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RESEARCH ARTICLE

Lipid Profiles as Markers for the Severity of Liver Diseases in Cirrhotic Patients

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Abstract:

Background

Liver cirrhosis is a diffuse process in which the anatomical structure and function of the liver are disturbed. Lipid metabolism occurs mainly in the hepatocytes. In liver cirrhosis, it is expected to detect abnormal lipid profile and abnormal neutrophil to lymphocyte ratio due to necro-inflammation and hepatocyte dysfunction. This study aimed to estimate the lipid profile in patients with liver cirrhosis and to assess its relation to the severity of the liver disease based on Child-Pugh Turcotte score and Neutrophil to Lymphocyte Ratio (NLR).

Methods:

This study included 500 cirrhotic patients. All patients are subjected to history taking, clinical examination, liver and renal function tests, lipid profile, and also abdomino-pelvic ultrasound. Child -Pugh score, fibrosis-4 score (FIB4), and neutrophil and platelet lymphocyte ratio were calculated.

Results:

A total of 500 patients were enrolled in this study; 12 patients were excluded (two patients were on the immunosuppressive drug, three patients had body mass index (BMI) >30, and seven patients took lipid-lowering drugs). Cholesterol level was significantly higher in patients with Child- Score A than B and C. Cholesterol, Low-Density Lipoprotein (LDL), and very-low-density lipoprotein (VLDL) cholesterol were significantly higher in Child B than C. A significant negative correlation was found between cholesterol level and each of FIB4 and NLR ratios.

Conclusion:

There was a significant negative correlation between the severity of liver cirrhosis and lipid profiles (except triglyceride), FIB4 and NLR ratio.

Keywords: Liver, Cirrhosis, Lipids, Cholesterol, Triglycerides, Liver failure.

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1. INTRODUCTION

Liver cirrhosis is a diffuse liver disease including fibrosis and disturbance of normal liver architecture with the formation of cirrhotic nodules [1].

The global prevalence of cirrhosis from autopsy studies ranges from 4.5% to 9.5% of the general population [1 - 32].

Multiple etiological factors contribute to the development of cirrhosis, as exemplified in epidemiological studies thatidentified regular (moderate) alcohol consumption, age above 50 years, and male gender as risk factors in chronic hepatitis C, or older age obesity, insulin resistance/type 2 diabetes, hypertension and hyperlipidemia (all features of the metabolic syndrome) in non-alcoholic steatohepatitis (NASH) [2, 27].

The most common important causes of liver cirrhosis are chronic hepatitis B, chronic hepatitis C, and alcoholic and (NASH) [2 - 4].

Several scoring systems have been developed to evaluate liver status as Child-Turcotte pugh score (CTP) and model for

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end-stage liver disease (MELD) [5, 6].

Neutrophil to lymphocyte ratio (NLR) test has been developed as a simple test to expect the presence of infection and to predict the severity of multiple malignancies [7 - 9]. NLR may be helpful in the prediction of liver disease severity because of the necroinflammatory changes occurring in different liver diseases and in liver cirrhosis [10 - 12].

Lipid metabolism and lipoprotein biosynthesis occur mainly in the hepatocytes; abnormal lipid profiles can be detected in patients with severe liver dysfunction. There is a prominent decrease in plasma cholesterol and triglyceride (TG) levels in patients with severe hepatitis and hepatic failure [13].

The preceding studies have reported that cirrhotic patients have abnormal metabolism of lipids, especially reduction in cholesterol level and hypobetalipoproteinemia, and the lipid profile may be considered a valuable method in assessing liver disease [33].

The aim of this study was to estimate the lipid profile in patients with liver cirrhosis and to assess its relation to the severity of the disease based on Child-Pugh Turcotte Score (CTP) and NLR

2. METHODS

It was a cross-section study. It included 500 subjects in the Department of Tropical Medicine and Infectious diseases in Tanta University Hospital and Assiut University Hospital from January 2017 to December 2018. Institutional ethical committee approval was obtained before the start of the study, and informed consent was signed by every patient before enrolment in the study; and by abiding the rules and regulations as per Helsinki Declaration. This study has been approved by the institutional review board of the, (registration number, 32382\06\18).

All authors had access to the study data, and reviewed and approved the final manuscript.

Patients more than 18 years old with chronic liver disease, etiologies were included in the study.

Diagnosis of liver cirrhosis was based on history, ultrasound, fibroscan and upper gastro-intestinal endoscopy. Patients are known to have dyslipidemia before detection of chronic liver disease, taking lipid-lowering drugs or immunosuppressive drugs, history of taking glucose, recent parenteral nutrition, patients with body mass index (BMI) >30, or patients unwilling to participate in the study were excluded.

A detailed history was taken. A clinical examination was made. Laboratory and radiological evaluations have been made, including complete blood count, fasting lipid profile (including cholesterol, triglycerides (TG), low- density lipoprotein(LDL), high- density lipoprotein (HDL) and very low - density lipoprotein (VLDL).

Serum cholesterol and triglyceride levels were analysed by *in vitro* enzymatic colorimetric kit method. HDL estimation was done by the enzymatic kit method after precipitation of serum by phosphotungstate and magnesium chloride [27].

Liver function tests, and renal function tests, and ultrasonography on the abdomen and pelvis were conducted. Child-Pugh Turcotte score [14], NLR and platelet to lymphocyte ratio, and FIB 4 were calculated for all patients.

A total Child-Pugh score of 5 to 6 is considered Child-Pugh class A (well-compensated disease), 7 to 9 is class B (significant functional compromise), and 10 to 15 is class C (decompensated disease).

Statistical Analysis: The normality of the different variables was tested by the Shapiro Wilks test. Statistical package for social science (IBM SPSS Statistics for Windows, version 23, IBM corp., Armonk, N.Y USA). V 23 was used to analyze the data. Quantitative data were compared using ANOVA for normally distributed data and Kruskal Wallis test for non-normally distributed data with LSD or Tamhane as post hoc test. Pearson and Spearman correlation coefficients were used. A two-sided P value <0.05 was considered statistically significant.

3. RESULTS

A total of 500 patients were enrolled in this study; 12 patients were excluded (two patients were on the immunosuppressive drug, three patients had BMI >30, and seven patients took lipid-lowering drugs). Four hundred and eighty-eight patients were analyzed during the period of the study. There were 338 (69.3%) males and 150 (30.7%) females. The mean age was 56.37 ± 11.13 years. Seventy patients had hypertension (14.3%) and 144 (29.5%) patients had Diabetes Mellitus (DM). The patients in this study were divided according to Child -Pugh Turcotte score, 96 patients (19.7%) were class A, 195 patients (40.0%) class B, and 197 patients (40.4%) class C. No significant difference in liver and kidney functions. Patients, characteristics and laboratory data are shown in Tables **1** and **2**.

Table 1. Patients' characteristics.

Variables	No (%)
Gender	
Male	338 (69.3)
Female:	150 (30.7)
Hypertension	
No	418 (85.7)
Yes	70 (14.3)
Diabetes mellitus	
No	344 (70.5)
Yes	144 (29.5)

(Table 1) contd.....

Variables	No (%)
Ascites	
No	151 (30.9)
Mild	104 (21.3)
Moderate	143 (29.3)
Marked	90 (18.4)
Jaundice	
No	266 (54.5)
Mild	55 (11.3)
Marked	167 (34.2)
Lower limb edema	
No	106 (21.7)
Mild	198 (40.6)
Moderate	143 (29.3)
Marked	41 (29.3)
Hepatitis C	344 (70.5)
Hepatitis B	80 (16.4)
Others	64 (13.11)
Child-Pughclassification	
A	96 (19.7)
B	195 (40.0)
C	197 (40.4)

A total Child-Pugh score of 5 to 6 is considered Child-Pugh class A (well-compensated disease), 7 to 9 is class B (significant functional compromise), and 10 to 15 is class C (decompensated disease).

Table 2. Laboratory characteristics of the patients.

Variables	Mean ±SD, Range
Age	56.37 ± 11.13, 18092
FIB4	6.14 ± 6.16, 0.22-74.79
FBS (mg/dL)	131.45 ± 57.92, 65.0-568.0
Total bilirubin (mg/dl)	2.66 ± 3.30, 0.3-27.7
Albumin (gm/dl)	2.85 ± 1.09, 1.2-21.0
ALT (U/ml)	42.75 ± 47.22, 5.0-498.0
AST (U/ml)	67.92 ± 58.90, 10.0-402.0
INR	1.48 ± 0.40, 0.99-3.91
S creatinine (mg/dl)	1.07 ± 0.43, 0.21-3.20
HB (gm/dl)	10.32 ± 2.45, 0.0-17.3
WBCs (cells/mcL)	8.44 ± 14.46, 0.03-160.0
Platelets (1000/cmm)	134.29 ± 84.65, 7.5-860.0
Neutrophils (cells/mcL)	1.40 ± 2.35, 0.24-21.13
Lymphocytes (cells/mcL)	0.87 ± 6.07, 0.03-134.0

The mean total cholesterol level and triglyceride level were 110.38 ± 43.09 mg\dl, and 80.43 ± 37.59 mg\dl, respectively. The mean LDL cholesterol was 77.69 ± 12.40 mg\ dl. The mean VLDL cholesterol was 19.35 ± 2.35 mg \dl. The mean HDL cholesterol was 33.42 ± 4.58mg\dl (Table **3**). Cholesterol level was significantly higher in patients with CTP class A than in other classes (P <0.001 for each). Also, it was significantly higher in patients with class B than in class C (P<0.001).

Table 3. Lipid profiles among the patients.

Variable Normal Value	Mean ± SD
Total cholesterol (mg/dl) >200 mg/dl	110.38 ± 43.09
LDL cholesterol (mg/dl) >130 mg/dl	77.69 ± 12.40
VLDL cholesterol (mg/dl) >30 mg/dl	19.35 ± 2.35
HDL cholesterol (mg/dl) <40 mg/dl	33.42 ± 4.58

(Table 3) contd.....

Variable Normal Value	Mean ± SD
Triglycerides (mg/dl) >150 mg/dl	80.43 ± 37.59

Table 4. Correlation of lipid profile with child grade.

	A (n=96)	B (n=195)	C (n=197)	P value	Post Hoc
Cholesterol (mg/dl)	135.47 ± 46.66	111.89 ± 38.26	96.67 ± 40.12	<0.001	P1 <0.001 P2 <0.001 P3 <0.001
Triglyceride(mg/dl)	80.47 ± 34.10	80.33 ± 33.42	80.51	0.99	-
LDL cholesterol (mg/dl)	80.33 ± 13.31	79.37 ± 12.01	74.74 ± 11.75	<0.001	P1 0.528 P2 <0.001 P3 <0.001
VLDL cholesterol (mg/dl)	20.00 ± 2.56	19.69 ± 2.30	18.69 ± 2.14	<0.001	P1 0.699 P2 <0.001 P3 <0.001
HDL cholesterol (mg/dl)	34.58 ± 4.90	33.98 ± 4.25	32.30 ± 4.51	<0.001	P1 0.675 P2 0.001 P3 <0.001

No significant difference in triglyceride level among the different classes (P =0.99). However, LDL cholesterol, VLDL cholesterol and HDL cholesterol were significantly higher in CTP class B than class C (P <0.001 for each); however, there was (Table **4**).

A significant negative correlation was found between each cholesterol level, LDL cholesterol, VLDL cholesterol and HDL cholesterol with CTP class (P <0.001 for each) (Table **5**). Also, there was a significant negative correlation between cholesterol level and each of NLR ratio and FIB4 (P <0.001 and 0.005 respectively) (Table **6**).

Table 5. spearman correlation of lipid profiles and CTP.

Variable	Child Pugh Grade	
	R	P value
Cholesterol (mg/dl)	-0.326	<0.001
Triglyceride (mg/dl)	0.001	0.984
LDL cholesterol (mg/dl)	-0.179	<0.001
VLDL cholesterol (mg/dl)	-0.230	<0.001
HDL cholesterol (mg/dl)	-0.208	<0.001
NLR	0.115	0.011

Table 6. Spearman correlation of cholesterol with liver disease severity markers.

-	Cholesterol	
	R	P Value
FIB 4	-0.280	<0.001
N/L ratio	-0.126	0.005
P/L ratio	0.02	0.662

4. DISCUSSION

This study was conducted to reveal the relation between the severity of liver disease and the lipid profile. In our study, all of the lipid markers were considerably greater in Child-Pugh A, although they began to decline with the progression of liver cirrhosis. The total cholesterol level was significantly higher in patients with Child-score A than B and C. Cholesterol, LDL, and VLDL cholesterol were significantly higher in Child B than C. A significant negative correlation was found between cholesterol level and each of FIB4 and NLR ratios. This could be explained by a decrease in the synthetic function of the diseased liver [12].

These findings were in agreement with the previous studies; Muhammed and Jayaraj [15] stated that all parameters of lipid profile, including triglycerides, were significantly lower in cirrhotic patients and were inversely correlated with the severity of cirrhosis [15].

Tauseef *et al*. [29] also supported our results and concluded that the amount of decrements measured in the levels of serum total cholesterol, LDL, and HDL in patients with cirrhosis are related to the progress in cirrhosis [29].

However, a study in 2013 conducted by Mandel *et al*. compared the lipid profile in 150 cirrhotic patients with healthy control detected those lipid profile parameters, other than serum TG and HDL levels, were reduced with the severity of liver cirrhosis but without significant correlation between the severity of liver disease and lipid profile. This could be because the majority of patients had cirrhosis due to non-alcoholic fatty liver disease [16]. Also, Mohammad Reza Ghadir *et al*. revealed that serum lipid levels diminished linearly with the progression of liver damage except for serum triglyceride level [17].

Sen *et al*. concluded that HDL and TG were significantly elevated in the patients with grade III fatty liver [18].

Due to the major role of inflammation in the process of advanced cirrhosis [19 - 21], and NLR is an indicator of inflammation (neutrophils present the inflammation and lymphocytes regulatory immune response) [22], NLR can act as a marker of severity of liver fibrosis. Our study was similar to the previous studies which detected a significant positive correlation between Child- score and N/L ratio as NLR was

higher in Child C patients [23 - 25].

Further studies are needed to confirm our results and to assess the predictive value of the lipid profile measurement in cirrhotic patients.

CONCLUSION

In conclusion, there was a significant negative correlation between the severity of liver cirrhosis and lipid profiles (except triglyceride), FIB4 and NLR ratio.

LIMITATION OF THE STUDY

It was a single-center study with a small number of patients. Further studies are needed.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study has been approved by the Institutional Review Board of the Faculty of Medicine, Tanta University, Tanta, Egypt (registration number,32382\06\18).

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All human research procedures were followed in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Informed consent was signed by every patient before enrolment in the study.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

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