International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

Ferritin Levels - As a Potential Biomarker to Predict the Clinical Outcome in Patients with Decompensated Liver Cirrhosis

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Abstract: ***This research brings to light an underutilized yet potent biomarker-serum ferritin-as a key predictor in the survival landscape of patients with decompensated cirrhosis. While traditional scoring systems like MELD-Na and Child-Turcotte-Pugh (CTP) have long guided clinical decisions, this study suggests that ferritin could add another dimension to risk stratification. It is evident that elevated serum ferritin levels (>400 ng/mL) are strongly linked with increased mortality, severe decompensation events such as upper gastrointestinal bleeding and hepatic encephalopathy, and high MELD-Na and CTP scores. What's especially compelling is the clear survival demarcation observed: all patients with ferritin levels below 200 ng/mL survived, while a staggering 88% of those above 400 ng/mL did not. This suggests that ferritin, while traditionally considered an inflammatory or iron overload marker, might also be a harbinger of systemic immune dysregulation and hepatic deterioration. Taking this further, incorporating ferritin into routine liver disease assessments could sharpen clinical foresight and allow for more nuanced patient prioritization, especially for transplant listing. That said, the study wisely cautions that ferritin should be interpreted contextually, given its nonspecific acute-phase nature. Overall, the work offers a nuanced, data-rich argument for integrating ferritin with established models to better predict outcomes and initiate earlier, targeted interventions in patients at greatest risk.***

Keywords: serum ferritin, decompensated cirrhosis, liver transplantation, MELD-Na score, mortality prediction

1. Introduction

Cirrhosis can manifest in either an asymptomatic or symptomatic phase. The symptomatic phase often presents with complications, which are critical indicators of the progression of liver disease. The clinical terminology used to describe these phases is 'compensated' and 'decompensated' cirrhosis[1]. Compensated cirrhosis refers to early - stage liver disease where the liver still functions relatively well, often without overt symptoms. In contrast, decompensated cirrhosis is characterized by the onset of complications such as jaundice, ascites, hepatic encephalopathy, or variceal bleeding, signaling a significant decline in liver function. Decompensated cirrhosis is associated with a substantially higher risk of morbidity and mortality. It is estimated that up to 50% of patients with decompensated cirrhosis die within two years[2], unless they undergo liver transplantation, which remains the only definitive treatment for end - stage liver disease. Given the grave prognosis, timely and accurate prediction of disease progression is crucial in determining the need for transplantation. Several prognostic models have been developed to predict outcomes and guide clinical decision - making, particularly in the allocation of organs for transplantation. Mathematical models play a pivotal role in medical practice by aiding in diagnosis, predicting outcomes, and guiding treatment strategies. Among these, the Model for End - Stage Liver Disease (MELD - Na) score is widely used for assessing prognosis in patients with advanced liver disease. Originally designed to predict outcomes in patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) [3] procedures, the MELD - Na score has since been validated as an accurate predictor of mortality in patients with advanced liver disease[4]. Importantly, it is statistically robust and is now routinely used to prioritize patients on liver transplant waiting lists. While the Child - Turcotte - Pugh (CTP) score has traditionally been used to assess prognosis in cirrhotic patients, it lacks the rigorous statistical foundation of the MELD - Na score. However, it remains a valuable tool in clinical practice, particularly for assessing the severity of liver disease on a day - to - day basis[5]. The MELD - Na score is generally preferred for organ allocation due to its precision in predicting mortality, whereas the CTP score continues to be useful in bedside clinical assessment[6]. In addition to these scoring systems, serum ferritin has emerged as a potential prognostic marker in liver disease. Serum ferritin is a widely available laboratory parameter and has been shown to predict survival in various liver conditions, including in patients undergoing liver transplantation. Although the exact mechanisms behind ferritin release are not fully understood, it is believed that ferritin leaks from damaged hepatocytes[7], making it a potential marker of liver injury. This study aims to evaluate the efficacy of serum ferritin as a prognostic marker in predicting future events and outcomes in patients with decompensated cirrhosis. By exploring the role of serum ferritin alongside established prognostic models, we hope to further refine the ability to predict survival and improve patient prioritization for liver transplantation

2. Materials and Methods

This prospective study was conducted at the Department of Medical Gastroenterology, Kurnool Medical College, and Government General Hospital, Kurnool. Andhra Pradesh. The evaluation period was from November 2022 to August 2024. Data were retrieved from prospectively enrolled medical records, with formal informed consent obtained from each participant. The study was approved by the institute's ethics committee.

Inclusion Criteria

Adult patients aged 18 years and above with decompensated chronic liver disease, diagnosed according to AASLD guidelines, were enrolled. Hepatic decompensation, defined by the presence of ascites, hepatic encephalopathy, and portal hypertensive gastrointestinal bleeding, was considered an important milestone in the natural history of cirrhosis.

Exclusion Criteria

1) Age below 12 years and above 80 years.
2) Pregnant women.
3) Patients with hepatocellular carcinoma.
4) Patients with any other malignancy.
5) Patients with acute liver failure or acute - on - chronic liver failure.
6) Patients with HIV.

Methods

Data were extracted by enrolling consecutive patients in a prospective database. Demographic data, including age, sex, medical history, comorbidities, and medication or native medicine history, were collected through patient interviews. Physical examinations, including anthropometric measurements, were conducted. Alcohol intake was assessed using the Alcohol Use Disorders Identification Test (AUDIT - C) questionnaire. Medical history was recorded from patients or their attendants, focusing on symptoms such as jaundice, ascites, confusion, oliguria, and upper GI bleeding. A detailed physical examination was performed, documenting clinical signs like icterus, ascites, pedal edema, spider nevi, gynecomastia, abdominal wall collaterals, hepatomegaly, and splenomegaly. Conscious patients underwent a Mini - Mental Status Examination and a thorough neurological assessment, with the presence of encephalopathy classified based on the modified West Haven criteria. Liver - related events during follow - up were recorded. Blood investigations included a complete hemogram, liver biochemistry, metabolic labs, renal function tests, coagulation profile, liver enzymes, serum ferritin (via fluorescence immunoassay), and serological markers for HBV and HCV. Plasma GGT, AST, and ALT were measured using Boehringer methods. Serum ceruloplasmin, immunoglobulins, and autoantibodies (antinuclear, mitochondrial, and smooth muscle antibodies) were also recorded if positive. The presence of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome (HRS) was documented according to the International Ascites Club and AASLD practice guidelines. Imaging studies, such as abdominal ultrasound with Doppler, CT, or MRI scans, were performed. Hepatocellular carcinoma (HCC) was diagnosed using radiological criteria based on AASLD guidelines. Gastroesophageal varices were identified via upper GI endoscopy and graded according to the Paquet classification. The Child - Turcotte - Pugh (CTP) score was calculated to assess the severity of liver disease.

The formula for calculating the MELD - Na score is as follows:

MELD - Na = MELD – Na – [0.025 × MELD × (140 - Na)] + 140

In this formula, sodium (Na) values below 125 are adjusted to 125, and values above 140 are adjusted to 140.

Patients were classified into three groups based on their serum ferritin levels:

- Group A: Serum ferritin < 200 ng/Ml
- Group B: Serum ferritin 200 to 400 ng/mL
- Group C: Serum ferritin > 400 ng/mL

Serum ferritin was analyzed as a trichotomous variable. All enrolled patients were followed up, and mortality was assessed during their hospital stay.

Statistical analysis:

Statistical analysis was performed to evaluate the baseline characteristics of the study cohort based on serum ferritin levels and survival status. Descriptive statistics were computed for continuous variables, reporting means with standard deviations (SD), while categorical variables were presented as counts and percentages.

1) Analysis of Variance (ANOVA): Used to compare continuous variables such as age across the three serum ferritin groups (Serum ferritin 400 ng/mL) to assess if there were any statistically significant differences. p - value <0.05 was considered statistically.
2) Chi - Square Test:
   a) This test was used to compare the categorical variables (e. g., gender, etiology of liver disease, decompensation events) between groups. The results were expressed as counts and percentages, with p - values reported for each comparison.
   b) Also used for comparing categorical variables such as CTP Score, MELD - Na Score, and outcomes (alive vs. dead). The results showed significant differences between groups in terms of disease severity and survival, with p values such as p = 0.0001 for outcomes and CTP score.
3) Fisher’s Exact Test: In instances where expected frequencies were less than five, Fisher's Exact Test was used instead of the Chi - Square Test to ensure robust results, particularly for comparisons involving smaller sample sizes.
4) Post - Hoc Analysis: If significant differences were identified in ANOVA, posthoc tests (e. g., Tukey's HSD) were conducted to determine which specific groups differed.

3. Results

A total of 176 participants were screened and 100 participants were included who met the inclusion criteria of the study as per protocol. At the time of recruitment Adult patients aged 18 years and above with decompensated chronic liver disease, diagnosed according to AASLD guidelines, were enrolled. Hepatic decompensation, defined by the presence of ascites, hepatic encephalopathy, and portal hypertensive gastrointestinal bleeding, was considered an important milestone in the natural history of cirrhosis.

Table 1: Baseline characteristics of the study cohort based on their serum ferritin concentration.

Characteristics	Serum ferritin <200 ng/mL (n=67)	Serum ferritin 200 - 400 ng/mL (n=16)	Serum ferritin >400 ng/mL (n=17)	p - value
Age (years), Mean (± SD)	47±12.85	51±74.45	43±14.33	0.22
Male [n (%)]	60 (90%)	15 (94%)	14 (82%)	0.56
Female [n (%)]	7 (10%)	1 (6%)	3 (18%)	
Etiology				
Alcohol	40 (60%)	7 (44%)	10 (59%)	0.60
Autoimmune	1 (1%)	None	None	
HbsAg	10 (15%)	3 (19%)	5 (29%)	
HCV	6 (9%)	1 (6%)	1 6%)	
NASH	10 (15%)	5 (31%)	1 (6%)	
Decompensation Event				
Ascites	57 (85%)	13 (81%)	17 (100%)	0.19
UGI Bleed	16 (24%)	12 (75%)	15 (88%)	0.0001
Hepatic Encephalopathy	7 (10%)	3 (19%)	11 (65%)	0.0001
CTP Score				
0 - 6	1 (1%)	None	None	0.0001
7 - 9	62 (93%)	14 (88%)	3 (18%)	
≥10	4 (6%)	2 (12%)	14 (82%)	
MELD - Na Score				
≤9	None	None	None	0.0001
10 - 19	26 (39%)	None	None	
≥20	41 (61%)	16 (100%)	17 (100%)	
Outcome				
Alive	67 (100%)	14 (88%)	2 (12%)	0.0001
Dead	None	2 (12%)	15 (88%)	

ANOVA and Chi Square test $p<0.05$ considered as significant.

This table summarizes the baseline characteristics of the cohort based on their serum ferritin levels, including age, gender, etiology, decompensation events, CTP score, MELD - Na score, and outcomes. The baseline characteristics of the study cohort, stratified by serum ferritin concentrations, highlight important clinical differences among the groups.

While the mean age appears to be similar across the three ferritin groups ($p = 0.22$), the gender distribution shows a predominance of males in all categories, though this difference was not statistically significant

Etiology of Liver Disease:

In terms of the underlying causes of liver disease, the proportion of alcohol - related etiology was high in all groups, but particularly so in the group with serum ferritin levels <200 ng/mL (60%). Interestingly, non - alcoholic steatohepatitis (NASH) was more prevalent in the intermediate ferritin group (31%) compared to the lower and higher ferritin groups, though this did not reach statistical significance ($p = 0.60$). Viral hepatitis (HbsAg and HCV) was relatively common in all groups, with a slightly higher prevalence of hepatitis B in the highest ferritin group (>400 ng/mL), but again, these differences were not statistically significant (Table 1) (Figure 2).

Decompensation Events:

When evaluating liver decompensation events, ascites was a common feature across all groups, affecting 85% of those with serum ferritin <200 ng/mL and 100% of those with serum ferritin >400 ng/mL. Although this trend suggests a greater degree of liver dysfunction in patients with 0.56) (Table 1). higher ferritin levels, the difference was not statistically significant ($p = 0.19$). However, gastrointestinal bleeding (UGI bleed) and hepatic encephalopathy showed significant variation across the groups. UGI bleeding was notably more frequent in patients with higher serum ferritin (88% in >400 ng/mL group) compared to just 24% in the <200 ng/mL group ($p = 0.0001$). Similarly, hepatic encephalopathy occurred in 65% of patients with ferritin >400 ng/mL, a marked increase compared to the lower ferritin groups ($p = 0.0001$) (Table 1).

CTP and MELD - Na Scores:

Liver disease severity, as measured by both CTP and MELD - Na scores, also differed significantly between groups. In the low ferritin group, 93% of patients had a CTP score between 7 - 9, indicating a moderate level of liver dysfunction, whereas 82% of those in the highest ferritin group had a CTP score ≥10, reflecting severe liver disease ($p = 0.0001$). This trend was mirrored in the MELD - Na scores, where all patients in the highest ferritin group had a score ≥20, compared to only 61% in the lowest ferritin group ($p = 0.0001$) (Table 1).

Outcomes:

Most notably, serum ferritin concentrations were strongly associated with patient outcomes. All patients in the low ferritin group (<200 ng/mL) survived during the study period, while the mortality rate was strikingly high in the >400 ng/mL group, with 88% of patients dying ($p = 0.0001$). This underscores the association between elevated serum ferritin and poor prognosis in patients with advanced liver disease (Table 1).

Table 2: Baseline characteristics of the study cohort based on their survival

Characteristics	Alive (n=83)	Dead (n=17)	p - value
Age (years), Mean (± SD)	47±12.64	45±15.86	0.22
Male [n (%)]	76 (92%)	13 (77%)	0.07
Female [n (%)]	7 (8%)	4 (23%)	
Etiology			
Alcohol	47 (57%)	10 (59%)	0.92
Autoimmune	1 (15%)	None	
HbsAg	14 (17%)	4 (24%)	
HCV	7 (8%)	1 (6%)	
NASH	14 (17%)	2 (11%)	
Serum ferritin ng/mL			
<200	67 (81%)	None	0.0001
200 - 400	14 (17%)	2 (12%)	
>400	2 (2%)	15 (88%)	
Decompensation Event			
Ascites	70 (84%)	17 (100%)	0.80
UGI Bleed	27 (33%)	16 (94%)	0.0001
Hepatic Encephalopathy	11 (13%)	10 (59%)	0.0001
CTP Score			
0 - 6	1 (1%)	None	0.0001
7 - 9	74 (89%)	5 (29%)	
≥10	8 (10%)	12 (71%)	
MELD - Na Score			
≤9	None	None	0.007
10 - 19	26 (31%)	None	
≥20	57 (69%)	17 (100%)	

Chi Square test or Fisher's Exact Test p<0.05 considered as significant

Analysis of Baseline Characteristics by Survival Status:
The baseline characteristics reveal distinct differences between patients who survived (n=83) and those who died (n=17) (Table 2).

Age and Gender:
The mean age between the two groups was not statistically different (p = 0.22), with survivors being slightly older on average (47 years) compared to those who died (45 years). Interestingly, there was a trend toward a higher proportion of males among survivors (92%) compared to the deceased group (77%), though this did not reach statistical significance (p = 0.07) (Table 2).

Etiology of Liver Disease:
Alcohol remained the predominant cause of liver disease in both groups (57% in survivors vs.59% in non - survivors), and there was no significant difference in the distribution of other etiologies such as hepatitis B (HbsAg), hepatitis C (HCV), or non - alcoholic steatohepatitis (NASH) across survival status (p = 0.92) (Table 2).

Serum Ferritin and Survival:
Serum ferritin levels were strongly associated with survival outcomes (p = 0.0001). Notably, 81% of survivors had serum ferritin levels <200 ng/mL, while none of the deceased patients had such low ferritin levels. Conversely, 88% of those who died had serum ferritin levels >400 ng/mL, highlighting the significant association between elevated ferritin and mortality (Table 2).

Decompensation Events:
Decompensation events were more frequent in non - survivors, particularly upper gastrointestinal (UGI) bleeding and hepatic encephalopathy. While ascites was common in both groups (84% of survivors vs.100% of non - survivors), UGI bleeding occurred in 94% of non - survivors compared to only 33% of survivors (p = 0.0001). Hepatic encephalopathy was similarly more prevalent in non - survivors, affecting 59% compared to just 13% of survivors (p = 0.0001) (Table 2).

CTP and MELD - Na Scores:
Both CTP and MELD - Na scores, which reflect liver disease severity, were significantly different between survivors and non - survivors. A striking 71% of non - survivors had a CTP score ≥10, indicative of severe liver disease, while only 10% of survivors were in this category (p = 0.0001). Similarly, all non - survivors had a MELD - Na score ≥20, compared to 69% of survivors (p = 0.007), underscoring the poor prognosis associated with high MELD - Na scores (Table 2).

The data indicate that elevated serum ferritin levels, advanced decompensation events (especially UGI bleeding and hepatic encephalopathy), and higher CTP and MELD - Na scores are significantly associated with mortality in patients with liver disease. These findings suggest that monitoring serum ferritin and decompensation events, in conjunction with CTP and MELD - Na scores, may help predict outcomes and identify patients at higher risk of death.

Table 3: Comparison of Ferritin Levels between Survivors and Non - Survivors

Ferritin Level (ng/ml)	Alive	Dead	p - value
<200	67 (81%)	None	0.0001
200 - 400	14 (17%)	2 (12%)	
>400	2 (2%)	15 (88%)	

Fisher's Exact Test p<0.05 considered as significant.

Table 4: Comparison of Median Ferritin Levels between Survivors and Non - Survivors

Ferritin Level (ng/ml)	Survivor (n=83)	Non - Survivor (n=17)	p - value
Median	95	550	<0.0001

Mann whitney test p<0.05 considered as significant

Analysis of Ferritin Levels in Survivors vs. Non - Survivors:
The comparison of ferritin levels between survivors and non - survivors reveals a striking difference in serum ferritin concentrations, which is strongly associated with survival outcomes (p = 0.0001) (Table 3).

Low Ferritin Levels (<200 ng/mL):
Among the 83 patients who survived, 81% had serum ferritin levels below 200 ng/mL. None of the patients in the non - survivor group had ferritin levels in this range, indicating that lower ferritin concentrations are strongly correlated with better survival outcomes (Table 3).

Intermediate Ferritin Levels (200 - 400 ng/mL):
Intermediate ferritin levels (200 - 400 ng/mL) were found in both survivors and non - survivors, though the distribution was still skewed towards the survivor group. Specifically, 17% of survivors had ferritin levels in this range compared to only 12% of non - survivors, suggesting that while

intermediate ferritin levels may not be as strongly predictive of mortality, they are more common in survivors (Table 3).

High Ferritin Levels (>400 ng/mL):
The most notable difference was observed in patients with serum ferritin levels greater than 400 ng/mL. A striking 88% of non - survivors had ferritin concentrations in this range, while only 2% of survivors exhibited such elevated ferritin levels. This finding highlights a significant association between high ferritin and poor prognosis, reinforcing that elevated serum ferritin levels are a strong predictor of mortality in this cohort (Table 3).

The data from this comparison clearly demonstrate that serum ferritin levels are a key factor in predicting survival in patients with liver disease. Low ferritin levels (<200 ng/mL) are strongly associated with survival, while elevated ferritin levels (>400 ng/mL) are linked to higher mortality. Monitoring ferritin concentrations may provide valuable insights into patient prognosis and help guide clinical decision - making (Table 3).

Table 5: Comparison of CTP Score between Survivors and Non - Survivors

CTP Score	Alive	Dead	p - value
0 - 6	1 (1%)	None	0.0001
7 - 9	74 (89%)	5 (29%)	
≥10	8 (10%)	12 (71%)	

Chi - Square test or Fisher's Exact Test p<0.05 considered as significant.

Analysis of CTP Score in Survivors vs. Non - Survivors:
The comparison of Child - Turcotte - Pugh (CTP) scores between survivors and non - survivors highlights a significant association between higher CTP scores and mortality, with a p - value of 0.0001 (Table 4).

Low CTP Score (0 - 6):
Only 1% of survivors had a low CTP score (0 - 6), indicating very mild liver disease in this small subset of patients. None of the non - survivors had CTP scores in this range, reinforcing the fact that a low CTP score is linked to better survival outcomes (Table 4).

Moderate CTP Score (7 - 9):
Most survivors (89%) had moderate liver dysfunction, as reflected by a CTP score between 7 and 9. In contrast, only 29% of non - survivors fell into this category, indicating that while moderate CTP scores are more common in survivors, a portion of non - survivors also had moderately severe liver disease (Table 4).

High CTP Score (≥10):
A marked difference was observed in patients with a CTP score ≥10, which indicates severe liver disease. Only 10% of survivors had a CTP score in this range, compared to 71% of non - survivors. This significant disparity underscores the association between higher CTP scores and increased mortality risk.

CTP scores are strongly predictive of survival in patients with liver disease. Patients with lower CTP scores (0 - 6) are more likely to survive, while those with higher scores (≥10) are at a substantially increased risk of death. These findings emphasize the importance of the CTP score in assessing liver disease severity and patient prognosis (Table 4).

Table 6: Comparison of MELD - Na Score between Survivors and Non - Survivors

MELD - Na Score	Alive	Dead	p - value
10 - 19	26 (31%)	None	0.0051
≥20	57 (69%)	17 (100%)	

Fisher's Exact Test p<0.05 considered as significant.

Analysis of MELD - Na Score in Survivors vs. Non - Survivors:
The comparison of MELD - Na scores between survivors and non - survivors highlights significant differences, particularly with respect to the distribution of higher MELD - Na scores (p = 0.007) (Table 5).

Low MELD - Na Score (≤9):
None of the patients, whether alive or deceased, had a MELD - Na score of 9 or below, indicating that very mild liver dysfunction was not present in this cohort of patients (Table 5).

Moderate MELD - Na Score (10 - 19):
A considerable portion of survivors (31%) had a MELD - Na score in the range of 10 - 19, suggesting moderate liver dysfunction. In contrast, none of the patients who died fell within this range, indicating that survival is more likely in patients with moderate MELD - Na scores (Table 5).

High MELD - Na Score (≥20):
Most survivors (69%) had a MELD - Na score ≥20, reflecting severe liver disease. However, all non - survivors (100%) had a MELD - Na score in this range, highlighting the strong association between high MELD - Na scores and increased mortality risk. This finding underscores the prognostic importance of MELD - Na scores in predicting poor outcomes in patients with advanced liver disease (Table 5).

The MELD - Na score is a significant predictor of survival in patients with liver disease. Moderate MELD - Na scores (10 - 19) are more common in survivors, while high MELD - Na scores (≥20) are strongly associated with mortality. Monitoring MELD - Na scores is crucial in identifying patients at higher risk of death, particularly those with scores ≥20 (Table 5).

Table 7: CTP Score among study patients

CTP Score	Number of Cases	Percentage
0 - 6	1	1%
7 - 9	79	70%
≥10	20	20%

Analysis of CTP Score Distribution among Study Patients:
The distribution of Child - Turcotte - Pugh (CTP) scores among the study patients reveals the following patterns (Table 6):

Low CTP Score (0 - 6):
Only 1% of the patients had a CTP score in the range of 0 - 6, indicating very mild liver dysfunction. This suggests that

most of the cohort consists of patients with more advanced liver disease.

Moderate CTP Score (7 - 9):
Most of the patients (70%) had a CTP score between 7 and 9, reflecting moderate liver dysfunction. This large proportion indicates that most patients in the study were in the mid - range of liver disease severity.

High CTP Score (≥10):
A significant subset of the cohort (20%) had a CTP score of 10 or higher, indicating severe liver dysfunction. These patients likely faced a higher risk of complications and poor outcomes due to the advanced stage of their liver disease.

The distribution of CTP scores among study patients highlights that most patients had moderate liver disease (CTP 7 - 9), with a smaller but notable proportion presenting with severe liver dysfunction (CTP ≥10). Monitoring CTP scores is essential in assessing disease severity and guiding management in liver disease patients

Table 8: MELD - Na Score among study patients

MELD - Na Score	Number of Cases	Percentage
<9	None	None
10 - 19	26	26%
≥20	74	74%

Analysis of MELD - Na Score Distribution among Study Patients:
The distribution of MELD - Na scores among the study patients provides insight into the severity of liver disease in the cohort (Table 7):

Low MELD - Na Score (<9):
No patients had a MELD - Na score below 9, indicating that none of the study participants had very mild liver disease. This suggests that the cohort consisted of individuals with more significant liver dysfunction.

Moderate MELD - Na Score (10 - 19):
A total of 26 patients (26%) had a MELD - Na score in the range of 10 - 19, reflecting moderate liver disease. These patients are likely to experience a moderate level of liver dysfunction but may still have a better prognosis compared to those with higher scores.

High MELD - Na Score (≥20):
Most patients (74%) had a MELD - Na score of 20 or greater, indicating severe liver disease. This large proportion of patients with high MELD - Na scores highlight the advanced stage of liver dysfunction in most of the cohort and suggests a greater risk for adverse outcomes.

The distribution of MELD - Na scores among study patients shows that a significant majority (74%) had severe liver disease with a MELD - Na score ≥20. Only a smaller subset (26%) had moderate liver disease (MELD - Na 10 - 19), and none had low MELD - Na scores. The high prevalence of elevated MELD - Na scores in this cohort emphasizes the advanced liver disease and associated risks for complications and poor outcomes.

4. Discussion

The current study aimed to assess the prognostic significance of serum ferritin levels in patients with decompensated chronic liver disease, focusing on its association with clinical outcomes such as mortality, decompensation events, and the severity of liver disease. Our findings highlight the critical role of elevated serum ferritin in predicting early mortality and worsened clinical parameters, which aligns with several previous studies that have explored ferritin as a key marker in liver disease prognosis.

Ferritin as a Prognostic Marker
Our study found that patients with serum ferritin levels exceeding 400 ng/mL exhibited significantly higher mortality rates (88%) compared to none of the patients with ferritin levels <200 ng/mL experiencing mortality ($p = 0.0001$) . This result is in line with the findings of **Maiwall *et al.* (2014),** who reported that elevated serum ferritin levels are strongly associated with early mortality in decompensated cirrhotic patients. In their cohort of 318 patients, the median ferritin level was 438 ng/mL, and patients with higher levels showed poor survival outcomes[8]. Our results further substantiate the use of serum ferritin as a marker of hepatic necro - inflammation, which is a major contributor to the progression of liver disease and mortality.

Similarly, another study **Meier *et al*. (2020)** demonstrated the independent prognostic value of serum ferritin in patients with end - stage liver disease (ESLD). Their study reported that patients with ferritin levels >1030.5 mg/L had a 50% risk of death within a median of 11 days[9]. The present study employed a lower threshold (>400 ng/mL), the correlation between elevated ferritin levels and poor prognosis is consistent. Both studies suggest that ferritin is a valuable biomarker for identifying high - risk patients who may benefit from intensive monitoring and early interventions.

Association with Decompensation Events
Our study also showed that patients with higher ferritin levels were more prone to severe decompensation events, including gastrointestinal bleeding and hepatic encephalopathy. In the >400 ng/mL ferritin group, 88% of patients experienced gastrointestinal bleeding, and 65% suffered from hepatic encephalopathy, in contrast to much lower rates in patients with ferritin <200 ng/mL. These findings are supported by **Tornai et al. (2021),** who found that high ferritin levels were associated with an increased risk of bacterial infections and mortality in cirrhotic patients. Tornai's et al study emphasized that ferritin, as an acute - phase reactant, reflects not only iron overload but also the systemic inflammation that exacerbates liver disease[10]. The increased incidence of decompensation events in our high ferritin group suggests that ferritin may act as a marker for both iron dysregulation and immune system activation, contributing to adverse clinical outcomes.

Furthermore, **Oikonomou et al. (2017)** reported similar results in their cohort of patients with stable decompensated cirrhosis, where high serum ferritin levels were linked to an increased incidence of spontaneous bacterial peritonitis (SBP) and hepatic encephalopathy[11]. The strong association between elevated ferritin and severe decompensation events observed in both our study and Oikonomou's et al study

reinforces the idea that ferritin is not merely a bystander but may be actively involved in the pathophysiology of liver decompensation.

Correlation with Liver Disease Severity (CTP and MELD - Na Scores)

Liver disease severity, as reflected by CTP and MELD - Na scores, was significantly higher in patients with elevated ferritin levels. In our study, 82% of patients with ferritin levels >400 ng/mL had a CTP score ≥10, indicating severe liver dysfunction, compared to none in the <200 ng/mL ferritin group ($p = 0.0001$) . These findings are consistent with the work of **Oikonomou et al. (2017),** who also demonstrated that patients with higher ferritin levels had worse CTP and MELD scores. Our study extends this by showing that elevated ferritin levels were similarly associated with higher MELD - Na scores, with all patients in the >400 ng/mL group having scores ≥20, signifying advanced liver disease.

Additionally, **Meier et al. (2020)** reported that serum ferritin levels, alongside MELD - Na scores, were strong predictors of 90 - day survival in patients with ESLD. Their study indicated that ferritin could complement traditional scoring systems like MELD - Na in predicting patient outcomes. Our study supports this notion, as patients with ferritin levels >400 ng/mL had a worse prognosis even when adjusting for MELD - Na scores. These findings suggest that integrating serum ferritin into routine assessments could improve the accuracy of existing prognostic models, particularly in identifying patients at risk for early mortality.

Ferritin's Role in the Pathophysiology of Liver Disease

Ferritin is widely recognized as an acute - phase protein involved in the inflammatory response. In the context of liver disease, ferritin levels rise due to hepatic necro - inflammation, iron overload, and systemic immune activation. Our study, along with previous research, suggests that ferritin not only reflects iron stores but also serves as an indicator of ongoing liver injury and inflammation. **Maiwall et al. (2014)** emphasized ferritin's role as a readily available, easily measured biomarker that can provide insights into the inflammatory processes driving liver disease progression. Another study by **Tornai et al. (2021)** further highlighted the dual role of ferritin in cirrhotic patients, where both low and high ferritin levels can have detrimental effects due to iron deficiency or overload, respectively. High ferritin levels, as observed in our study, may signal a state of immune dysregulation and bacterial translocation, leading to endotoxemia and systemic inflammation, which are key drivers of mortality in decompensated cirrhosis.

Clinical Implications and Future Directions

The findings of this study, in conjunction with those of previous research, underscore the utility of serum ferritin as a prognostic marker in patients with decompensated chronic liver disease. Elevated ferritin levels were consistently associated with higher mortality, increased decompensation events, and worse liver function scores (CTP and MELD - Na). Given its role in reflecting both iron overload and inflammation, ferritin could be incorporated into routine clinical assessments to enhance the prediction of adverse outcomes in cirrhotic patients.

However, while serum ferritin shows great promise as a prognostic tool, it is important to acknowledge its limitations. Ferritin is an acute - phase reactant and may be elevated in a range of conditions unrelated to liver disease, such as infections and malignancies. Therefore, it should be used alongside established scoring systems like CTP and MELD - Na to provide a more comprehensive assessment of liver disease severity.

In conclusion, this study reinforces the prognostic significance of serum ferritin in decompensated liver disease, particularly in predicting early mortality and severe decompensation events. Future research should focus on validating these findings in larger, multicentred studies and exploring the underlying mechanisms by which ferritin contributes to liver disease progression and patient outcomes. Integrating ferritin into existing prognostic models could improve the management of high - risk patients, enabling earlier interventions and potentially better outcomes.

5. Conclusion

The findings of this study highlight the significant relationship between serum ferritin levels and patient outcomes in individuals with liver disease. The analysis demonstrates that patients with elevated serum ferritin (>400 ng/mL) are at a markedly increased risk of mortality, with an alarming 88% of non - survivors exhibiting high ferritin levels. Conversely, all patients with ferritin levels <200 ng/mL survived throughout the study period, indicating a strong correlation between low ferritin concentrations and better survival outcomes.

Furthermore, the study reveals that gastrointestinal bleeding and hepatic encephalopathy are significantly more common in non - survivors, suggesting that these decompensation events may serve as critical indicators of disease severity and prognosis. The Child - Turcotte - Pugh (CTP) and MELD - Na scores also exhibit strong associations with survival, with higher scores correlating with increased mortality risk. Notably, most non - survivors had a CTP score ≥10 and a MELD - Na score ≥20, both markers of severe liver dysfunction.

Overall, this study underscores the importance of monitoring serum ferritin levels, along with CTP and MELD - Na scores, as valuable tools in assessing liver disease severity and predicting patient outcomes. These findings may guide clinical decision - making and management strategies for patients with advanced liver disease, emphasizing the need for targeted interventions in those at higher risk of adverse outcomes. Further research is warranted to validate these results in larger, multicentre cohorts, ensuring a comprehensive understanding of the prognostic implications of serum ferritin and other clinical parameters in liver disease.

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