Original Research Article

A study of serum ferritin as a prognostic marker in patients with decompensated liver disease

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Abstract

Introduction: Decompensated liver disease caused by various modifiable and non-modifiable factors leads to the progression of cirrhosis, jaundice, bleeding varies and other complications which leads to high complications and mortality. This study was carried out to predict whether serum ferritin a marker of body iron stores and inflammation is a valid prognostic marker in advanced liver disease.
Aim of the study: To study whether serum ferritin levels as an independent prognostic marker to predict the mortality of patients with decompensated liver disease.
Materials and methods: It was a prospective and analytical study of 100 patients admitted to our hospital with DCLD and its complications. The study period was from August 2017 to July 2018. After informed consent patients were evaluated with laboratory investigations, clinical examination.
Results: It was found that among enrolled 100 patients after getting informed consent, the majority were male patients but sex wise both female and male patients that P- the value of the comparison non-significant. This indicated that there was a low correlation between, LFT values with SF values. This also proved that high SF values were having a low association with LFT values which needs more investigation.
Conclusion: Serum ferritin is one of the surrogate markers to predict prognosis in the patients of DCLD. Compared with a well established prognostic model like MELD score, to assess the mortality with SF level is statistically valid one. So, in future SF levels will be a one of the best screening independent prognostic markers in people with liver disease.

Key words

American Association for the study of liver disease, Serum ferritin, Decompensated liver disease, Jaundice.

Introduction

Cirrhosis represents a late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules. It is generally considered to be irreversible in its advanced stages at which point the only option may be liver transplantation [1]. Various etiological factors have been associated with chronic liver disease e.g. alcohol, hepatitis B, C, alpha-1 antitrypsin deficiency cystic fibrosis etc. Among these causes, hepatitis C is one of the leading causes of cirrhosis. Pathogenesis behind liver fibrosis is liver fibrogeneis [2]. Early detection of liver fibrogenesis is important for timely treatment of patients. Various markers and scoring systems have been used for assessing the severity of chronic liver disease. Child Turcotte-Pugh (CTP) and Model of End-Stage Liver Disease (MELD) scoring system are widely used for classification of severity of chronic liver disease and to prioritize the patients for liver transplant [3]. CTP class A patients have a good prognosis with medium-term survival, class B patients have a variable prognosis. They may survive for a year or more or may deteriorate rapidly whereas class C patients need liver transplantation urgently. Similarly, studies have shown MELD score predicting 3 months mortality in patients with chronic liver disease [4]. As cirrhosis, secondary to any cause, is one of the leading cause of death so it is really important that there should be some marker which can predict prognosis in decompensated chronic liver disease as earlier as one month. Serum ferritin is an acute phase reactant. It plays a defensive role against inflammatory stress on the body. Ferritin levels can be measured in serum easily. It is increased in the inflammatory process and malignancy. Raised ferritin levels in the context of chronic liver disease are seen in hereditary hemochromatosis, NAFLD and virus-related chronic liver diseases [5]. In a patient of chronic liver disease without iron overload, serum ferritin levels are related to the histological liver parenchymal damage rather than iron accumulation [6]. Purpose of this study is to find a biochemical marker such as serum ferritin level as a predictor of early mortality at 30 days in hospitalized patients with decompensated chronic liver disease. So, in future, serum ferritin may be used as a surrogate marker or may be used in conjunction with another scoring system such as CTP in predicting early mortality in patients with chronic liver disease [6].

Materials and methods

It was a prospective and analytical study of 100 patients admitted to our hospital with DCLD and its complications. The study period was from June 2017 to July 2018. After informed consent patients were evaluated with laboratory investigations, clinical examination. After arriving the provisional diagnosis of chronic liver disease demographic data retrieved which includes Age, Sex, Co-morbidity, medical history, any native medications, and drugs. Information gathered from patient and attenders in the case of the liver disease with hepatic encephalopathy and entered in the proforma designed for this study. Using AUDIT-C questionnaires alcohol intake identified. Lab investigations included complete hemogram, PT/INR, LFT, RFT, serum electrolytes, serum ferritin by using Roche electrochemiluminance assay, VCTC, viral markers including HBV and anti HCV.

Inclusion criteria

- Patients selected with referral to AASLD guidelines.
- Both male and female with chronic liver disease with decompensation.
- Around 35 to 60 years age groups were included.

Exclusion criteria

- Ageless than35 years and more than 60 years.
- Prenatal women with the liver disease.
- Primary or secondary malignancy of liver
- Patients were on hepatotoxic drugs.
- PLWHA
- Chronic illness like tuberculosis.

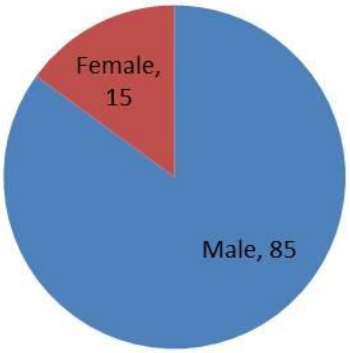
Statistical analysis

To describe about data, descriptive statistics frequency analysis was used. Percentage analysis was used for categorical analysis. For continuous variables, the Mean and SD were used. To find the significant difference between the bivariate samples in independent groups, the unpaired sample t-test was used. By using correlation analytical method we assess how much significant to predict mortality in decompensated liver disease with serum ferritin.

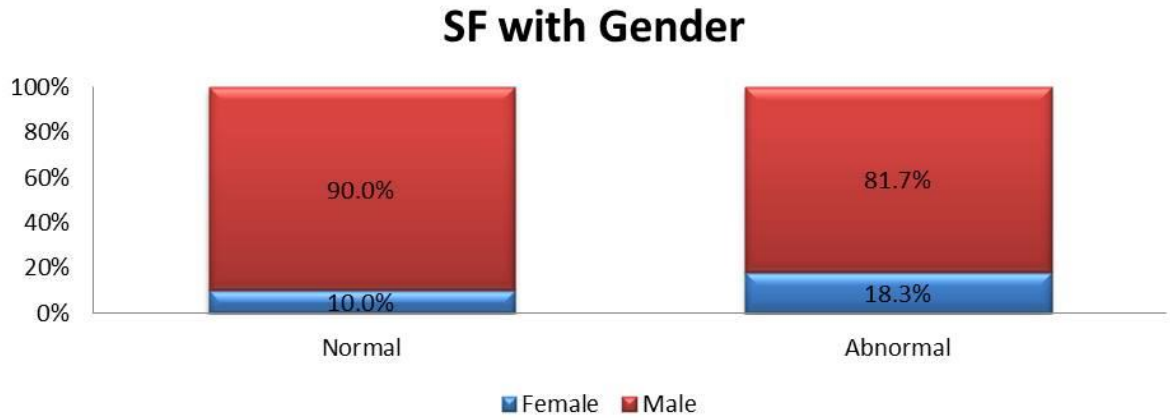
Results

Totally 100 patients were included in the study. 15% were females and 85% were males. A male preponderance was more in our study (**Graph – 1**).

Graph – 1: The gender distribution in the studied population.



Graph – 2: Correlation between SF with gender.

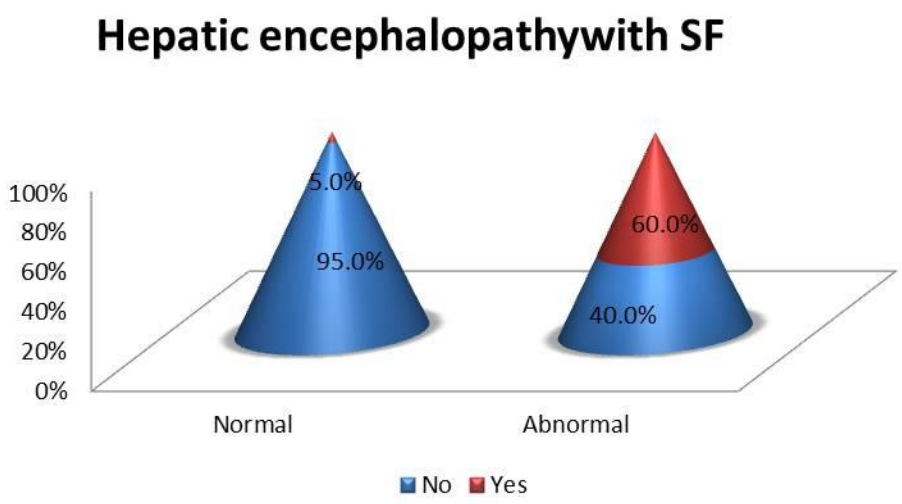


18.3% of females and 81.7% of males showed elevated serum ferritin.in our study group, a maximum number of enrolled patients are males. Since in India alcoholism and liver disease higher in males than females, we were not able to come to conclusion whether SF level associated with gender specificity (**Graph – 2**).

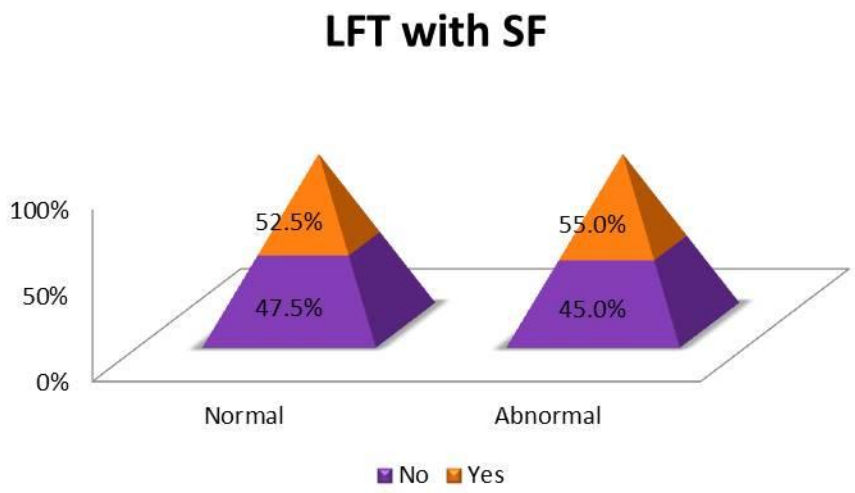
This indicated that there was a high correlation between, Hepatic encephalopathy values with SF values. This also proved that high SF values were highly associated with Hepatic encephalopathy values which lead to high mortality (**Graph – 3**).

This indicated that there was a low correlation between, LFT values with SF values. This also proved that high SF values were having a low association with LFT values which NEEDS more investigation (**Graph – 4**).

Graph – 3: Correlation hepatic encephalopathy with serum ferritin.



Graph – 4: Correlation with LFT and serum ferritin.



Discussion

Chronic liver disease is an important medical condition because of its high morbidity and mortality. Early diagnosis of cirrhosis is important for timely management of disease, to avoid its complications and to prioritize patients for liver transplantation. Various classification systems having been established to access the severity and outcome of disease like CP and MELD scoring system. These scoring systems access 3, 6 months mortality. So, it's really important to have a marker which can access mortality as early as 30 days. Serum ferritin is an acute phase reactant and it has been shown in various studies that its levels increase as the liver disease advances [7]. Patients having ferritin <200ng/ml had 100% survival while patients

having serum ferritin 200400ng/ml had 50% mortality and 50% survival. It was important to note that patients having serum ferritin >400 ng/ml had 93% mortality. It was also noted that with increasing ferritin level, CTP class increased as well as MELD Score. Patients who were higher ferritin were among non-survivors (p<.001). Of these three factors, strongest correlation of mortality with outcome was seen with ferritin e.g. 28 out of 30 (93.3%) patients having ferritin level greater than 400 died (p <.001) but for high CTP class and high MELD score, the case is not exactly like that e.g. 35 patients in class C died out of 54 (64.8%) [8]. Our study results were comparable with other similar studies. In one study, serum ferritin had been taken like 6 months and 1-year mortality predictor and was found that serum ferritin greater than 200 microg/L was an independent factor predicting increased 180-day and 1year waiting list mortality [9]. Results of our study were also similar to another study in which serum ferritin was taken as a predictor of mortality as early as 15 days and 30 days. In this study ferritin levels > 500, ng/ml were strongly associated with 15 days and 30 days mortality (p=0.006, HR 1.42). In one study done on best predictors in post-transplant patient and it was found that serum ferritin levels > 365 ng/ml and transfusion saturation <55% were associated with higher mortality in post-liver transplant patients. It was seen in one study that serum ferritin is a marker of advanced fibrosis in patients of Non-alcoholic Steatohepatitis [10]. Results of our study and various other studies showed that serum ferritin can be taken mortality predictor in patients with early cirrhosis as early as 30 days with high accuracy of results and such patients can be prioritized for the liver transplant list. Serum transferrin level has been shown to correlate with short-term mortality in acute-on-chronic organ failure in patients with decompensated cirrhosis [11]. The investigators found that among the various markers for iron metabolism, serum transferrin level was the best predictor of 30day mortality. In this study serum, ferritin was significantly different between survivors and non-survivors but did not predict mortality [12]. More studies are needed to elucidate the relationship of markers of iron metabolism with early mortality in patients with decompensated cirrhosis. Our study did not look at the relationship of transferrin as a marker for predicting mortality and thus we are unable to comment on its utility in our patient group [13]. Apart from predicting early mortality in patients with decompensated cirrhosis, serum ferritin has recently been shown to be associated with increased long-term mortality not only in patients with hemochromatosis and iron overload but also those with non-alcoholic fatty liver disease. This shows that serum ferritin is an important marker for predicting survival in liver disease. Further studies involving the full spectrum of patients from acute liver failure to decompensated cirrhosis as well as acute on chronic liver failure are needed to further characterize this association [14, 15].

Conclusion

Serum ferritin levels well correlated with complications of liver cell failure. Helps us to predict early mortality in liver disease patients especially with decompensation and we conclude that like MELD score, levels of serum ferritin it is the independent best prognostic score to predict death and early mortality in DCLD patients. So in future, this could be considered one of significant therapeutic and assessment implication in liver disease patients.

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References

1. Schuppan D, Stolzel U, Oesterling C, Somasundaram R. Serum assays for liver fibrosis. J Hepatol., 1995; 22(2 Suppl): 82–8.
2. Keeffe EB. Summary of guidelines on organ allocation and patient listing for

liver transplantation. Liver Transpl Surg., 1998; 4(5Suppl 1): S108–14.
3. Oellerich M, Burdelski M, Lautz HU, Binder L, Pichlmayr R. Predictors of one-year pretransplant survival in patients with cirrhosis. Hepatology, 1991; 14(6): 1029–34.
4. Freeman RB Jr, Wiesner RH, Harper A, McDiarmid SV, Lake J, Edwards E, et al. The new liver allocation system: moving toward evidence-based transplantation policy. Liver Transpl., 2002; 8(9): 851–8.
5. Beaton MD, Adams PC. Treatment of hyperferritinemia. Ann Hepatol., 2012; 11(3): 294–300.
6. Bugianesi E, Manzini P, D'Antico S, Vanni E, Longo F, Leone N, et al. Relative contribution of iron burden, HFE mutations, and insulin resistance to fibrosis in the nonalcoholic fatty liver. Hepatology, 2004; 39(1): 179–87.
7. Walker NM, Stuart KA, Ryan RJ, Desai S, Saab S, Nicol JA, et al. Serum ferritin concentration predicts mortality in patients awaiting liver transplantation. Hepatology, 2010; 51(5): 1683–91.
8. Maiwall R, Kumar S, Chaudhary AK, Maras J, Wani Z, Kumar C, et al. Serum ferritin predicts early mortality in patients with decompensated cirrhosis. J Hepatology, 2014; 61(1): 43–59.
9. Weismüller TJ, Kirchner GI, Scherer MN, Negm AA, Schnitzbauer AA, Lehner F, et al. Serum ferritin concentration and transferrin saturation before liver transplantation predict decreased long-term recipient survival. Hepatology, 2011; 54(6): 2114–24.
10. Kowdley KV, Belt P, Wilson LA, Yeh MM, Neuschwander Tetri BA, Chalasani N, et al. Elevated serum ferritin is an independent predictor of histologic severity and advanced fibrosis among patients with nonalcoholic fatty liver disease. Hepatology, 2012; 55(1): 77–85.
11. Noor M T, Tiwari M, Kumar R. Non-HFE iron overload as a surrogate marker of disease severity in patients of liver cirrhosis. Indian J. Gastroenterol., 2016; 35: 33.
12. Vague C, Sultana C, Ruta S. Serum iron markers in patients with chronic hepatitis C infection. Hepat. Mon., 2013; 13(10).
13. Olmez S, Alan M, Saritas B, Yalcin MS, Tas A, Balaharogou R. Serum ferritin levels in patients with HBV and HDV-related cirrhosis. Acta Medica Mediterranea, 2016; 32: 1813.
14. Khare S, Garg V K. Serum iron and TIBC parameters in chronic liver disease. SJAMS, 2015; 3: 2128-31.
15. Weismüller T J, Kirchner G I, Scherer MN, Negm A A, Schnitzbauer AA, Lehner F, Strassburg C P. Serum ferritin concentration and transferrin saturation before liver transplantation predict decreased long-term recipient survival. Hepatol., 2011; 54(6): 2114–24.