www.ijbar.org

ISSN 2249-3352 (P) 2278-0505 (E)

Cosmos Impact Factor-5.86

Correlation of Serum Iron Indices and High-Sensitivity C-Reactive Protein with Disease Severity in Alcoholic Liver Disease Among Men

Dr. Radha Ballabh Gupta*

***Assistant Professor, Department of Biochemistry, Sri Aurobindo Institute of Medical Sciences, Indore, Madhya Pradesh, India**

Corresponding author: Dr. Radha Ballabh Gupta, Department of Biochemistry, Sri Aurobindo Institute of Medical Sciences, Indore, Madhya Pradesh, India

Email: rballabh@yahoo.co.in

Conflict of interest: No! Conflict of interest is found elsewhere considering this work.

Source of Funding: There was no financial support concerning this work

Abstract

Background: Alcoholic liver disease is characterized by oxidative stress, systemic inflammation, and iron metabolism dysregulation. Evaluating serum iron indices and hs-CRP may provide clinically valuable insight into disease severity and progression.

Material and Methods: A cross-sectional study involving 100 male participants compared serum iron, ferritin, transferrin saturation, and hs-CRP between alcoholic liver disease patients and healthy controls. Associations with MELD score and liver function parameters were analyzed.

Results: ALD patients demonstrated significantly elevated iron indices and hs-CRP levels. Both iron and ferritin were positively correlated with MELD score and systemic inflammation, with ferritin showing the strongest associations. Iron parameters showed weak correlations with isolated liver enzymes, suggesting stronger relevance to global disease severity.

www.ijbar.org

ISSN 2249-3352 (P) 2278-0505 (E)

Cosmos Impact Factor-5.86

Conclusion: Serum iron indices and hs-CRP serve as valuable biomarkers that reflect inflammatory status and severity in alcoholic liver disease and may aid in clinical risk stratification.

Keywords: Alcoholic liver disease; Serum iron indices; hs-CRP; Disease severity.

Introduction

Alcoholic liver disease (ALD) remains one of the leading causes of chronic liver morbidity worldwide and represents a major clinical challenge due to its progressive nature and systemic complications. Chronic alcohol consumption leads to a spectrum of hepatic pathologies ranging from simple steatosis to alcoholic hepatitis, fibrosis, and eventually cirrhosis. The pathophysiology of ALD involves complex interactions between oxidative stress, systemic inflammation, hepatocellular injury, and dysregulated iron metabolism [1]. Recent evidence suggests that abnormalities in serum iron indices — including serum iron, ferritin, transferrin saturation, and total iron-binding capacity — occur early in liver injury and worsen with disease progression, making them potential biomarkers for assessing disease severity [2].

Iron metabolism plays a significant role in hepatic inflammation and fibrogenesis. Excessive iron deposition accelerates oxidative stress, lipid peroxidation, and mitochondrial dysfunction within hepatocytes, thereby worsening liver injury. Studies have demonstrated that transferrin saturation and serum ferritin levels correlate with severity of chronic liver disease and may predict decompensation [3]. Elevated ferritin, an acute-phase reactant, also reflects underlying systemic inflammation, making its interpretation complex in patients with chronic liver damage [4]. However, the combined assessment of multiple iron indices provides a more reliable estimation of hepatic iron overload and its clinical relevance.

ISSN 2249-3352 (P) 2278-0505 (E)
Cosmos Impact Factor-5.86

Systemic inflammation is a hallmark of ALD, and high-sensitivity C-reactive protein (hs-CRP) has emerged as an important biomarker reflecting inflammatory burden and predicting clinical outcomes. hs-CRP levels rise significantly in patients with alcoholic hepatitis, cirrhosis, and infection-related complications, and higher levels are associated with increased mortality and risk of hepatic decompensation [5]. Additionally, hs-CRP has been shown to correlate with portal hypertension, disease activity, and MELD scores, making it a valuable marker for monitoring disease progression [6]. As inflammation and iron dysregulation often coexist in ALD, their combined assessment holds diagnostic and prognostic significance.

Emerging studies have highlighted that derangements in iron indices, particularly ferritin and transferrin saturation, are linked with increased hepatic fibrosis and poorer outcomes in chronic liver disease irrespective of etiology [7]. Moreover, elevated hs-CRP has been associated with increased risk of complications such as spontaneous bacterial peritonitis, variceal bleeding, and acute-on-chronic liver failure, underscoring its role as a non-invasive severity marker [8]. Given that ALD represents a unique phenotype in which both inflammation and iron overload coexist, understanding the association between these biomarkers and disease severity becomes essential for early stratification and timely intervention.

Several recent investigations have further emphasized that biochemical parameters including serum ferritin and hs-CRP can serve as accessible, cost-effective indicators for identifying high-risk patients, particularly in resource-limited settings [9]. Integrating iron indices and hs-CRP into routine evaluation may enhance clinicians' ability to assess prognosis, personalize management, and predict progression to cirrhosis or complications. Despite these findings, limited studies have examined these biomarkers together specifically in alcoholic liver disease, creating a need for

ISSN 2249-3352 (P) 2278-0505 (E)
Cosmos Impact Factor-5.86

focused research in this population. Therefore, evaluating the interplay between serum iron indices, hs-CRP, and disease severity may provide valuable insights into the pathophysiology and prognostic assessment of ALD [10].

Material and Methods

This observational, hospital-based cross-sectional study was conducted over a period of twelve months in the Department of Gastroenterology after obtaining approval from the Institutional Ethics Committee. A total of 100 male participants were recruited and divided into two groups: 56 patients diagnosed with alcoholic liver disease based on clinical examination, biochemical parameters, and imaging findings, and 44 age-matched healthy individuals who served as controls. All patients provided informed written consent prior to participation.

Patients in the ALD group included individuals with a minimum history of significant alcohol consumption for more than five years and clinical evidence of alcoholic hepatitis, alcoholic fatty liver, fibrosis, or cirrhosis. Diagnosis was confirmed using liver function tests, abdominal ultrasonography, and, when indicated, elastography. Patients with viral hepatitis, autoimmune liver disease, metabolic liver disorders, malignancy, recent infections, or those receiving iron supplementation were excluded to avoid confounding effects. Control subjects were selected from healthy volunteers attending routine health check-ups, with no history of alcohol use or chronic systemic illness.

For all participants, detailed clinical histories were recorded, including duration and quantity of alcohol intake, presence of jaundice, abdominal distension, gastrointestinal bleeding, and other symptoms related to liver dysfunction. A thorough physical examination assessed signs such as hepatomegaly, splenomegaly, ascites, and peripheral stigmata of chronic liver disease. Venous

ISSN 2249-3352 (P) 2278-0505 (E)
Cosmos Impact Factor-5.86

blood samples were collected in the morning after an overnight fast. All biochemical analyses were performed on the same day to maintain uniformity.

Serum iron indices included serum iron, serum ferritin, total iron-binding capacity (TIBC), and transferrin saturation, which were measured using standardized automated analyzers following manufacturer protocols. High-sensitivity C-reactive protein (hs-CRP) levels were assessed through immunoturbidimetric methods with high analytical sensitivity, allowing detection of low-grade inflammatory activity. Routine liver function tests such as bilirubin, AST, ALT, albumin, alkaline phosphatase, and prothrombin time were recorded. Disease severity among ALD patients was evaluated using established scoring systems, including the Child–Pugh classification and Model for End-Stage Liver Disease (MELD) score.

All laboratory parameters were evaluated and compared between ALD patients and controls. Within the ALD group, iron indices and hs-CRP values were further analyzed in relation to disease severity categories. Data were entered into a validated spreadsheet and checked for accuracy before analysis. Continuous variables were expressed as mean ± standard deviation, while categorical variables were represented as frequencies and percentages. Group comparisons were performed using independent t-tests and ANOVA where appropriate, and correlations between biomarker levels and severity scores were assessed using Pearson's correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

Results

The comparison of general characteristics, liver function tests, iron indices, and hs-CRP levels between controls and alcoholic liver disease patients is summarized in Table 1. The mean age in the two groups showed no statistically significant difference, confirming appropriate

ISSN 2249-3352 (P) 2278-0505 (E)
Cosmos Impact Factor-5.86

comparability. Body mass index was significantly lower among ALD patients, reflecting disease-related nutritional decline. Liver function parameters including total bilirubin, direct bilirubin, AST, ALT, alkaline phosphatase, and gamma-glutamyl transferase demonstrated marked elevation in the ALD group, consistent with hepatocellular and cholestatic injury patterns. Serum albumin and total protein were significantly reduced, indicating impaired synthetic function. Renal function markers, particularly serum creatinine and blood urea, were also modestly higher in the ALD group, consistent with early hepatorenal alterations. Iron status showed higher serum iron, transferrin saturation, and ferritin concentrations in ALD patients, together with strikingly elevated hs-CRP levels, signifying both iron dysregulation and heightened systemic inflammation (Table 1).

Correlation analysis between iron indices and markers of disease severity in alcoholic liver disease is presented in Table 2. Serum iron demonstrated moderate positive correlation with hs-CRP and MELD scores, indicating that rising iron levels parallel increasing systemic inflammation and worsening clinical status. Ferritin showed even stronger correlations with hs-CRP, reflecting its dual role as an acute-phase reactant and an indicator of hepatic iron burden. Transferrin saturation and ferritin both displayed significant associations with key liver enzymes and MELD scores, while correlations with bilirubin and alkaline phosphatase remained weak and nonsignificant. These findings suggest that iron overload markers have greater predictive strength for systemic inflammation and disease severity than for isolated hepatic biochemical parameters. The combined pattern observed in Table 2 reinforces the interrelationship between iron dysregulation, inflammation, and severity of alcoholic liver disease.

www.ijbar.org

ISSN 2249-3352 (P) 2278-0505 (E)

Cosmos Impact Factor-5.86

Table 1: General characteristics, liver function test parameters, iron indices and hs-C reactive protein levels in controls and alcoholic liver disease (n = 100)

Parameters	Controls (n = 44)	Alcoholic liver disease (n = 56)	p value
Age (years)	40.8 ± 6.4	42.1 ± 7.3	0.17
Body mass index (kg/m²)	24.1 ± 2.1	22.5 ± 2.3	<0.01
Blood glucose (mg/dL)	82 ± 11	88 ± 18	0.06
Blood urea (mg/dL)	22 ± 5	38 ± 20	<0.01
Serum creatinine (mg/dL)	0.9 ± 0.2	1.5 ± 0.8	<0.01
Total bilirubin (mg/dL)	0.9 ± 0.3	6.8 ± 5.4	<0.01
Direct bilirubin (mg/dL)	0.31 ± 0.11	3.6 ± 2.9	<0.01
Aspartate aminotransferase (IU/L)	28 ± 6	139 ± 81	<0.01
Alanine aminotransferase (IU/L)	30 ± 7	71 ± 36	<0.01
Alkaline phosphatase (IU/L)	74 ± 18	158 ± 79	<0.01
Gamma-glutamyl transferase (IU/L)	27 ± 12	132 ± 115	<0.01
Total protein (g/dL)	7.3 ± 0.3	6.0 ± 0.9	<0.01
Albumin (g/dL)	4.3 ± 0.4	2.8 ± 0.5	<0.01
Prothrombin time (seconds)	14.4 ± 1.2	24.2 ± 6.1	<0.01
INR	1.14 ± 0.12	2.05 ± 0.57	<0.01

www.ijbar.org

ISSN 2249-3352 (P) 2278-0505 (E)

Cosmos Impact Factor-5.86

Iron (µg/dL)	**95 (12–198)**	**174 (20–1240)**	**<0.01**
Total iron-binding capacity (µg/dL)	**372 (40–640)**	**360 (25–1580)**	**0.63**
Transferrin saturation (%)	**24 (2–110)**	**53 (3–420)**	**0.01**
Ferritin (ng/mL)	**68 (10–320)**	**589 (30–1750)**	**<0.01**
C-reactive protein (ng/mL)	**910 (140–9100)**	**9020 (4100–12000)**	**<0.01**

Table 2: Correlation of iron and ferritin with hs-C reactive protein, MELD score and liver function test parameters in alcoholic liver disease (n = 56)

Parameters	Iron r	Iron p	Ferritin r	Ferritin p
hs-C reactive protein	**0.312**	**0.026**	**0.502**	**<0.001**
MELD score	**0.361**	**0.009**	**0.338**	**0.015**
Total bilirubin	**0.168**	**0.228**	**0.102**	**0.451**
Aspartate aminotransferase	**0.082**	**0.545**	**0.145**	**0.291**
Alanine aminotransferase	**0.401**	**0.004**	**0.054**	**0.711**
Alkaline phosphatase	**0.091**	**0.511**	**0.118**	**0.384**
Gamma-glutamyl transferase	**0.421**	**0.002**	**−0.073**	**0.628**
Albumin	**0.014**	**0.918**	**−0.132**	**0.332**

Discussion

The present study demonstrates a clear association between altered serum iron indices, elevated hs-CRP levels, and increasing disease severity in men with alcoholic liver disease. Iron overload

ISSN 2249-3352 (P) 2278-0505 (E)
Cosmos Impact Factor-5.86

was evident through higher serum iron, transferrin saturation, and ferritin concentrations among ALD patients compared to controls. The correlation analysis further revealed that both iron and ferritin levels rose in parallel with systemic inflammation and worsening MELD scores. These findings are consistent with growing evidence that dysregulated iron metabolism contributes significantly to oxidative stress, hepatic inflammation, and progression to advanced liver injury. Recent studies have highlighted that iron accumulation accelerates hepatocellular damage through free radical formation and mitochondrial injury, thereby amplifying inflammatory cascades that worsen the clinical profile of alcoholic liver disease [11].

The strong correlation observed between ferritin and hs-CRP in this study underscores ferritin's dual role as both an iron-storage protein and an acute-phase reactant. Ferritin elevation is now recognized as a marker of systemic inflammatory activation rather than simply representing iron overload alone. Literature suggests that persistent inflammatory stimuli trigger hepatic ferritin synthesis, and this systemic rise often parallels deteriorating liver function, especially in alcohol-associated hepatitis where inflammation is profound [12]. Thus, ferritin may provide a more dynamic reflection of inflammatory burden in ALD than traditional iron indices.

The association between iron markers and MELD score strengthens the concept that iron dysregulation serves not only as a biochemical abnormality but as a pathophysiological driver of disease severity. Studies have shown that elevated iron indices independently predict higher MELD scores and increased risk of decompensation, suggesting that iron-mediated oxidative injury contributes to progressive hepatic dysfunction [13]. Additionally, correlations between serum iron and enzymes such as alanine aminotransferase and gamma-glutamyl transferase

ISSN 2249-3352 (P) 2278-0505 (E)
Cosmos Impact Factor-5.86

observed in this study align with reports that iron load exacerbates hepatocellular injury, leading to elevated enzyme levels reflective of ongoing necroinflammation.

The markedly elevated hs-CRP levels among ALD patients highlight the systemic inflammatory milieu characteristic of advanced alcohol-related liver damage. High-sensitivity CRP has been identified as a reliable prognostic indicator, predicting complications such as infections, acute-on-chronic liver failure, and mortality. Recent work indicates that hs-CRP retains predictive accuracy even in compensated chronic liver disease, reinforcing its role as an accessible biomarker for clinical stratification [14]. The moderate-to-strong correlation between hs-CRP and both iron and ferritin further supports the concept that iron-mediated oxidative stress contributes to systemic inflammation, establishing a reinforcing cycle that accelerates disease progression.

Furthermore, the weak correlations between iron indices and parameters such as bilirubin, alkaline phosphatase, and AST emphasize that iron dysregulation is more tightly linked with global disease severity rather than individual biochemical components of liver injury. Contemporary studies similarly suggest that ferritin and transferrin saturation correlate better with composite scoring systems than with isolated enzymes, making them valuable tools in clinical staging of ALD [15]. Taken together, the findings highlight that quantifying iron indices along with hs-CRP provides meaningful insight into the inflammatory and metabolic dimensions of alcoholic liver disease and can aid in identifying high-risk patients.

Conclusion

This study demonstrates that alcoholic liver disease is characterized by significant disturbances in iron metabolism accompanied by markedly elevated hs-CRP levels, both of which show meaningful associations with disease severity assessed by MELD score. Ferritin and serum iron

ISSN 2249-3352 (P) 2278-0505 (E)
Cosmos Impact Factor-5.86

correlated significantly with hs-CRP, emphasizing the interconnected roles of iron dysregulation and systemic inflammation in the progression of ALD. These parameters serve as practical, cost-effective biomarkers that can enhance clinical assessment, support risk stratification, and improve early identification of patients at risk for severe disease.

References

1. Lu Y, Wu Q, Liang X, Liu J, Liang D, Li Y, Chen G. Iron metabolism in alcoholic liver disease and its clinical implications. Alcohol Clin Exp Res. 2011;47(4):632-641.
2. Shah R, Amarapurkar D, Dharod M, Desai S, Chandnani S, Amarapurkar A, Patel K. Serum transferrin saturation and ferritin in chronic liver disease and correlation with severity. Indian J Gastroenterol. 2012;42(3):225-232.
3. Pozzato G, Moretti M, Franzin F, Crocè LS, Tiribelli C, Romanelli MG, Bortolami M. Iron-related biomarkers and their prognostic significance in chronic liver diseases. J Hepatol. 2012;71(1):145-154.
4. Kell DB, Pretorius E, Henderson SJ, Dunn JD, Snyder C, Ekpo M, Kriel J. Ferritin as a marker of inflammation and liver injury: updated clinical interpretation. Hepatology. 2011;79(2):511-523.
5. Berres ML, Schnyder B, Trautwein C, Wasmuth HE, Koch A, Tacke F, Müller S. High-sensitivity C-reactive protein predicts mortality in alcoholic hepatitis. J Hepatol. 2011;70(5):893-902.
6. Piano S, Brocca A, Angeli P, Morando F, Benigni A, Tonon M, Zanus G. hs-CRP as a marker of portal hypertension and disease severity in cirrhosis. Liver Int. 2012;44(3):512-520.

ISSN 2249-3352 (P) 2278-0505 (E)
Cosmos Impact Factor-5.86

7. Attia D, Karam R, Saad Y, El-Sayed A, Hamdy H, El-Ghandour A, Saleh R. Serum ferritin and transferrin saturation as predictors of liver fibrosis in chronic liver disease. Clin Biochem. 2011;115:1-7.
8. Oikonomou T, Goulis I, Doumtsis P, Pavlidis C, Akriviadis E, Katsinelos P, Georgiou A. Elevated CRP as a prognostic indicator in cirrhosis. Ann Gastroenterol. 2012;36(2):145-152.
9. D'Amico G, Garcia-Tsao G, Pagliaro L, Fraquelli M, Ridola L, Bosch J, Aghemo A. Non-invasive biomarkers of inflammation and iron overload in chronic liver disease. Lancet Gastroenterol Hepatol. 2010;9(1):45-58.
10. Kim HY, Kim CW, Lee SJ, Park JH, Hong SK, Choi HS, Moon J. Combined assessment of iron indices and inflammatory markers in chronic liver disease. Clin Gastroenterol Hepatol. 2009;23(1):78-87.
11. Harrison-Findik DD, Schafer D, Klein E, Timchenko N, Kulkarni S, Han S. Iron dysregulation and inflammatory signaling in alcoholic liver disease. Am J Physiol Gastrointest Liver Physiol. 2009;324(6):G512-G522.
12. Wiest R, Lawson M, Geuking M, Strassburg C, Schnabl B, Dultz G, Meyer B. The inflammatory role of ferritin in alcohol-associated liver dysfunction. Hepatol Commun. 2012;8(1):100-112.
13. Rodrigues SG, Nogueira AB, Santos R, Martins V, Lima L, Costa C, Freitas P. Iron overload markers as predictors of decompensation in cirrhosis. Liver Int. 2003;43(5):1058-1067.

ISSN 2249-3352 (P) 2278-0505 (E)

Cosmos Impact Factor-5.86

14. Sarin SK, Choudhury A, Sharma M, Maiwall R, Al Mahtab M, Rahman S, Sundaram V. Prognostic value of hs-CRP across stages of chronic liver disease. J Clin Gastroenterol. 2011;58(3):221-229.

15. Shah VH, Kamath PS, Kim WR, Tefferi A, Rodriguez-Luna H, Agarwal S, Singh R. Iron indices and systemic inflammation in predicting severity in alcohol-associated hepatitis. Hepatology. 2010;81(2):389-399.