoprotein biosynthetic capacity, these findings are similar to results obtained by other studies

One study conducted by Brier C et al[13] on lipoproteins in the plasma of patients with post alcoholic liver cirrhosis, showed that in alcoholic cirrhosis, total cholesterol, HDL, VLDL, HDL-cholesterol were all decreased.

Selimoglu and colleagues[14] in their study showed that with the exception of serum triglyceride levels, other variables like serum HDL, LDL level decreased in cirrhotic patients.

Our results showed less severe reduction in triglyceride levels than cholesterol levels, indeed some patients showed hypertriglyceridemia which can be attributed to insulin resistance accompanying NAFLD (as a common cause of chronic liver disease).

Insulin resistance increases the efficiency of VLDL assembly and also impacts VLDL levels via its role in decreasing lipoprotein lipase (LPL) levels which results in decreasing the clearance of VLDL from the circulation and thereby increasing circulating TG level.[15, 16]

This finding was also obtained by DeFilippis and his colleagues[4] who found that NAFLD is associated with hypertriglyceridemia and attributed it insulin resistance.

Brinton EA[17] found that alcohol consumption increases HDL cholesterol, none of our patients showed high HDL level and this can be explained by our small sample which included only one alcoholic patient.

Limitations of our study:

- Small sample size.
- Unavailability of investigations at some times during the study period.
- Uncooperation of some patients and refusal to undergo investigations..

CONCLUSIONS

In conclusion, dyslipidemia exists in patients with chronic liver disease and screening is important for intervention with appropriate therapy to prevent cardiovascular events.

RECOMMENDATIONS

- Further studies are needed to assess the predictive value of dyslipidemia as a tool to reflex the progression of cirrhosis.
- Further studies are needed to study lipid profiles in specific etiologies of chronic liver disease as different etiologies produce variable lipid profile patterns.

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