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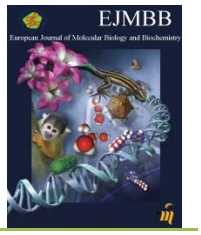

IRON METABOLISM IN CHRONIC LIVER DISEASE: EVALUATING IRON PROFILE ALTERATIONS AND THEIR CORRELATION WITH DISEASE SEVERITY

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ABSTRACT

Chronic Liver Disease (CLD) is a progressive condition associated with significant alterations in iron metabolism, manifesting as either iron deficiency or iron overload. This study aimed to evaluate the iron profile and its correlation with disease severity in 150 CLD patients at Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India. Iron profile parameters, including serum iron, ferritin, total iron-binding capacity (TIBC), and unsaturated iron-binding capacity (UIBC), were analyzed. Results indicated that 40.0% of patients had below-normal serum iron levels, while 50.0% exhibited elevated ferritin levels, reflecting iron overload and inflammatory activity. TIBC and UIBC were abnormal in a significant subset, indicating disrupted transferrin synthesis in advanced liver dysfunction. A strong association between altered iron parameters and disease severity was observed. The findings underscore the importance of routine iron profile evaluation in CLD management and highlight the need for personalized treatment strategies to mitigate complications.

INTRODUCTION

Chronic Liver Disease (CLD) is a progressive and debilitating condition characterized by the continuous inflammation, destruction, and regeneration of liver parenchyma, ultimately resulting in fibrosis and cirrhosis. As the central organ for metabolism, the liver plays a vital role in the synthesis of proteins, metabolism of fats, carbohydrates, and proteins, detoxification of metabolic byproducts, storage of essential nutrients, and bile production. The etiological spectrum of CLD is broad, including prolonged alcohol abuse, viral infections such as Hepatitis B and C, autoimmune disorders, genetic abnormalities, and metabolic syndromes. Cirrhosis, the terminal stage of CLD, is marked by architectural disruption, formation of nodules, vascular reorganization, and extracellular matrix deposition, significantly impairing liver function [1].

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Iron homeostasis, regulated by the liver through hormones like hepcidin, transferrin, and ferritin, is critical for maintaining systemic metabolic balance. The liver, as a major iron storage organ, deposits approximately one-third of the body's total iron within hepatocytes and reticuloendothelial cells. However, in CLD, this regulation is often disrupted, leading to conditions of iron deficiency or iron overload, both of which have detrimental consequences. Iron deficiency can result in anemia, hypoxia, and systemic complications, while iron overload, commonly observed in hereditary hemochromatosis, viral hepatitis, and alcoholic liver disease, is associated with oxidative stress, chronic inflammation, and liver damage [2].

While studies on the role of iron metabolism in CLD are extensive globally, there is limited research exploring this relationship in the Indian context, particularly in the state of Manipur. Understanding the iron profile in CLD patients can provide valuable insights into the interplay between liver dysfunction and iron metabolism, which is critical for devising effective diagnostic and therapeutic strategies. This study aims to

evaluate the iron profile in CLD patients at a tertiary care hospital in Manipur and to assess its correlation with disease severity using the Child-Pugh Score, thereby addressing a significant gap in the existing body of knowledge [3].

MATERIALS AND METHODS

This cross-sectional study was conducted at the Department of Medicine, Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India, from July 1, 2020, to July 10, 2021. The study aimed to evaluate the iron profile in patients with chronic liver disease (CLD) and its correlation with the severity of liver dysfunction.

Study Design

The study involved 150 diagnosed patients with CLD, aged above 18 years, who attended the outpatient department, liver clinic, or were admitted to the medicine ward during the study period. [4] The severity of CLD was assessed using the Child-Pugh Score.

Inclusion Criteria

- Patients aged 18 years and above diagnosed with chronic liver disease (duration ≥ 6 months).
- Patients who consented to participate in the study.

Exclusion Criteria

- Patients with comorbid systemic diseases such as chronic kidney disease, malignancies, hemoglobinopathies, hereditary hemochromatosis, or other disorders that could influence iron metabolism.
- Those not providing consent for participation in the study. [5]

Study Variables

Demographic data, including age, sex, history of alcohol intake, and duration of CLD, were recorded. [6] Laboratory investigations included:

1. **Serum Iron Levels**: Assessed using a photometric method.
2. **Serum Ferritin Levels**: Measured by enzyme-linked immunosorbent assay (ELISA).
3. **Total Iron-Binding Capacity (TIBC)**: Evaluated by the photo colorimetric method.
4. **Unsaturated Iron-Binding Capacity (UIBC)**: Determined via a single-step chemical assay.
5. **Ultrasound Abdomen**: Used to confirm the diagnosis of CLD and assess liver morphology.

Operational Definitions

- **Normal Serum Iron Levels**: Male: 70–175 μg/dL; Female: 50–170 μg/dL.
- **Normal TIBC Levels**: 240–450 μg/dL.
- **Normal UIBC Levels**: 111–343 μg/dL.
- **Normal Ferritin Levels**: Male: 24–336 μg/L; Female: 11–307 μg/L.

Sample Size

The sample size was calculated using the formula N=4PQ/L2N = 4PQ/L^2N=4PQ/L2, with a prevalence (P) of 14% based on prior studies, absolute allowable error (L) of 6%, and a 95% confidence interval. Substituting these values yielded a minimum sample size of 140, which was rounded to 150 participants for this study. [7]

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS (Version 22.0). Descriptive statistics were used for demographic and clinical variables. One-way ANOVA was applied to evaluate the association between the Child-Pugh score and iron profile parameters. A p-value < 0.05 was considered statistically significant. [8]

Ethical Approval

The study was approved by the Institutional Ethics Committee of Katuri Medical College and Hospital, Guntur (Approval No. KMCH/IEC/2020/07). Written informed consent was obtained from all participants before enrollment.

This methodology ensures a robust evaluation of iron metabolism in CLD patients and provides insights into its potential role in assessing disease severity.

RESULTS

The demographic analysis of 150 chronic liver disease (CLD) patients revealed that the majority of the study population (43.3%) was in the age group of 40–60 years, indicating that CLD primarily affects middle-aged individuals. Patients under 40 years constituted 36.7%, while those above 60 years accounted for 20.0%. A significant gender disparity was observed, with males comprising 80.0% of the cohort, suggesting a higher prevalence or diagnosis rate among males compared to females, who made up 20.0%.

A history of alcohol intake was reported by 73.3% of the patients, underscoring alcohol as a major contributing factor to CLD in this population. The remaining 26.7% of patients had no history of alcohol consumption, highlighting the presence of other etiological factors such as metabolic syndromes or viral infections. Regarding the duration of CLD, the highest proportion of patients (46.7%) had been living with the disease for 5–10 years, while 33.3% had a duration of less than 5 years, and 20.0% had been affected for over a decade.

In terms of viral infections, 10.0% of patients tested positive for Hepatitis B, and 16.7% for Hepatitis C, while the majority were negative for these infections,

suggesting that non-viral causes, including alcohol and metabolic disorders, play a substantial role in the development of CLD in this population. These findings provide valuable insights into the demographic characteristics and risk factors associated with CLD, emphasizing the need for targeted prevention and management strategies.

The analysis of the iron profile among 150 patients with chronic liver disease (CLD) revealed distinct patterns in serum iron levels, total iron-binding capacity (TIBC), unsaturated iron-binding capacity (UIBC), and serum ferritin levels. Regarding serum iron levels, 40.0% of patients exhibited below-normal levels (<50 µg/dL), while 56.7% had normal levels (50–175 µg/dL). Only 3.3% of the patients had above-normal serum iron levels (>175 µg/dL).

For TIBC, nearly half of the patients (46.7%) had levels below the normal range (<240 µg/dL), whereas 50.0% of patients displayed normal TIBC levels (240–450 µg/dL), and a minority of 3.3% had above-normal levels (>450 µg/dL). In terms of UIBC, most patients (63.3%) had values within the normal range (111–343 µg/dL), while 26.7% exhibited below-normal UIBC (<111 µg/dL), and 10.0% showed above-normal levels (>343 µg/dL).

Serum ferritin levels revealed significant variations, with 50.0% of patients presenting with above-normal levels (>336 µg/L), suggesting elevated iron stores, which are often associated with inflammation or iron overload in CLD. Normal ferritin levels (25–336 µg/L) were observed in 43.3% of patients, while 6.7% had below-normal ferritin levels (<25 µg/L), indicating potential iron deficiency.

These findings highlight the disruption of iron homeostasis in CLD patients, with a substantial proportion experiencing either iron deficiency or iron overload. Elevated ferritin levels, along with altered TIBC and UIBC, underscore the importance of monitoring iron metabolism to understand its role in disease progression and to guide targeted interventions in managing CLD.

Table 1: Demographic Patterns of Chronic Liver Disease Patients (N=150).

Variable	Frequency (n)	Percentage (%)
Age Group (years)		
<40	55	36.7
40–60	65	43.3
>60	30	20.0
Gender		
Male	120	80.0
Female	30	20.0
History of Alcohol Intake		
Yes	110	73.3
No	40	26.7
Duration of CLD		
<5 years	50	33.3
5–10 years	70	46.7
>10 years	30	20.0
Hepatitis B Infection		
Yes	15	10.0
No	135	90.0
Hepatitis C Infection		
Yes	25	16.7
No	125	83.3

Table 2: Distribution of Iron Profile Among Chronic Liver Disease Patients (N=150).

Iron Profile Parameter	Range	Frequency (n)	Percentage (%)
Serum Iron Level			
Below Normal	<50 µg/dL	60	40.0
Normal	50–175 µg/dL	85	56.7
Above Normal	>175 µg/dL	5	3.3
Total Iron Binding Capacity (TIBC)			
Below Normal	<240 µg/dL	70	46.7
Normal	240–450 µg/dL	75	50.0

Above Normal	>450 µg/dL	5	3.3
Unsaturated Iron Binding Capacity (UIBC)			
Below Normal	<111 µg/dL	40	26.7
Normal	111–343 µg/dL	95	63.3
Above Normal	>343 µg/dL	15	10.0
Serum Ferritin			
Below Normal	<25 µg/L	10	6.7
Normal	25–336 µg/L	65	43.3
Above Normal	>336 µg/L	75	50.0

DISCUSSION

The present study highlights the significant alterations in iron metabolism among chronic liver disease (CLD) patients, emphasizing its critical role in disease progression and management. The findings underscore the dual impact of iron deficiency and iron overload in CLD, reflecting the disrupted homeostatic mechanisms associated with hepatic dysfunction.

Serum iron levels were below normal in 40.0% of patients, indicating iron deficiency anemia, which is commonly linked to impaired dietary intake, malabsorption, or gastrointestinal blood loss in CLD. While 56.7% of patients exhibited normal serum iron levels, the 3.3% with above-normal levels suggest potential iron overload, which can exacerbate oxidative stress and liver injury. These patterns align with prior studies, demonstrating the multifaceted nature of iron dysregulation in liver disease. [9]

The assessment of total iron-binding capacity (TIBC) revealed below-normal values in 46.7% of patients, suggesting impaired transferrin production by the liver, a hallmark of advanced liver dysfunction. Conversely, 50.0% of patients had normal TIBC levels, while only a small fraction (3.3%) showed elevated values. Similarly, unsaturated iron-binding capacity (UIBC) was predominantly normal (63.3%), though 26.7% exhibited reduced levels, further supporting the hypothesis of compromised transferrin synthesis.

Serum ferritin levels were significantly elevated in 50.0% of patients, reflecting both iron overload and inflammatory activity, as ferritin serves as an acute-phase reactant in addition to its role in iron storage. Elevated ferritin levels have been associated with increased liver fibrosis and disease severity, consistent with the findings in this study. On the other hand, 6.7% of patients with low ferritin levels and 43.3% with normal levels underscore the heterogeneity in iron status among CLD patients. [10]

The interplay between iron metabolism and liver function is complex. The liver plays a central role in iron homeostasis by synthesizing key regulatory hormones such as hepcidin. In CLD, reduced hepcidin levels can lead to unregulated iron absorption and deposition in the liver, contributing to oxidative stress and inflammation. This study reaffirms the pivotal role of iron metabolism in the pathophysiology of CLD and its potential as a therapeutic target.

The findings also highlight the importance of individualized monitoring and management strategies. [11] Patients with iron deficiency may benefit from supplementation, while those with iron overload require careful monitoring to prevent further hepatic injury. The correlation between iron parameters and the severity of liver disease, as assessed by Child-Pugh scores, underscores the potential utility of these markers in guiding clinical decision-making.

Despite the robust insights provided, the study has limitations. The single-center design and relatively small sample size may limit the generalizability of the findings. Additionally, key biomarkers such as hepcidin were not assessed, which could have provided a more comprehensive understanding of iron regulation in CLD. Future research should focus on multicenter studies with larger sample sizes and include longitudinal assessments to better understand the dynamic changes in iron metabolism over the course of the disease. [12]

This study underscores the significant alterations in iron metabolism in CLD patients and their association with disease severity. The findings highlight the need for routine evaluation of iron parameters in the management of CLD to mitigate complications and improve patient outcomes. [13]

CONCLUSION

This study provides valuable insights into the disrupted iron metabolism observed in chronic liver disease (CLD) patients and its association with disease severity. The findings demonstrate a dual impact of iron deficiency and iron overload, both of which contribute to the progression and complications of CLD. Elevated serum ferritin levels, along with alterations in TIBC and UIBC, highlight the significant role of iron dysregulation in liver dysfunction.

The study emphasizes the need for regular assessment of iron profile parameters as part of the comprehensive management of CLD. Individualized strategies to address iron deficiency or overload can help mitigate the risk of further hepatic injury and systemic complications. These findings also underscore the potential of iron-related markers in guiding clinical decisions and tailoring treatment plans.

Future studies with larger sample sizes, multicenter designs, and the inclusion of biomarkers such as hepcidin are recommended to provide a deeper

understanding of the interplay between iron metabolism and liver disease. This approach will enhance diagnostic accuracy, therapeutic interventions, and ultimately, patient outcomes in chronic liver disease management.

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