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Original Research Article

Role of HDL-C as a Predictor of Development of Complications in Patients with Stable Decompensated Cirrhosis

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Abstract:

Background: Chronic liver disease (CLD) is a major global health issue, with a growing number of cases and a significant impact on patient health and survival. The liver plays a crucial role in lipid metabolism, including synthesizing and regulating lipoproteins. The study was done to determine the development of more accurate predictive models for CLD progression, complementing existing tools such as the Model for End-Stage Liver Disease (MELD) and Child-Pugh scores.

Materials and methods: A prospective observational cohort study was conducted at the Department of Gastroenterology, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, India. The study has been conducted for 15 months after obtaining ethical clearance, i.e., from December 2022 to March 2024. Ethical approval has been obtained from the Institutional Ethics Committee (IEC), IGIMS, Patna, Bihar, India under letter number 836/IEC/IGIMS/2022 dated 10 December 2022.

Results: The mean age ± standard deviation is 48.45 ± 13.72 years. The range is 15 to 75. Eighty-one males make up the study population, which is 81% male. Nineteen females represent 19% of the total. P-values were found to be significant at less than 0.05 at three months, six months, and twelve months in both CTP and MELD levels while correlating with HDL. The main complications that were observed were acute kidney injury, ascites, variceal bleeding, and SBP.

Conclusion: Serum HDL-C has emerged as a strong predictor of complication in patients with stable decompensated patients. It has the potential to become an essential part of management strategies, aiding in the prioritization of patients with decompensated CLD for liver transplantation. However, larger, multicenter prospective studies are necessary to validate these findings before recommending the routine use of HDL-C in clinical settings.

Keywords: Chronic liver disease, cirrhosis, High-density lipoprotein, Liver, ascites, Acute Kidney Injury

Introduction

Chronic liver disease (CLD) is a major global health issue, with a growing number of cases and a significant impact on patient health and survival [1]. The progression of CLD involves a range of clinical symptoms, from a stable condition to decompensation and, ultimately, acute-on-chronic liver failure (ACLF). Stable decompensated cirrhotic liver disease (SDC) is characterized by common complications like ascites, low systemic inflammation, and the ability to recover quickly [2, 3]. Patients with SDC typically don't require further hospitalization due to decompensation, and severe organ failure is rare. However, as the disease progresses, those with stable decompensated CLD are at risk of developing additional complications that can significantly affect their outlook and quality of life [4,5].

In recent years, there has been growing interest in identifying reliable biomarkers that can predict the development of complications in patients with stable decompensated CLD. One such potential biomarker is High-Density Lipoprotein Cholesterol (HDL-C), a protein-rich lipoprotein known for its role in reverse cholesterol transport and anti-inflammatory properties [6].

The liver plays a crucial role in lipid metabolism, including synthesizing and regulating lipoproteins. In chronic liver disease, impaired liver function alters lipoprotein levels and composition, particularly affecting HDL-C. These changes are directly proportional to the severity of liver disease and may have significant implications for disease progression and patient outcomes [7].

HDL-C, especially its HDL3 subclass, has been recognized for its anti-inflammatory activities and potential to facilitate the removal of bacterial lipopolysaccharides from circulation. In the context of CLD, where systemic inflammation and susceptibility to infections are vital concerns, the role of HDL-C becomes particularly relevant [8].

Recent studies have suggested that changes in HDL-C levels and functionality may be associated with the risk of decompensation and progression to acute-on-chronic liver failure in patients with CLD. Lower levels of HDL-C and a shift from the HDL3 to HDL2 subclass have been observed in CLD patients, potentially affecting their inflammatory response and overall prognosis [9, 10].

This research aims to investigate the potential of HDL-C as a prognostic marker in patients with stable decompensated chronic liver disease. By examining the relationship between HDLC levels and the development of complications, we seek to enhance our understanding of disease progression in CLD and potentially improve risk stratification and management strategies for these patients.

The findings of this study may contribute to the development of more accurate predictive models for CLD progression, complementing existing tools such as the Model for End-Stage Liver Disease (MELD) and Child-Pugh scores. Ultimately, this research could pave the way for improved patient care and more targeted interventions in managing chronic liver disease.

Methodology

Study Design- A prospective observational cohort study was conducted at the Department of Gastroenterology, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, India. The study has been conducted for 15 months after obtaining ethical clearance, i.e., from December 2022 to March 2024.

Study Population- A total of 100 patients were enrolled in the study. The criteria for enrolment of patients into the study were patients of any gender and age 18 years above, patients ready to provide informed

consent and consecutive patients diagnosed with Stable decompensated cirrhosis during the study period will be considered for the study. The exclusion criteria for participants were patients with liver transplants, hepatocellular carcinoma, patients with cholestatic liver diseases, and patients with other malignancies like intrahepatic cholangiocarcinoma and metastatic liver disease were excluded from the analysis. All patients were followed up for a minimum of 12 months.

Study Procedure- A total of 125 patients of acute decompensation were enrolled and observed for 3 months with all previous history and investigation. During the 3-month observational period-20 patients were excluded. A total of 100 patients were included as per inclusion criteria with all necessary details and followed up in three, six, and twelve months. Liver severity of scores has been compared at different time periods. The complication was managed as per institution protocol after hospital admission.

Data Collection- All relevant clinical data include demographics such as age at diagnosis, gender, and underlying comorbidities, relevant radiological/histological reports, and endoscopy reports. Relevant laboratory values at recruitment and each follow-up were meticulously recorded. Tests of liver dysfunction such as total bilirubin, albumin, and liver enzymes were measured at baseline. Routinely used prognostic scores like the Child-Pugh (CP) classification score and Model for End-Stage Liver Disease (MELD) score were calculated for each patient at entry into the study and on subsequent follow-up. Total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL-C), triglycerides (TG), and very low-density lipoprotein (VLDL) were estimated at baseline and further correlation was performed.

Statistical Analysis- All statistical data analysis will be done using SPSS software 24.0. Pearson's Correlation test and unpaired t-test were conducted to obtain the p-value. All statistical tests were conducted exploratively on a significance level of <0.05.

Ethical Clearance- Ethical approval has been obtained from the Institutional Ethics Committee (IEC), IGIMS, Patna, Bihar, India under letter number 836/IEC/IGIMS/2022 dated 10 December 2022.

Results

Table 1 represents the patient's demographics. The mean age ± standard deviation is 48.45 ± 13.72 years. The range is 15 to 75. Eighty-one males make up the study population, which is 81% male. Nineteen females represent 19% of the total. Comorbidities in the study population included: hypertension (HTN) at 06%, diabetes mellitus (DM) at 14%, and hypothyroidism at 09%.

Table 1: Patients Demographics

Characteristics	**Value**
Age (in years)	48.45 ± 13.72
Male Participants	81 (81%)
Female Participants	19 (19%)
Etiology of Chronic Liver Disease	
Alcohol with portal hypertension	46 (46%)
Hepatitis B	21 (21%)
Hepatitis C	08 (08%)
Cryptogenic	08 (08%)
Autoimmune Hepatitis	02 (02%)
Non-alcoholic steatohepatitis (NASH)	15 (15%)

Comorbidities	
Hypertension	06 (06%)
Diabetes Mellitus	14 (14%)
Hyperthyroidism	09 (09%)
Hemoglobin	8.43±0.67
Total Bilirubin	1.66±0.69
Total Protein	5.26±0.55
Albumin	3±0.35
Alanine aminotransferase (ALT)	42.89±22.32
Aspartate aminotransferase (AST)	64.6±23.
Alkaline Phosphatase (ALP)	103.9±22.7
Total Cholesterol	107.4±17.5
Triglycerides	84.3±13.4
High-Density Lipoprotein (HDL)	30.9±4.4
Low-Density Lipoprotein (LDL)	60.2±14.3
Very-low Density Lipoprotein (VLDL)	16.9±2.7

Data were presented as either mean±SD or n (%)

The mean Child-Turcotte-Pugh (CTP) score is 7.31± 0.77, while the average Model for End-Stage Liver Disease (MELD) score is 12.15±3.19. The mean Fibro scan score is 36.54±6.49. Table 2 depicts liver disease severity scores at the baseline.

Table 2: Liver disease severity scores at the Baseline

Severity at baseline	**Scores**
Child-Turcotte-Pugh (CTP)	7.31±0.77
Model for End-Stage Liver Disease (MELD)	12.15±3.19
Fibro scan (in kPa)	36.54±6.49

Data were presented as mean±SD

Table 3 depicts liver disease severity scores for patients with and without complications at 3 months, 6 months, and 12 months follow-up. All the scores were found to be significant in both the complication and without complication cases except MELD scores at follow-up visits at twelve months.

Table 3: Liver disease severity scores for patients with and without complications at 3months follow-up

Score	**Without Complication**	**With Complications**	**p-value**
CTP (at 3 months)	6.87±0.89	9.67±0.47	**<0.001**
MELD (at 3 months)	11.79±2.75	15.33±0.47	**0.01**
CTP (at 6 months)	7.0±0.89	9.19±1.28	**<0.00001**
MELD (at 6 months)	11.5±2.52	18.62±3.61	**<0.00001**
CTP (at 12 months)	7.8±0.96	10.35±0.68	**<0.001**
MELD (at 12 months)	1.53±2.82	1.95±3.84	0.621

Data were presented as mean±SD
p-value was considered significant at <0.05

Table 4 depicts the correlation of HDL with CTP and MELD at 3 months, 6 months, and 12 months. P-values were found to be significant at less than 0.05 at three months, six months, and twelve months in both CTP and MELD levels while correlating with HDL.

Table 4: Correlation of HDL with CTP and MELD at 3 months, 6 months, and 12 months

	CTP	MELD
At 3 months	-.495** **(<0.001)**	-0.199 **(0.02)**
At 6 months	-.495** **(<0.001)**	-0.371 **(<0.001)**
At 12 months	-0.775 **(<0.001)**	-0.518 **(<0.001)**

Data has been presented as correlation coefficient (p-value)
p-value was considered significant at <0.05
Pearson's Correlation test was used to obtain the correlation coefficient and p-value

Table 5 represents complications in participants at three months, six months, and twelve months respectively. The main complications that were observed were acute kidney injury, ascites, variceal bleed, and SBP.

Table 5: Complications at three months, six months, and twelve months follow up

Complications	At three months	At six months	At twelve months
Acute Kidney Injury and Ascites	02 (2%)	04 (4%)	08 (8%)
Ascites	01 (1%)	08 (8%)	11 (11%)
Variceal Bleed	-	17 (17%)	27 (27%)
SBP	-	03 (3%)	03 (3%)

Data was presented as n (%)

Discussion

In this study, patients with stable decompensated cirrhosis were enrolled. A baseline investigation was done. HDL at baseline was noted and patients were followed up at 3,6,12 months for prediction of complications in patients with stable decompensated cirrhotic patients.

In our study, the mean age (years) of study objects was 49.94 ± 12.30 and 81% of patients were male and 19% were female. In accordance with the present study, Tauseef A. et al reported that their younger populations were similar to our results with mean ages of 47.09 ± 12.30 years [11]. Cirrhosis tends to manifest in middle-aged adults, particularly between the ages of 40 and 60 years, as liver damage often accumulates over decades before clinical decompensation occurs.

In comparison to Rao BH et al.'s study, our study shows similarities and differences in chronic liver disease (CLD) causes. Both studies indicate a high prevalence of alcohol-related CLD. However, our study reports a 29% viral hepatitis-related CLD prevalence (21% HBV, 8% HCV), while Rao BH et al. report only 6.4%. Cryptogenic CLD prevalence also varies, with our study at 8% compared to Rao BH et al.'s reported 50% [6].

The prevalence of diabetes varies significantly across the three studies. Rao BH et al reported the highest prevalence at 64.7%, while Tauseef A et al reported 58.19% respectively [6, 11]. And, in contrast, the present study reported a much lower prevalence of 14%.

Rao BH et al., Feng R et al., and the present study at the last follow-up of 12 months reveals these studies present a spectrum of liver disease severity, with the present research occupying an intermediate position with Child C (47%) [6, 12]. Rao BH et al. reported the highest proportion of Child C patients (76.3%), indicating a population with advanced liver disease [6].

The present study, with a mean CTP score of 10.34 in the complications group, aligns more closely with Rao BH et al., indicating

a predominantly advanced liver disease population [6].

Rao BH et al. reported total high rates of ascites (69%), hepatic encephalopathy (42.3%), variceal bleed (21%), and hepatorenal syndrome (46.4%) at the end of the follow-up period of 1year [6]. In contrast, in the present study at 12 months of follow-up, variceal bleeding was the most common complication (51%), ascites (21%), and acute kidney injury with ascites (15%).

The current study also highlights the negative correlation of HDL with CTP at 3,6,12 months. Initially, the relation was moderately negative at 3 months (HDL and CTP scores $r = -0.495$, $p < 0.001$, HDL and MELD $r = -0.199$, $p = 0.029$), but as time progressed it became stronger at 12 months (HDL and CTP $r = -0.775$, $p < 0.001$, HDL and MELD $r = -0.518$, $p < 0.001$).

There are several limitations to the current study. First, this study relied on total HDL-C levels without considering the various subtypes of HDL particles, each of which may play different roles. Another limitation was that this study did not examine the relationship between HDL-C and portal hypertension, which is closely linked to decompensation in CLD patients.

Conclusion

Serum HDL-C has emerged as a strong predictor of complication in patients with stable decompensated patients. It has the potential to become an essential part of management strategies, aiding in the prioritization of patients with decompensated CLD for liver transplantation. Also, the correlation of HDL with CTP and MELD at follow-ups showed significant results. It has been observed that the number of complications increased with an increase in follow-up visits. However, larger, multicenter prospective studies are necessary to validate these findings before recommending the routine use of HDL-C in clinical settings.

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