RESEARCH PAPER

Serum Hepcidin, Ferritin and Iron Levels in Alcohol-Related Cirrhosis and Their Correlation with Disease Severity

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ABSTRACT

Introduction: Alcohol-related liver disease (ALD) represents a major global health burden and is one of the leading causes of cirrhosis. Disturbances in iron metabolism are frequently observed in chronic liver disease, largely due to dysregulation of the hepatic hormone hepcidin, which plays a central role in systemic iron homeostasis. Alterations in serum ferritin and iron levels have also been linked to hepatic inflammation and iron overload. These biomarkers may reflect disease severity and provide additional insight into the progression of alcohol-related cirrhosis.

Aim: To estimate serum hepcidin, ferritin and iron levels in patients with alcohol-related cirrhosis and to correlate these parameters with disease severity according to the Child–Turcotte–Pugh (CTP) score.

Materials and Methods: This descriptive cross-sectional study was conducted in the Department of Medicine at Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, over a period of 18 months. A total of 106 patients aged >18 years diagnosed with alcohol-related cirrhosis were included. Serum hepcidin levels were measured using enzyme-linked immunosorbent assay (ELISA), serum ferritin by chemiluminescent immunoassay (CLIA), and serum iron using a colorimetric method. Patients were classified into Child-Turcotte-Pugh classes A, B, and C. Statistical analysis included ANOVA and Spearman correlation tests.

Results: The mean age of patients was 46.08±8.6 years, with a predominance of males (81.13%). The mean serum hepcidin level was 6.36±3.66 ng/mL and showed a strong negative correlation with CTP score ($r=-0.882$, $p<0.0001$). Serum ferritin levels were markedly elevated with a mean of 870.51±736.25 ng/mL and demonstrated a strong positive correlation with CTP score ($r=0.905$, $p<0.0001$). Serum iron levels (81.58±25.83 µg/dL) did not show a significant correlation with disease severity ($r=-0.073$, $p=0.458$). A significant negative correlation was observed between serum hepcidin and ferritin levels ($r=-0.863$, $p<0.0001$).

Conclusion: Serum hepcidin levels decrease while ferritin levels increase with advancing severity of alcohol-related cirrhosis. These findings suggest that hepcidin and ferritin may serve as useful non-invasive biomarkers for assessing disease severity and iron dysregulation in alcoholic liver disease.

Keywords: Alcohol-related cirrhosis; Child-Turcotte-Pugh score; Ferritin; Hepcidin; Iron metabolism.

How to cite this article: Kumar A, Kathuria P, Singh P, Serum Hepcidin, Ferritin and Iron Levels in Alcohol-Related Cirrhosis and Their Correlation with Disease Severity. Int J Drug Deliv Technol. 2026;16(14s): 742-747. DOI: 10.25258/ijddt.16.14s.84.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Chronic liver disease (CLD) is a major global health problem associated with significant morbidity and mortality. Among the various etiologies, alcohol-related liver disease (ALD) remains one of the most common causes of liver cirrhosis worldwide. Chronic and excessive alcohol consumption results in progressive liver injury through mechanisms such as oxidative stress, inflammation, mitochondrial dysfunction, and metabolic disturbances, ultimately leading to fibrosis and cirrhosis (1,2). Alcohol-related cirrhosis represents the advanced and irreversible stage of ALD and is associated with multiple systemic complications and poor prognosis.

Alcohol-related liver disease encompasses a spectrum of hepatic abnormalities ranging from simple steatosis and alcoholic hepatitis to cirrhosis. Long-term alcohol consumption exceeding 30–50 g/day significantly increases the risk of liver injury, and approximately one-third of individuals with sustained heavy alcohol intake may develop cirrhosis (3). In India, alcohol consumption has emerged as one of the leading causes of cirrhosis, accounting for a considerable proportion of chronic liver

disease cases in tertiary care centres (4). However, only a subset of individuals with chronic alcohol exposure progress to cirrhosis, suggesting that additional metabolic and molecular factors influence disease progression (5).

The liver plays a central role in systemic iron homeostasis. It regulates iron storage and produces hepcidin, a peptide hormone that is the principal regulator of iron metabolism. Iron balance in the body is tightly controlled through regulation of intestinal absorption because there is no physiological mechanism for active iron excretion (6). In chronic liver disease, this regulatory mechanism may become disrupted, leading to abnormal iron accumulation in hepatic tissue. Excess iron promotes oxidative stress through generation of reactive oxygen species, resulting in lipid peroxidation, cellular injury, and progression of hepatic fibrosis (7).

Hepcidin regulates iron metabolism by binding to ferroportin, the only known iron exporter present on enterocytes and macrophages, thereby reducing iron absorption and release into circulation (8). In alcohol-related liver disease, hepcidin production is often suppressed due to hepatocellular injury and altered inflammatory signaling. Reduced hepcidin levels may lead to increased intestinal iron absorption and subsequent iron overload, which further aggravates hepatic injury (9,10).

Ferritin, an intracellular iron storage protein, serves as an indirect marker of body iron stores. Elevated serum ferritin levels are commonly observed in chronic liver disease and may reflect iron overload, hepatocellular damage, or systemic inflammation (11). Several studies have reported that elevated ferritin levels are associated with advanced liver disease and worse clinical outcomes in cirrhotic patients (12).

Assessment of disease severity in cirrhosis is commonly performed using the Child–Turcotte–Pugh (CTP) classification, which categorises patients into three classes (A, B and C) based on clinical and biochemical parameters (13). Biomarkers related to iron metabolism may provide additional insight into disease progression and severity.

Therefore, the present study was undertaken to estimate serum hepcidin, ferritin and iron levels in patients with alcohol-related cirrhosis and to evaluate their correlation with disease severity according to the Child–Turcotte–Pugh score (14,15).

MATERIALS AND METHODS

Study Design and Participants

This hospital-based descriptive cross-sectional study was conducted in the Department of Medicine in collaboration with the Departments of Biochemistry and Haematology at Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India. The study was carried out over a period of 18 months after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrolment.

A total of 106 patients aged more than 18 years with a diagnosis of alcohol-related cirrhosis were included in the study. The diagnosis of cirrhosis was based on clinical presentation, biochemical investigations and radiological findings suggestive of chronic liver disease. Patients with cirrhosis due to other causes such as viral hepatitis, autoimmune liver disease or metabolic liver disorders were excluded. Patients with hepatocellular carcinoma, active infection, recent blood transfusion or iron supplementation, chronic kidney disease, or other systemic illnesses affecting iron metabolism were also excluded.

Severity of liver disease was assessed using the Child–Turcotte–Pugh (CTP) classification, which categorises patients into Class A, B and C based on clinical and biochemical parameters including serum bilirubin, serum albumin, prothrombin time or INR, presence of ascites and hepatic encephalopathy.

Laboratory Investigations

Five millilitres of venous blood was collected from each participant under aseptic precautions. Serum was separated by centrifugation and analysed for iron metabolism parameters. Serum hepcidin levels were estimated using enzyme-linked immunosorbent assay (ELISA) (Human HepC ELISA Kit). Serum ferritin levels were measured using ELISA kit (Calbiotech Inc, El Cajon,CA, USA) while serum iron levels were estimated using a standard colorimetric method. Routine laboratory investigations including liver function tests, complete blood count and coagulation profile were also performed as part of the clinical evaluation.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) version 25. Continuous variables were expressed as mean±standard deviation, whereas categorical variables were presented as frequencies and percentages. Comparison of biochemical parameters among different Child–Turcotte–Pugh classes was performed using one-way analysis of variance (ANOVA). Correlation between serum hepcidin, ferritin and iron levels with disease severity was assessed using Spearman's correlation coefficient. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 106 patients with alcohol-related cirrhosis were included in the study. The mean age of the study

population was 46.08±8.60 years. Majority of the participants were males (81.13%), while females constituted 18.87% of the study population. Based on the Child–Turcotte–Pugh (CTP) classification, most patients belonged to Class B (44.34%), followed by Class C (33.96%) and Class A (21.70%) (table 1)

Table 1: Baseline Characteristics of Study Population

Variable	Value
Mean age (years)	46.08 ± 8.60
Gender	
Male	86 (81.13%)
Female	20 (18.87%)
Mean CTP score	9.05 ± 2.77
CTP class	
Class A	35 (33.02%)
Class B	35 (33.02%)
Class C	36 (33.96%)

The mean serum hepcidin level among study participants was 6.36±3.66 ng/mL, while the mean serum ferritin level was 870.51±736.25 ng/mL. The mean serum iron level was 81.58±25.83 µg/dL. (table 2)

Table 2: Mean Serum Hepcidin, Ferritin and Iron Levels

Parameter	Mean ± SD
Serum Hepcidin (ng/mL)	6.36 ± 3.66
Serum Ferritin (ng/mL)	870.51 ± 736.25
Serum Iron (µg/dL)	81.58 ± 25.83

Serum hepcidin levels showed a significant decreasing trend with increasing severity of cirrhosis, whereas serum ferritin levels showed a progressive increase with worsening Child–Pugh class. However, serum iron levels did not demonstrate a statistically significant association with disease severity.

Correlation analysis revealed a strong negative correlation between serum hepcidin and CTP score, while serum ferritin showed a strong positive correlation with CTP score. Serum iron levels did not show a significant correlation with disease severity (table 3).

Table 3: - Correlation of CTP score with serum iron, serum ferritin, serum hepcidin

Variables	Serum iron (mcg/dL)	Serum ferritin (ng/mL)	Serum hepcidin (ng/mL)
Correlation coefficient	-0.073	0.905	-0.882
P value	0.458	<0.0001	<0.0001

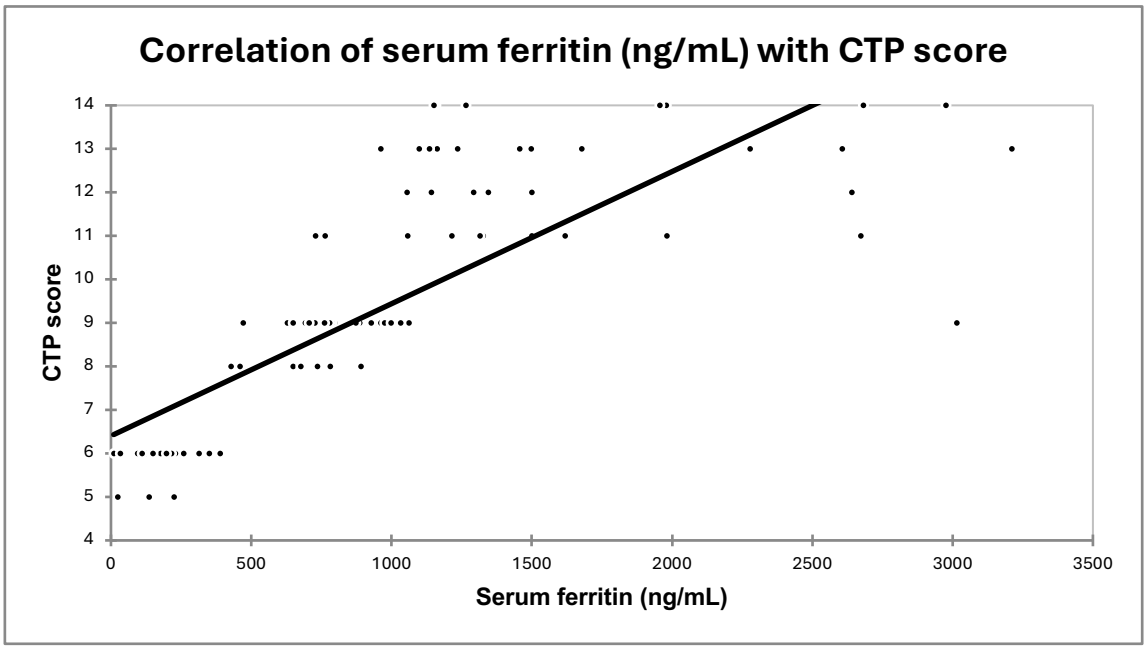

Figure 1: - Correlation of serum ferritin (ng/mL) with CTP score

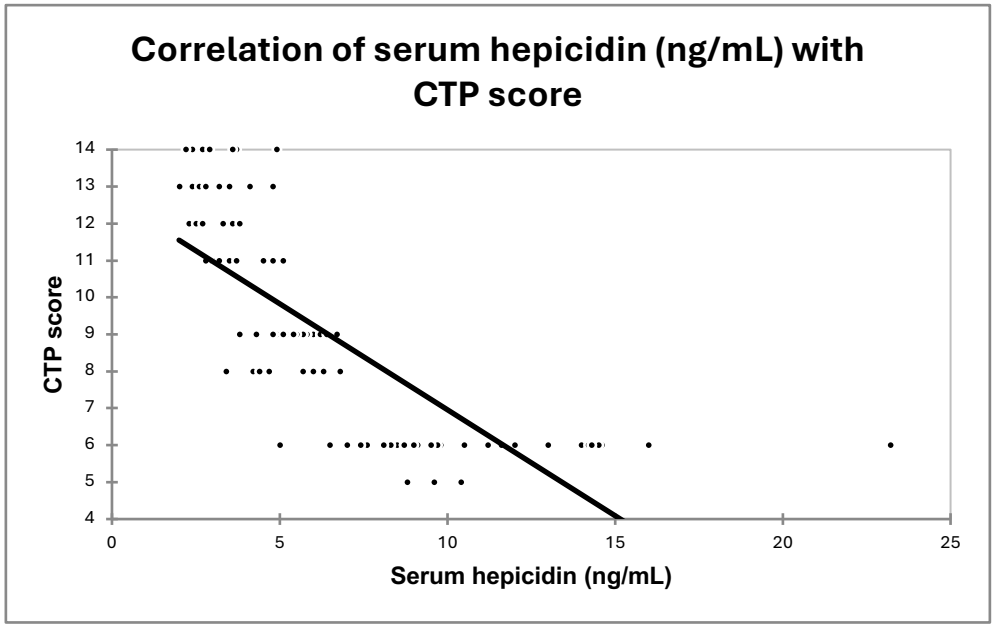

Figure 2: - Correlation of serum hepcidin (ng/mL) with CTP score

DISCUSSION

Alcohol-related liver disease is one of the most important causes of chronic liver disease and cirrhosis worldwide. Chronic alcohol consumption leads to progressive liver injury through mechanisms such as oxidative stress, inflammation and metabolic dysregulation, eventually resulting in hepatic fibrosis and cirrhosis (1,2). Disturbances in iron metabolism are frequently observed in patients with alcohol-related cirrhosis and may contribute to disease progression through enhanced oxidative stress and hepatocellular injury (6,7). In recent years, increasing attention has been focused on iron-regulatory hormones, particularly hepcidin, and their role in the pathogenesis of chronic liver disease.

In the present study, the mean age of patients with alcohol-related cirrhosis was 46.08±8.60 years, with a clear male predominance (81.13%). This demographic pattern is consistent with previous studies which have reported that alcohol-related cirrhosis occurs more frequently in middle-aged males due to higher prevalence of chronic alcohol consumption in this group (3,4). Similar age distribution and male predominance have been reported in several studies evaluating alcoholic liver disease in tertiary care settings (4,5).

In the present study, the majority of patients belonged to Child–Turcotte–Pugh Class B, followed by Class C and Class A. This observation suggests that many patients seek medical attention only after significant progression of liver disease. Similar distributions of Child–Pugh classes have been described in earlier studies of cirrhotic patients in hospital-based settings (13). The Child–Turcotte–Pugh classification remains a widely used and reliable tool for assessing severity and prognosis in cirrhosis.

One of the major findings of the present study was the significant decrease in serum hepcidin levels with increasing severity of cirrhosis. Hepcidin is a key regulator of systemic iron metabolism and is primarily synthesised by hepatocytes (8). Under physiological conditions, hepcidin regulates iron homeostasis by inhibiting ferroportin-mediated iron export from intestinal enterocytes and macrophages (8). In alcohol-related liver disease, chronic hepatocellular injury and altered inflammatory signalling pathways suppress hepcidin synthesis, resulting in increased intestinal iron absorption and systemic iron overload (9,10).

The present study demonstrated a strong negative correlation between serum hepcidin levels and Child–Turcotte–Pugh score, indicating that hepcidin levels decline as liver disease severity increases. These findings are consistent with previous studies which have reported reduced hepcidin expression in patients with alcoholic liver disease due to impaired hepatic synthetic function and direct inhibitory effects of alcohol on hepcidin gene expression (9,10). Reduced hepcidin levels may contribute to progressive hepatic iron accumulation, thereby exacerbating oxidative stress and hepatocellular damage.

Another important observation in the present study was the marked elevation of serum ferritin levels in patients with alcohol-related cirrhosis. Ferritin is an intracellular iron storage protein and an important marker of body iron stores (11). Elevated serum ferritin levels in chronic liver disease may reflect iron overload, hepatocellular injury and systemic inflammation. In the present study, serum ferritin levels showed a strong positive correlation with the Child–Turcotte–Pugh score, indicating that ferritin levels increased with worsening liver disease severity.

Similar findings have been reported in previous studies which have demonstrated elevated ferritin levels in patients with advanced liver disease and cirrhosis (11,12). Increased ferritin levels may result from release of ferritin from damaged hepatocytes as well as from increased iron stores associated with reduced hepcidin activity. Furthermore, ferritin acts as an acute-phase reactant and may increase in response to inflammatory processes occurring in advanced liver disease (12).

In contrast to hepcidin and ferritin, serum iron levels in the present study did not show a significant correlation with disease severity. Although iron metabolism is altered in cirrhosis, serum iron concentration may be influenced by multiple factors including nutritional status, inflammation and diurnal variation, which may limit its usefulness as an independent marker of disease severity (6). Similar findings have been reported in earlier studies where serum iron levels did not consistently correlate with severity of chronic liver disease.

The findings of the present study highlight the importance of iron metabolism disturbances in alcohol-related cirrhosis. Reduced hepcidin production and elevated ferritin levels may reflect impaired hepatic regulation of iron homeostasis and increased oxidative stress in advanced liver disease (7,9). Evaluation of these biomarkers may therefore provide additional insights into disease progression and hepatic dysfunction.

Overall, the results of this study suggest that serum hepcidin and ferritin may serve as useful non-invasive biomarkers for assessing disease severity in patients with alcohol-related cirrhosis, whereas serum iron appears to have limited diagnostic utility in this context. Further large-scale prospective studies are required to validate these findings and to explore the potential role of iron metabolism markers in predicting clinical outcomes in patients with chronic liver disease.

CONCLUSION

The present study demonstrates significant alterations in iron metabolism among patients with alcohol-related

cirrhosis. Serum hepcidin levels were significantly reduced with increasing severity of liver disease, whereas serum ferritin levels were markedly elevated and showed a strong positive correlation with the Child–Turcotte–Pugh score. These findings highlight the dysregulation of iron homeostasis that occurs in alcohol-related liver injury. Reduced hepcidin production may lead to increased intestinal iron absorption and subsequent hepatic iron overload, which may further aggravate oxidative stress and hepatocellular damage. In contrast, serum iron levels did not show a significant association with disease severity in the present study.

The results suggest that serum hepcidin and ferritin may serve as useful non-invasive biomarkers for assessing disease severity in alcohol-related cirrhosis, while serum iron appears to have limited diagnostic value in this context. Evaluation of these markers may provide additional insights into iron metabolism disturbances in chronic liver disease and may help in identifying patients with advanced disease. However, further large-scale multicentric studies are required to validate the clinical utility of these biomarkers and to explore their potential role in predicting prognosis and therapeutic outcomes in patients with alcohol-related cirrhosis.

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