Original Article

Analysis of Serum Ferritin Level in Patients of Decompensated Chronic Liver Disease

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ABSTRACT

Objective: To observe the different levels of ferritin among NAFDL and conducted to find a significant relationship between them.

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Pakistan Railway Hospital Rawalpindi within 1 year from Jan 2019 to Jan 2020.

Materials and Methods: We select 30 participants who undergone through NAFLD/NASH biopsy for the collection of their demographic, histological, laboratory data. All the patients were selected to form the Hepatology and gastroenterology department of Pakistan railway hospital Rawalpindi hospital.

Results: With the help of the Pearson formula, we found a significant relationship (0.011) between ferritin and the male gender. This value proves the statement that men had increased ferritin levels as compared to the female population.

Conclusion: Our studies conclude that in young people with 0 levels of obesity, ferritin serum is not only a single way to find disease severity.

Key Words: Serum ferritin, Histological analysis, Steotosis grade, fibrosis stage, liver biopsy, 0 Obesity

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INTRODUCTION

Globally chronic liver due to cirrhosis has a high mortality rate[1]. It has no specific signs or symptoms and only diagnosed incidentally during a medical examination. At the initial stage, cirrhosis is usually compensated. Cirrhosis at the compensated stage is harmless and can be treated with a high life expectancy[2]. But due to the asymptomatic at the initial stage, cirrhosis eventually reaches to decompensated form. Decomposition of compensated cirrhosis is defined as a situation in which ascites occurs very first time along with the oesophageal variceal bleeding, hepatic encephalopathy[3]. Some patients report an increase in bilirubin concentration during decomposition[3,4]. At the stage of decay, patients need rapid medical attention and frequent medical assistance. Mortality and morbidity rate risen to 80% reached its peak in a year after dissolution[5].

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Mostly the death rate of chronic liver disease is noted due to decompensated cirrhosis This disease causes acute, chronic liver failure, a condition in which critical hepatic decomposition caused the liver failure with cirrhosis[6]. Different studies explore the relationship between chronic liver disease and cirrhosis. They assume that chronic liver sometimes ends in the development of cirrhosis[6]. Decompensated cirrhosis is usually correlated with a viral infection, drug and alcohol consumption, ischemic hepatitis. These factors worsen the patient's situation and result in extrahepatic organ failure[7].

Due to the absence of laboratory test, imaging, liver biopsies, lack of standardized definition total number of cirrhosis cases are unknown[8]. Meanwhile, in 2017, in the whole world, 440,000 deaths were reported due to cirrhosis. The male population has more encounters with cirrhosis as compared to the female population (66.7% and 33.3%, respectively). Globally in 2017, death ration of cirrhosis increased from 1.9% to 2.4%. The high rates of death are reported in undeveloped countries due to their weak economy and inaccessible health care opportunities[9].

Some researchers demonstrate that nonalcoholic fatty liver disease (NAFLD) is a second major prevalent cause of cirrhosis. In the future, it will be the leading cause of cirrhosis and liver transplantation[10]. It arises due to the high obesity rate and increases the risk of cardiovascular disease, diabetes mellitus, and chronic kidney disease along with cirrhosis. The nonalcoholic fatty disease creates complications like hepatocellular

carcinoma that leads to death[11,12]. The pathogenesis of nonalcoholic fatty acid is still not defined yet.

In previous years, researchers notice ferritin serum for the best possible prediction for the NASH versus simple steatosis[13,14]. In one-third of the NAFLD patients, iron overload was originated as a significant issue[15]. Ferritin is an acute-phase reactant in NAFLD, but it is not a single predictor of disease. Many researchers define an association of serum ferritin with hepcidin level (a hormone that regulates the iron)[16]. Some other studies found a relationship of serum ferritin with hepatic iron in NAFLD patients[16]. Still, significant literature is missing to define a correlation between serum ferritin and NAFLD. This study aims to observe the different levels of ferritin among NAFDL and conducted to find a significant relationship between them.

MATERIALS AND METHODS

This study was conducted in Islamic international college Hepatology department in 1 year. We select 30 participants who undergone through NAFLD/NASH biopsy for the collection of their demographic, histological, laboratory data. All the patients were selected to form the Hepatology and gastroenterology department of Pakistan railway hospital Rawalpindi hospital. For better results, we asked senior hepatologists to confirm the severity of disease among patients chosen and recommend us for biopsy patients so that we further conduct a study for the evaluation of abnormal liver and biopsies. Senior radiologists conducted all the liver biopsies through ultrasonography. The results were also sent to the lab for further processing. During the investigation, if large fat vacuoles were found in liver parenchyma and had any impacts on the nuclei border of the cells, then it was counted in fatty liver disease. Affected hepatocytes, less than 33%, were considered as grade 1, whereas 33-60% affected hepatocytes were marked into category 2. For class 3, we prefer changed hepatocytes higher than 66%. This grading score was selected from the Brunt et al. study[17].

After the biopsy, serum ferritin was computed through an enzyme-linked immunosorbent assay (ELISA) test in which we further observed monoband and unstable angina. These readings were obtained within two weeks of biopsy. For analyzing serum iron and total iron-binding capacity, we used colorimetric. Both testings were administered at a parallel timeline. For a reasonable understanding of complete iron-binding, transferrin saturation was also noticed. All those victims who lack NAFLD in their chronic liver disease were avoided from the research. Patients have Hepatitis B or C, any rheumatologic disorders, using any iron supplements, access consumption of alcohol, or having any infectious disease were excluded from the research. Patients who are already using any medication for fatty liver disease at the time of studies, and patients using steroids, methotrexate, and tamoxifen and any other medicines that trigger the fatty liver disease among them were also excluded from the research. Only male participants were selected to check the validity of previous researches. All the young NAFLD patients were referred for the biopsy. All the patients underwent laboratory testing for measuring, hepatic, metabolic, and hematologic readings. A lipid test was also conducted on the selected population. For the formulating correlation in results, we measured blood pressure, body weight, and height of all patients.

All the data was measured through SPSS 23.0. One sample Kolmogorov test, t-test, and Pearson coefficient of Correlation were applied to the gathered information. For this study, p-value, 0.05, is supposed as significant[18].

RESULTS

A total of 30 biopsy proven NAFLD male patients were selected for the research. Recent studies show a high ratio of NAFLD, so we chose only male patients with a mean age of 37.9 years. After measuring the height and weight of patients, we get an average of 26.6 BMI in the study. Data was divided into four groups; mild, moderate, severe, and no steotoheptic for further laboratory testing. We observed 19 mild cases, four moderate, five non-steotoheptic. In contrast, only two severe cases were found.

Table No.1: Demographic and histological analysis of Participants[18]

Characteristics	Severe Steotoheptic 2	Moderate Steotoheptic 4	Mild Steotoheptic 19	No Steotoheptic 5	All patients 30
Age mean	44.5 ± 17.6	32.75 ± 7.4	39.15 ± 12.7	34.8 ± 14.8	37.93 ± 12.5
Male sex (n%)	0	3 (75%)	13 (68.4%)	1 (20%)	17 (56.7%)
BMI mean (kg/m2)	29 ± 1.4	25 ± 1.8	26.8 ± 3.7	25.3± 8.3	26.45 ± 4.4
AST (IU/L)	112 ± 110	79.2 ± 34.7	49.8 ± 25.5	31.6± 20.7	54.8 ±37.7
ALT (IU/L)	151 ± 115.9	134.3 ± 92.2	71.1± 37.9	46.2± 29.3	85.7 ± 57.1
ALP (IU/L)	233.5 ± 89.8	204.5 ± 29.7	205.6± 75.8	338.4± 154.9	229.4 ± 98.7
Serum Ferritin (ng/mL)	241.6 ± 146.2	268.5 ± 61.8	212.1± 236	88.0 ± 106	200.8 ± 200.6
Fasting blood sugar (mg/dL)	225 ± 193	179 ± 153.3	95.3 ± 26.1	94.8 ± 13	115 ± 76.7

After a complete analysis, we found 43.3% patients at 0 stage, 10% cases at stage 1, 26.7% cases at stage 2. For stage 3 and 4 ratios were comparatively low (13.3% and 6.7% respectively).

Coming towards the steotoheptic analysis, we found 16.7% cases with no steotoheptic, 13.3% cases of moderate, and only 6.7% of severe steotoheptic. The ratio of mild cases was high (63.3%), where the disease was at its initial stage.

Among the selected population, in 36.3% ferritin level was above 200 ng/L. At the same time, 45% of ferritin saturation was found among the people. With the help of the Pearson formula, we found a significant relationship (0.011) between ferritin and the male gender. This value proves the statement that men had increased ferritin levels as compared to the female population.

Table No.2: Correlation among serum ferritin with histological examination[28]

Variables	Pearson correlation	p-value
Age	0.296	0.112
BMI	-0.032	0.869
AST	0.039	0.839
Cholesterol	-0.150	0.429
ALP	-0.351	0.057
Fasting plasma glucose	0.057	0.763
ALT	0.096	0.615
Triglycerides	-0.160	0.399
Transferrin saturation	0.312	0.093

DISCUSSION

We found no significant correlation between histopathological findings, especially stages, and with ferritin serum. An increase in the age of age had a severe impact on NAFLD. All the younger patients in our studies had mild and moderate, which was against our expectations. In the past, many studies were conducted to analyze the serum ferritin level among NAFLD[19,20]. In many studies, researchers demonstrate an association of high serum ferritin with severe histological disorders of the liver in NASH instead of iron overload[21]. A survey conducted by Kowdly observed an association of serum ferritin with a high risk of NAFLD. In their study, they found that the use of patients with metabolic syndrome had hight predatory liver fibrosis because of their higher serum level (>1.5 scales)[22].

A study conducted by Manousou explored an association of fibrosis with serum ferritin and BMI. They argued that increase BMI rate and change in ferritin levels cause adverse effects on fibrosis, which lobular inflammation among the NAFLD patients[23].

Meanwhile, retrospective study of Angulo did not find any significant relationship between ferritin with any liver fibrosis grade. They further argued that serum ferritin does do not affect the accuracy of non-invasive liver fibrosis. They also stated that the inclusion of serum ferritin could not explain the improvement in the accuracy rate. Thus they conclude serum ferritin had limited accuracy for the diagnosis and categorization of NAFLD patients[24].

A cohort study conducted in Japan depicts that other factors like age, sex, and metabolism of patients are the obstacles in the predictive test of liver fibrosis through serum ferritin. They further examine the association of independent serum ferritin with steatosis grade and fibrosis stage but unable to find its influence on predictive values of liver fibrosis[25].

In correspondence to these studies, we were also unable to find a significant association of serum ferritin with histological grades and stages. One of the reasons of insignificance among variables is the minimal population of our research. Only 30 participants were referred to as the biopsy and meet inclusion criteria at the time of examination. We had limited exposure with the elder age group due to their physician prohibition. We were unable to include them in studies. They might have increased risk of complications, so they were not suggested for biopsy and treated with comorbidities and using anti platelet medications at the time of research. Another reason for the insignificant relation could be the younger age of our participants with healthy BMI. Obesity is a factor that affects the iron profile. There is a possibility that a significant relationship will be found among young anemic NAFLD patients because anemia affects the iron profile.

CONCLUSION

Our studies conclude that in young people with 0 levels of obesity, ferritin serum is not only a single way to find disease severity. With a unique marker of ferritin, it's hard to find relevant information regarding the histology of NAFLD.

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Author's Contribution:

Concept & Design of Study:	Shabir Ahmed Orakzai
Drafting:	Mohibullah Khan
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Roth GA, Abate D, Abate KH, et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and

territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018;392: 1736-1788.
2. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. J Hepatol 2006; 44: 217-23.
3. Fleming KM, Aithal GP, Card TR, West J. The rate of decompensation and clinical progression of disease in people with cirrhosis: a cohort study. Aliment Pharmacol Ther 2010; 32: 1343-1350.
4. Moreau R, Jalan R, Gines P, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology. 2013;144(37.e1-9):1426.
5. Fleming KM, Aithal GP, Card TR, West J. All-cause mortality in people with cirrhosis compared with the general population: a population-based cohort study. Liver Int 2012; 32:79-84.
6. Kamath PS. Acute chronic liver failure. Clin Liver Dis 2017;9(4): doi.org/10.1002/cld.625
7. Ge PS, Runyon BA. Treatment of patients with cirrhosis. N Engl J Med 2016;375: 767-777.
8. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. J Hepatol 2019;70: 151-171.
9. Sepanlou, Sadaf G, et al. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study. Lancet Gastroenterol Hepatol 2017;5(3):245-266.
10. Lusida MI, Juniastuti YY. Current hepatitis B virus infection situation in Indonesia and its genetic diversity. World J Gastroenterol 2016; 22(32):7264.
11. Wong RJ, Aguilar M, Cheung R, Perumpail RB, Harrison SA, Younossi ZM, et al. Nonalcoholic steatohepatitis is the second leading etiology of liver disease among adults awaiting liver transplantation in the United States. Gastroenterol 2015;148:547-55.
12. Zezos P, Renner EL. Liver transplantation and nonalcoholic fatty liver disease. World J Gastroenterol 2014;20:15532-8.
13. Tsochatzis EA, Gurusamy KS, Ntaoula S, Cholongitas E, Davidson BR, Burroughs AK. Elastography for the diagnosis of severity of fibrosis in chronic liver disease: a meta-analysis of diagnostic accuracy. J Hepatol 2011;54:650-9.
14. Feldstein AE, Wieckowska A, Lopez AR, Liu YC, Zein NN, McCullough AJ. Cytokeratin-18 fragment levels as noninvasive biomarkers for nonalcoholic steatohepatitis: a multicenter validation study. Hepatol 2009;50:10728.
15. Sumida Y, Yoneda M, Hyogo H, Yamaguchi K, Ono M, Fujii H, et al. A simple clinical scoring system using ferritin, fasting insulin, and type IV collagen 7S for predicting steatohepatitis in nonalcoholic fatty liver disease. J Gastroenterol 2011;46:257-68.
16. Dongiovanni P, Fracanzani AL, Fargion S, Valenti L. Iron in fatty liver and in the metabolic syndrome: a promising therapeutic target. J Hepatol 2011;55:920-32.
17. Brunt EM, Janney CG, Di Bisceglie AM, NeuschwanderTetri BA, Bacon BR. Nonalcoholic steatohepatitis: a proposal for grading and staging the histological lesions. Am J Gastroenterol 1999;94:2467-74.
18. Modares Mousavi S, Geramizadeh B, Anushiravani A, Ejtehadi F, et al. Correlation between Serum Ferritin Level and Histopathological Disease Severity in Non-alcoholic Fatty Liver Disease. Middle East J 2018;10 (2):90-95.
19. Brudevold R, Hole T, Hammerstrom J. Hyperferritinemia is associated with insulin resistance and fatty liver in patients without iron overload. PloS one 2008;3:e3547.
20. Farigson S, Mattioli M, Fracanzani AL, Sampietro M, Tavazzi D, Fociani P, et al. Hyperferritinemia, iron overload, and multiple metabolic alterations identify patients at risk for nonalcoholic steato-hepatitis. Am J Gastroenterol 2001;96:2448-55.
21. 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 nonalcoholic fatty liver. Hepatol 2004;39:179-87.
22. Kowdley KV, Belt P, Wilson LA, Yeh MM, NeuschwanderTetri BA, Chalasani N, et al. Serum ferritin is an independent predictor of histologic severity and advanced f ibrosis in patients with nonalcoholic fatty liver disease. Hepatol 2012; 55:77-85.
23. Manousou P, Kalambokis G, Grillo F, Watkins J, Xirouchakis E, Pleguezuelo M, et al. Serum ferritin is a discriminant marker for both fibrosis and inflammation in histologically proven non-alcoholic fatty liver disease patients. Liver Int 2011;31:730-9.
24. Angulo P, George J, Day CP, Vanni E, Russell L, De la Cruz AC, et al. Serum ferritin levels lack diagnostic accuracy for liver fibrosis in patients with nonalcoholic fatty liver disease. Clin Gastroenterol Hepatol 2014;12:11639.e1.
25. Yoneda M, Thomas E, Sumida Y, Imajo K, Eguchi Y, Hyogo H, et al. Clinical usage of serum ferritin to assess liver fibrosis in patients with non-alcoholic fatty liver disease: Proceed with caution. Hepatol Res 2014;44:499502.