Research Article

Clinical usefulness of serum ferritin level in patients with fatty liver.

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Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease worldwide. Recently several parameters, such as serum ferritin, have emerged as possible predictors for the severity of NAFLD and insulin sensitivity. We aimed to investigate the value of serum ferritin level as a useful biomarker for the prediction of disease severity in patients with NAFLD. **Methods:** This was a prospective cross sectional study in which demographic, clinical and laboratory data of 101 adult patients with NAFLD were analyzed. **Results:** In our patients population with mean age of 49.2 years and mean BMI of 31.9, it was also observed that ferritin level did not have a significant correlation with the stage of fibrosis (p = 0.835). **Conclusion:** Hyperferritinemia is common in patients with NAFLD but the extent of serum ferritin elevations do not predict the stage of underlying NAFLD disease.

Keywords: Ferritin, Non-alcoholic Fatty Liver Disease, Hepatic steatosis score.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the 2nd most common cause of cirrhosis and liver transplantation worldwide. It will probably be the leading cause of chronic liver disease in forth-coming years[1]. As the hepatic manifestation of the metabolic syndrome; NAFLD is gaining prevalence worldwide due to the obesity epidemic[2].

Fatty liver is characterized histologically by the accumulation of triglycerides within the cytoplasm of the hepatocytes1 and refers to the fat accumulation in the liver exceeding 5–10% by weight[3].

There is a wide spectrum of liver diseases ranging from simple steatosis to non-alcoholic steato-hepatitis (NASH) to cirrhosis and its related complications such as hepatocellular carcinoma and death at the end in NAFLD[4].

In the clinical setting, there is still no consensus about whether liver biopsy is required to confirm a diagnosis of NAFLD. Due to the many potential errors, due to sampling, inter/intra-observer variability, biopsy is the "best" not the "gold" standard for diagnosis[5].

Recently, several non-invasive markers such as serum ferritin have emerged as possible predictors for the presence of NASH versus simple steatosis[6,7]. Iron overload is found in as many as one third of the patients with NAFLD[8]. Steatosis, insulin resistance, and inflammation cause an altered regulation of iron transport[9]. Elevated serum ferritin has been found to be correlated with hepcidine level, which is an iron regulatory hormone, and also with the level of hepatic iron in patients with NAFLD, which may point to the pathological role of iron metabolism in such patients[10].

It has been suggested that serum ferritin levels could potentially be used to predict presence and severity of liver fibrosis in patients with NAFLD. However, the evidence associating elevated serum ferritin with severity of liver fibrosis in NAFLD comes, at the best, from the results of multiple logistic regression analyses. The accu-racy of serum ferritin levels in diagnosing presence and severity of liver fibrosis has not been formally evaluated[11].

Patients and Methods

This study is an observational cross-sectional one that was conducted at the Minia university hospital during the period from January to May, 2019. It included 101 patients. Approval from the Research and Ethics Committee of the Faculty of Medicine, Minia University is obtained in accordance with local research governance requirements. Informed consent is obtained from all individual participants included in the study.

Inclusion criteria:

- Patients with NAFLD with or without hepatic fibrosis.
- Both sexes are included.
- Age more than 18 years.

Exclusion criteria:

1- Age less than 18 years.
2- Patients with medical history, clinical or laboratory evidence of any other liver diseases, such as alcoholic or viral hepatitis, schistose-miasis, autoimmune hepatitis, hereditary liver disease, and those with decompensated liver cirrhosis.
3- Patients with a history of drug usage in the last 2 months.
4- Serum ferritin levels > 1000ng/ml.

All patients are subjected to the following:

1-Complete medical history and clinical examination, including abdominal examination, waist circumference measurement, and body mass index (BMI).
Body mass index (BMI) was calculated as weight (kg) divided by the square of height (meters). Waist circumference (WC) was measured while standing at the level of umbilicus.
2- Laboratory investigations.
3- Abdominal ultrasound.
4- NAFLD liver fat score (NLFS score) and Hepatic steatosis index (HSI score) were selected for the scoring model for NAFLD.

Results

They included 33 males (32.3%) and 68 females (67.6%), and their ages ranged between 20-80 years with a mean 49.2±11.5. Table (1).

Table (1): Demographic data

Demographic data		N=101
Age	*Range*	(20-80)
	Mean ±SD	49.2±11.5
Gender	*Male*	33(32.3%)
	Female	68(67.7%)
M. State	*Single*	1(1%)
	Married	95(94.9%)
	Widow	5(4%)
Occupation	*Housewife*	65(65.7%)
	Worker	7(7.1%)
	Retired	4(4%)
	Deriver	4(4%)
	Nurse	1(1%)
	Employee	1(1%)
	Farmer	16(16.2%)
	Student	1(1%)
DM	*No*	85(84.8%)
	Yes	16(15.2%)
HTN	*No*	80(79.8%)
	Yes	21(20.2%)
Smoking	*No*	79(78.8%)
	Smoker	16(15.2%)
	X-Smoker	6(6.1%)

M. State: marital state, DM: diabetes mellitus, HTN: hypertension.

On assessment of liver fibrosis by the FIB-4 index, there was 68 had F0 (67.7%), 28 had F1-2 (27.3%) and 5 had F3-4 (5.1%). Table (2).

Table (2): Liver fibrosis as assessed by the FIB-4 index in patients with NAFLD

Scores		N=101
Fibrosis	*No*	68(67.7%)
	Yes	33(32.3%)
Fibrosis stage	*F0*	68(67.7%)
	F1-2	28(27.3%)
	F3-4	5(5.1%)

FIB-4: fibrosis-4.

Discussion

Non-alcoholic fatty liver disease (NAFLD) is the 2nd most common cause of cirrhosis and liver transplantation worldwide. It will probably be the leading cause of chronic liver disease in upcoming years[12]. As the hepatic manifestation of the metabolic syndrome; NAFLD is gaining prevalence worldwide due to the obesity epidemic[13].

Our study was an observational cross-sectional that included 99 patients, at the Minia university hospital. We aimed to study the evaluation of serum ferritin in patients with NAFLD.

There is conflicting evidence of the usefulness of serum ferritin as a prognosticator in observational studies of adults with fatty liver[14].

Although ferritin is the chief iron storage protein and can closely reflect body iron stores, it is an acute phase reactant, leading to difficulty in its interpretation in the presence of co-existing liver injury. In NAFLD, mild hepatic iron deposition is seen in up to 30% of patients while increased hepatic and systemic inflammation are also common[15].

Serum ferritin, but not serum iron, transferrin saturation, or hepatic iron concentration has been proposed to be higher in patients with severe (stages 3–4) than with mild (stages 1–2) fibrosis, but not steatosis or inflammation, and could independently predict severe fibrosis[16].

Ferritin has been identified as a predictor of advanced fibrosis and hyperferritinaemia has been associated with obesity, insulin resistance (IR) and cardiovascular disease, conditions inherently related to NAFLD [17].

Some evidence suggests an association between increased serum ferritin and mild iron overload, unrelated to hereditary hemochromatosis, in conditions associated to the metabolic syndrome including NAFLD [18]

The non-alcoholic fatty liver disease activity score (NAS) is independently associated with fibrosis progression. However, there is considerable overlap in clinical progression between NAFLD subgroups. [19].

In our study, we found that serum ferritin was significantly higher in males than females. However, we found no significant correlation between serum level of ferritin and fibrosis stage or hepatic steatosis score.

Our findings were in agreement with a study done by Modares et al., who reported no significant correlation between serum ferritin level and histopathological grade or stage of the disease. In addition, no correlation between serum ferritin level and age, body mass index (BMI), the level of liver enzymes, fasting plasma sugar, or serum lipids was seen[19].

On the other hand, our results disagreed with a study performed by Kowdley and colleagues that showed an independent association between serum ferritin level and increased risk of advanced fibrosis in NAFLD. They proposed that levels > 1.5× upper normal limits can have a predictive value for liver fibrosis in their patients with severe obesity and metabolic syndrome. Serum ferritin levels and BMI were strongly associated with fibrosis, and portal and lobular inflammation in patients with biopsy proven NAFLD. Serum ferritin could be due to the genetic, environmental factors, and diet habituates differences in the study population[20].

Our study has some limitations; firstly, it included a relatively small number of patients. Secondly, lack of control group. Thirdly, NASH was diagnosed based on noninvasive paramters such as NLFS, HSI...etc and not liver biobsy.
In conclusion, our study indicates that serum ferritin levels are elevated in most NAFLD patients but the extent of elevation does not predict the stage of the underlying liver disease.

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