

## ASSESSMENT OF SERUM LIPID PROFILE AS PROGNOSTIC MARKER IN CIRRHOSIS OF LIVER - A CROSS SECTIONAL STUDY

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### ABSTRACT

#### BACKGROUND

Liver plays a vital role in lipid metabolism. Hence, it is not unusual to expect perturbation in lipid profile in patients with liver cirrhosis. We evaluated lipid profile in patients of cirrhosis of liver and correlated their levels with severity of liver dysfunction. We also evaluated lipid profile as prognostic marker in cirrhosis of liver.

#### MATERIALS AND METHODS

Cross-sectional observational study was conducted among 139 patients of cirrhosis of liver. Patient were classified according to severity of cirrhosis based on child pugh's classification and MELD scoring. Apart from routine tests prescribed in patients of cirrhosis of liver, fasting lipid profile (Total cholesterol, triglycerides, HDL-C, VLDL-C, LDL-C) were assessed.

#### RESULTS

Significant decrease in total Cholesterol, HDL-C, LDL-C, VLDL-C and triglyceride levels observed in enrolled patient as compared to reference range value. Total cholesterol, HDL-C and VLDL-C levels were inversely related to severity of liver disease as measured by Child Pugh and MELD score. The decline in total cholesterol, HDL-C & VLDL-C was much greater in HCV related cirrhosis as compared to other aetiologies of cirrhosis.

#### CONCLUSION

Serum total cholesterol, HDL-C, VLDL-C can be used to assess the disease severity in patients with cirrhosis of liver and to predict the disease outcome. Screening for dyslipidaemia may be an important tool to initiate appropriate therapy to prevent adverse cardiovascular events in patients of cirrhosis of liver.

#### KEYWORDS

Cirrhosis of Liver, Serum Lipid Profile, Child Pugh Classification, MELD Score.

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#### BACKGROUND

Liver plays a vital role in various aspects of lipid metabolism. It facilitates digestion and absorption of lipids by production of bile and is responsible for active synthesis and oxidation of fatty acids by increasing activation of transcription factors.<sup>1</sup>

In chronic liver disease, lipid profile is profoundly disturbed.<sup>2</sup> The abnormality in serum lipoprotein are mainly due to decreased synthesis of lipoprotein, decreased clearance of lipoprotein complex by the liver and regurgitation of biliary content into the serum. Endogenous lipids, lipoproteins and Apo lipoproteins are largely produced

in the liver. Hepatocellular microsomes synthesise more than 80% of endogenous cholesterol, therefore in chronic liver disease; the synthesis and metabolism of cholesterol are impaired resulting in their decreased plasma levels.<sup>3</sup> High density lipoprotein (HDL-C), VLDL-C and triglyceride level are reduced in patients with cirrhosis of liver as compared to the normal individuals.

So, we conducted a cross sectional study to evaluate levels of serum lipid profile in cirrhosis of liver. We also correlated levels of lipid profile with severity of liver disease and to find out its prognostic implications.

#### MATERIALS AND METHODS

A cross-sectional observational study was conducted in the Department of Medicine, King George Medical University (KGMU), Lucknow, India over a period of one year. All patients admitted in medical ward who were diagnosed as cirrhosis of liver as evidenced by liver cell failure and portal hypertension (portal vein diameter >13 mm and presence of oesophageal varices) with or without liver biopsy were

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enrolled in our study. Patients with diabetes mellitus, hypertension, symptomatic cerebrovascular disease, symptomatic coronary disease, renal dysfunction, septicaemia, hepatorenal syndrome, pregnancy were excluded from the study.

All enrolled patients were carefully evaluated by detailed history and physical examination. All patients were investigated for complete blood count, serum Na<sup>+</sup>, K<sup>+</sup>, blood urea, serum creatinine, prothrombin time, international normalized ratio, liver function test, ultrasound-abdomen, chest X-ray postero-anterior view, upper gastrointestinal endoscopy, ascitic fluid analysis, antibodies against hepatitis B and C virus. A 12 hour fasting lipid profile (Total cholesterol, triglycerides, HDL-C, VLDL-C, LDL-C were also carried out in all patients.

Reference range of various lipoproteins taken from pathology laboratory of KGMU which is accordance with the National Cholesterol Education Programme (NCEP) ATP III guidelines as shown in Table 1.

Total cholesterol (mg/dl)	150-200 mg/dl
LDL cholesterol (mg/dl)	<150 mg/dl
HDL cholesterol (mg/dl)	Male: 35-65, Female: 45-75 mg/dl
Triglyceride (mg/dl)	75-170 mg/dl
VLDL cholesterol (mg/dl)	15-34 mg/dl

**Table 1. Reference Range of Various Lipoproteins**

All enrolled patients were graded for severity of liver disease by using Child-Pugh score and MELD score.

**Statistical Analysis**

All the statistical analysis was performed using SPSS version 22.0 (SPSS Inc. Chicago, USA). Data were presented as mean ± S.D or number (%) unless specified. All parametric data were analysed using student's t test. All nonparametric data were analysed by Chi-square test. A p-value of <0.05 was considered statistically significant.

**OBSERVATION AND RESULTS**

A total of 139 patients fulfilling inclusion criteria were enrolled in the present study. The mean age of population was 43.20 ± 12.22 years, with 105 male and 34 female patients.

Table 2 shows distribution of patients according to etiology of cirrhosis of liver. Most of the patients in our study had hepatitis B virus (HBV) related cirrhosis.

Etiology	Number of Patients	Age
Alcoholic liver disease	34 (24.46%)	45.81 ± 12.08
HBV related cirrhosis	55 (39.57%)	42.82 ± 13
HCV related cirrhosis	11 (7.9%)	46.82 ± 14.9
Others	39 (28.05%)	42.95 ± 11.2
<b>Total</b>	<b>139</b>	<b>43.20 ± 12.22</b>

**Table 2. Distribution of Study Population according to the Etiology**

Table 3 shows distribution of patients according to severity of cirrhosis as assessed by Child Pugh criteria. Most

of the patients in our study belonged to Child Pugh class C. Among Child Pugh class C, 32 patients were HBV related cirrhosis, 18 were alcoholic cirrhosis and 7 were HCV related cirrhosis.

Child Pugh Class	Number of Patients
A	10 (7.2%)
B	58 (41%)
C	71 (51%)
<b>Total</b>	<b>139</b>

**Table 3. Distribution of Patients according to Child Pugh Classification**

Table 4 shows distribution of patient according to severity of cirrhosis as assessed by MELD score. Maximum number of patients were of MELD score >24. Out of 56 patients having a MELD score >24, 24 were HBV related cirrhosis, 8 were alcoholics and 4 were HCV related cirrhosis.

MELD Score	Number of Patients
<10	8
10-17	33
18-24	42
>24	56
<b>Total</b>	<b>139</b>

**Table 4. Distribution of Patients according to MELD Score**

Table 5 shows distribution of serum total cholesterol level in study population. The reference range of total cholesterol was taken as 150-200 mg/dl. A total of 134 patients (97%) were having serum cholesterol level below 150 mg/dl, out of which maximum number of patients (55%) were having serum cholesterol level between 100-150 mg/dl. This decline in serum total cholesterol level was significant as compared to the reference range (p<.001).

Serum Cholesterol (mg/dl)	Number of Patients
<50	3
51-100	54
101-150	77
151-200	5

**Table 5. Distribution of Serum Total Cholesterol Level in Patients**

Table 6 shows the distribution of serum triglyceride levels in study population. The reference range of serum triglyceride was taken as 75-150 mg/dl. 32 (23%) patients were found to have serum triglyceride levels less than 75 mg/dl. A total of 118 patients (85%) showed serum triglyceride levels less than 125 mg/dl. This decline in serum triglyceride level was significant as compared to the reference range (p<.005).

Serum Triglyceride (mg/dl)	Number of Patients
<50	2
50-75	30
76-100	49
101-125	37
126-150	13
151-175	6
>176	2

**Table 6. Distribution of Serum Triglyceride Level in Patients**

Table 7 shows distribution of serum HDL-C levels in study population. The reference range of serum HDL-C was taken as 35-65 mg/dl for males and 45-75 mg/dl for females. In our study, 122 patients (81%) had serum HDL-C below 30 mg/dl. When compared with the reference range, this decline in serum HDL-C was found to be significant (p value <0.001).

Serum HDL-C (mg/dl)	Number of Patients
<20	34
21-30	88
31-40	11
41-50	5
>50	1

**Table 7. Distribution of Serum HDL-C Level in Patients**

Table 8 shows distribution of serum VLDL-C levels in study population. Reference range for serum VLDL-C was taken as 15-34 mg/dl. Among study population, 101 patients (77%) had serum VLDL-C levels below 20 mg/dl. When compared with the reference range, the decline in serum VLDL-C levels was found to be significant (p value <0.001).

Serum VLDL-C (mg/dl)	Number of Patients
<15	19
15-20	82
21-25	23
26-30	12
>30	3

**Table 8. Distribution of Serum VLDL-C Level in Patients**

Table 9 shows distribution of serum LDL-C levels in study population. Reference range of serum LDL-C was taken as <150 mg/dl. All the patients included in the study had serum LDL-C levels less than 125 mg/dl and among them 117 patients (84%) had serum LDL-C <75 mg/dl. This decline in serum LDL-C was found to be significant as compared to the reference range (p value <0.001).

Serum LDL-C (mg/dl)	Number of Patients
<50	22
50-75	95
76-100	18
101-125	4

**Table 9. Distribution of Serum LDL-C Level in Patients**

Table 10 shows lipid profile of patients of cirrhosis of liver as assessed by Child Pugh and MELD criteria. It can be concluded that there was significant decrease in serum cholesterol, HDL-C and VLDL-C levels with increase in severity of cirrhosis. Serum triglyceride were significantly reduced in Child Pugh C group (p<0.036), although no correlation was found between decline in triglyceride levels with severity of cirrhosis of liver as assessed by MELD score. There was no significant correlation between decline in LDL-C and severity of cirrhosis as assessed by Child Pugh and MELD score.

Groups	Number of Patients	Serum Cholesterol	Serum HDL-C	Serum LDL-C	Serum VLDL-C	Serum Triglyceride
Child Pugh A	10	119.06 ± 17.0	32.11 ± 7.9	67.45 ± 16.4	20.78 ± 4.4	101.71 ± 42.8
Child Pugh B	58	108.52 ± 16.8	27.56 ± 7.4	62.49 ± 16.3	20.52 ± 4.4	96.93 ± 24.5
Child Pugh C	71	96.81 ± 21.6	22.68 ± 6.8	63.59 ± 15.5	18.43 ± 5.5	88.51 ± 21.6
MELD <10	8	118.69 ± 18.9	28.5 ± 4.7	70.11 ± 18.0	21.93 ± 4.1	85.14 ± 43.5
MELD 10-17	33	106.87 ± 17.9	27.15 ± 8.5	61.54 ± 14.3	19.64 ± 4.4	105.33 ± 22.2
MELD 18-24	42	100.66 ± 15.6	26.49 ± 7.2	63.67 ± 16.4	19.05 ± 4.4	97.14 ± 26.3
MELD >24	56	94.04 ± 13.7	22.79 ± 7.3	61.81 ± 16.1	16.49 ± 4.1	101.25 ± 43.7

**Table 10. Distribution of Lipid Profile among Different Classes of Child Pugh and MELD Score**

Table 11 compares lipid profile in patients with liver cirrhosis according to aetiology. It shows that there is statistically significant decline in total cholesterol (p=0.00394), HDL-C (p=0.0029), LDL-C (p=0.0034) and serum VLDL-C levels in HCV group when compared with other aetiologies of cirrhosis of liver.

Etiology	Number of Patients	Serum Cholesterol	Serum HDL-C	Serum LDL-C	Serum VLDL-C	Serum Triglyceride
Alcoholic liver Disease	34	104.81 ± 35.08	25.01 ± 7.2	63.43 ± 15.4	19.77 ± 5.9	109.02 ± 36
HBV related Cirrhosis	55	104.23 ± 22.5	25.58 ± 7.6	63.58 ± 15.3	19.14 ± 4.2	101.49 ± 34.8
HCV related Cirrhosis	11	82.55 ± 24.9	18.04 ± 9.6	46.82 ± 14.9	17.99 ± 3.09	100.83 ± 25.7
Others	39	95.26 ± 26.2	24.95 ± 7.5	62.9 ± 15.2	18.95 ± 6.01	99.35 ± 35.98
<b>Total</b>	<b>139</b>	<b>102.56 ± 22.34</b>	<b>24.40 ± 7.7</b>	<b>61.20 ± 15.72</b>	<b>19.21 ± 5.1</b>	<b>100.06 ± 34.6</b>

**Table 11. Comparison of Lipid Profile in Patients with Liver Cirrhosis According to Etiology**

**DISCUSSION**

The mean age of enrolled patients was  $43.20 \pm 12.2$  years with majority of the patients between 41 to 50 years, with a male to female ratio of 3:1. The most common cause of cirrhosis of liver in our study was HBV related cirrhosis (39%). Most of the patients belonged to Child Pugh class C, with a MELD score  $>24$ , showing that majority of patients were in advanced stage of cirrhosis.

Most of the patients in our study had serum cholesterol, HDL-C, triglyceride, LDL-C and VLDL-C levels significantly below the reference range suggesting hypolipidemic state in cirrhotic patients. This is also supported by previous studies.<sup>4,5,6</sup> However, Okeka et al<sup>7</sup> found that serum triglycerides level was not decreased, although median total cholesterol and HDL-C levels were significantly decreased in patients of cirrhosis of liver.

The decline in serum cholesterol, HDL-C & VLDL-C level correlated with severity of liver cirrhosis as assessed by both Child Pugh & MELD score. The decline in triglyceride level correlated with severity of cirrhosis of liver as assessed by Child Pugh classification only and not by MELD score. However, LDL-C levels did not correlated with severity of liver disease. Sposito et al<sup>8</sup> also found that VLDL-C, LDL-C and HDL-C levels were lower in the liver failure and there was inverse correlation between HDL and severity of liver disease as assessed by Child Pugh's classification. Similarly, Feher et al<sup>9</sup> also found that with increase in severity of liver cirrhosis, VLDL-C levels were markedly decreased.

In HCV related liver cirrhosis, the decline in serum HDL-C, LDL-C, and total cholesterol levels were highest as compared to other cause of cirrhosis, although the decline in VLDL-C and triglyceride level were comparable with other causes of cirrhosis of liver. Corey KE et al<sup>10</sup> also that observed total cholesterol and LDL-C were significantly lower in chronic hepatitis C. Similarly, Carlo Fabris et al<sup>11</sup> observed that mean cholesterol was lower in HCV infected patients as compared to HBV infected patients. This decline in TC, HDL-C & LDL-C levels is probably because that HCV virions circulating in serum bound to lipoproteins and lipids modulate life cycle of HCV.<sup>12</sup>

**CONCLUSION**

The present study shows that serum lipid levels are lower in most of the liver cirrhosis patients. Serum total cholesterol, HDL-C, VLDL-C and triglyceride levels were found to be

inversely correlated with severity of liver cirrhosis. Hence, serum total cholesterol, HDL-C, VLDL-C and triglyceride level may be used to assess severity of cirrhosis of liver and to predict the disease outcome.

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