VOLUME-9, ISSUE-5, MAY -2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Biochemistry

SERUM FERRITIN LEVELS: A POTENTIAL BIOMARKER IN LIVER CIRRHOSIS PATIENTS

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ABSTRACT

Background: Liver cirrhosis and the child-Turcotte-Pugh (CTP) score are closely associated entities. CTP score is called as the mortality and prognosis predictor. Although, Ferritin emerges as a potential biomarker related to prognosis. To study that ferritin could be used as a prognostic marker in liver cirrhosis patients.

Methods: The study analyzed 54 cirrhotic patients including 17 females and 37 males at Gandhi medical college and Hamidia hospital,Bhopal,Madhya-Pradesh between May 2018 and December 2019. Ferritin levels were, then, divided into trichotomous cut-off value (< 200 ng/mL, n = 22; 200–400 ng/mL, n = 5; and > 400 ng/mL, n= 27). Data was analyzed using SPSS version 12.0 (continuous variables were assessed by the Kruskal-Wallis test and Chi-square test was used for categorical variables). In addition, Spearman correlation test was used to determine any significant correlation between ferritin levels and CTP score.

Results: Based on data analysis, gender and CTP score were related to higher ferritin levels (P= 0.002 and P = 0.018, respectively). Furthermore, a significant correlation between serum ferritin levels and CTP score was obtained in to moderate degree (P= 0.000;r= 0.487).

Conclusions: There might be a significant role of serum ferritin levels in predicting mortality and prognosis among cirrhosis patients but it still needs further attention.

KEYWORDS :

INTRODUCTION

Liver cirrhosis has been a condition where normal liver parenchyma was replaced with connective tissue producing nodule formation. The condition is described as the end stage of chronic liver disease. The etiologic causes are viral infection, excessive alcohol consumption or cryptogenic agent (1). The symptoms varies from compensated, no clinical manifestation, to decompensate stage consist of ascites, spontaneous bacterial peritonitis, hepatic encephalopathy or variceal bleeding (2).

Serum ferritin is elevated in several clinical conditions including patients with both acute and chronic liver diseases [3].Ferritin synthesis is produced by macrophages and hepatocytes (4). Its raised levels can be seen either in iron overload conditions or in several pathologies, inflammation, infection and liver diseases(5,6).

Ferritin is a 24-subunit protein and an acute phase-reactant,represent iron levels in the human body indirectly but not in a liver cirrhotic patient (7).although in recent studies, ferritin as prognostic marker in cirrhotic patients is emphasized(8).Hyperferritinemia might be related to poor prognosis of liver cirrhosis because ferritin secretion and inflammatory surges depend on certain cytokines(9,10).In fact, recent studies confirmed the above observation: Walker *et al* showed that serum ferritin could be used as an independent predictor of mortality in cirrhotic patients awaiting Liver Transplant and high levels were associated with a higher frequency of liver-related complications (11), while Maiwall *et al* found that ferritin was an independent prognostic biomarker for early liver-related death, at 15 days and at 1 month, in hospitalized patients with cirrhosis (12).The study aimed to assess serum ferritin levels as a Potential Biomarker among liver cirrhosis patients.

MATERIAL AND METHOD-

The cross-sectional study was carried out in Gandhi Medical College and Hamidia hospital, Bhopal, Madhya Pradesh between May 2018 and December 2019. Patients admitted to the internal medicine ward and diagnosed with liver cirrhosis were considered for the study subjects. The written informed consent has been taken.

The exclusion criteria in the study were malignancy condition, or severe co morbidity, end-stage renal disease and chronic pulmonary, obstructive disorder, blood transfusion in the previous three months, positive HIV status, dyslipidemia and diabetes mellitus, acute liver failure, and pregnancy.Several laboratory findings were noted from the medical record registry, such as serum ferritin levels, thrombocyte, international normalized ratio, bilirubin, serologic marker related to viral cirrhosis, and endoscopy for the presence of esophageal varices .

CTP Score

The five indicators included in CTP score were assessed using physical and ultrasonography examination for ascites and encephalopathy while bilirubin, albumin, and INR were noted from central pathology laboratory record registry on the admission day. CTP score was calculated using the free online calculator provided by MdCacl (https://www.mdcalc.com/child-pugh-scorecirrhosis-mortality). CTP score was, then, divided into three class, A (5–6), B (7–9), and C (10–15). Thereafter, the mean difference of demographical characteristic comparison in each class and correlation analysis between serum ferritin and CTP score were carried out.

Statistical analysis

The analysis was performed using Statistical Package for the Social Science (SPSSInc, Chicago, IL) version 12.0 and depicted in percentage and medians or means with standard deviation. The data was not normally distributed, it was statistically proven based consequently, and the data was analyzed using non-parametric test (Kruskal-Wallis test). In exception to age variables, the data normal distribution was obtained; it was analyzed using ANOVA test.

RESULTS

The study enrolled 54 liver cirrhotic patients, 17 females and 37 males, with a mean age of 52.76 ± 12.57 years. The study subjects are divided into three group according to the serum ferritin levels (ferritin under 200, 200–400, and over 400).

In addition, creatinine and bilirubin levels were consistently and descriptively higher in patients with ferritin levels more than 400 μg/L. The other findings consisting of albumin, INR and creatinine were also depicted in Table 1. The correlation between the serum ferritin level and CTP score was evaluated using Spearman correlation test (P-value < 0.05 was stated as significant results statistically with 95% confidence interval).Thus the serum ferritin levels were significantly correlated with CTP score (r = 0.487; P= 0.000).

Table1: Clinical characteristics and laboratory findings based on serum ferritin levels Variables

Variables	Ferritin < 200 (n= 22)	Ferritin 200–400 (n= 5)	Ferritin > 400 (n= 27)	P-value
Age (years)	52.25±13.14	58.4±11.19	51.89±12.50	0.574
Gender Male/ Female	15/7	0/5	22/5	0.002*
Albumin	2.45 (1.5–3.3)	1.9 (1.6–3.1)	2.2 (1.7–3.7)	0.419
INR(International normalised ratio)	1.28 (0.99–1.84))	1.54 (1.07–2.96	1.32 (0.81–2.45)	0.266
Creatinine	0.9 (0.6–2.37)	0.88 (0.55–2.06)	1.18 (0.52-13.58)	0.198
Total bilirubin	1.0 (0.3–4.6)	1.9 (0.6–16.3)	2.41 (0.29–29.8)	0.183
CTP score c	8 (6–12)	9 (7–12)	10 (5–12)	0.018
CTP class (A/B/C)	1/18/3	0/3/2	1/12/14	0.089

DISCUSSION

In the study, the significant and positive correlation between serum ferritin levels and CTP score was seen among liver cirrhosis patients. Most findings had higher levels in accordance with high serum ferritin levels (> 400 μg/L), particularly CTP score. Thus patient with Hyperferritinemia has a higher CTP score with moderate correlation.

Ferritin as cytosolic protein leaks from necrotic liver cells, and Hyperferritinemia will occur. Therefore ferritin is correlated with the extent of liver cell necrosis and same was proved by recent studies (13). Liver biopsy was a golden standard to diagnose iron overload in liver tissue but it could produce complications outweighing its beneficial aspects, particularly among advanced-cirrhosis and low-platelet patients (14).

The study proved the significant finding that ferritin was correlated with CTP score. Ripoll et al. (15) similarly found a significant correlation between hyperferritinemia and CTP score . In other perspectives, ferritin and CTP score were associated with poor prognosis through multivariate analysis among waiting list pre-transplant patients independently (16). Buyukasik et al. (17) showed that higher level of serum ferritin was confined to CTP class C patients Although,the association between ferritin and prognosis or the outcome still becomes inconsistent. There was a finding that ferritin could not be used solely to predict prognosis and the clinical outcome. Uchino et al. (18) stated that serum ferritin did not affect the prognosis among hepatocellular carcinoma patients who underwent radiofrequency ablation (RFA), in addition, there were lower serum ferritin levels among CTP score class C and it is more likely affected by tumor size and liver function (19).

The study has certain limitations. First, the causal relationship between ferritin and certain dependent variables could not be described since it was designed as a cross-sectional (point-time design). Second, serum ferritin levels would be affected by the presence of C282Y homozygosity producing iron overload (20) Finally, the study also did not provide the output related to prognosis and outcome.

CONCLUSIONS

The study concluded that ferritin is a potential biomarker that represents CTP among liver cirrhotic patients. Ferritin level is affected by several factors; therefore, longitudinal studies are need to provide evidence of ferritin as a important biomarker of prognosis since Hyperferritinemia is a hallmark of liver inflammation instead of iron overload among cirrhotic patients.

REFERENCES

1. Wiegand J, Berg T. The etiology, diagnosis andprevention of liver cirrhosis: part 1 of a series onliver cirrhosis. Dtsch Arztebl Int. 2013;110(6):85. https://doi.org/10.3238/arztebl.2013.0085
2. Tsochatzis EA, Bosch J, Burroughs AK. Livercirrhosis. Lancet. 2014;383(9930):1749–1761. https://doi.org/10.1016/S0140-6736(14)60121-5
3. Prieto J, Barry M, Sherlock S. Serum ferritin in patients with iron overload and with acute and chronic liver diseases. Gastroenterology 1975;68:525-533.
4. Harrison PM, Arosio P. The ferritins: molecular properties, iron storage function and cellular regulation. Biochim Biophys Acta 1996;1275:161-203.
5. Knovich MA, Storey JA, Coffman LG, Torti SV, Torti FM. Ferritin for the clinician. Blood Rev 2009;23:95-104.
6. Hearnshaw S, Thompson NP, McGill A. The epidemiology of hyperferritinaemia. World J Gastroenterol 2006;12:5866-5869.
7. Knovich MA, Storey JA, Coffman LG, Torti SV,Torti FM. Ferritin for the clinician. Blood reviews.2009;23(3):95–104. https://doi.org/10.1016/j.blre.2008.08.001
8. Wang W, Knovich MA, Coffman LG, Torti FM,Torti SV. Serum ferritin: past, present and future.Biochim Biophys Acta. 2010;1800(8):760–769. https://doi.org/10.1016/j.bbagen.2010.03.011
9. Wessling-Resnick M. Iron homeostasis andthe inflammatory response. Ann Rev Nutr.2010;30:105–122. https://doi.org/10.1146/annurev.nutr.012809.104804
10. Milic S, Mikolasevic I, Orlic L, Devcic E, Starcevic-Cizmarevic N, Stimac D, et al. The role of iron andiron overload in chronic liver disease. MedicalSci Monit. 2016;22:2144–2151. https://doi.org/10.12659/MSM.896494
11. Walker NM, Stuart KA, Ryan RJ, et al. Serum ferritin concentration predicts mortality in patients awaiting liver transplantation. Hepatology 2010;51:1683-1691.
12. Maiwall R, Kumar S, Chaudhary AK, et al. Serum ferritin predicts early mortality in patients with decompensated cirrhosis. J Hepatol 2014;61:43-50.
13. Kowdley KV. Iron overload in patients with chronic liver disease. Gastroenterol Hepatol. [Internet]. 2016 [Retrieved 2018 December 3];12(11):695–698. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5193089/pdf/GH-12-695.pdf
14. Seeff LB, Everson GT, Morgan TR, Curto TM, Lee WM, Ghany MG, et al. Complication rate of percutaneous liver biopsies among persons with advanced chronic liver disease in the HALT-C trial. Clin Gastroenterol Hepatol. 2010;8(10):877–883. https://doi.org/10.1016/j.cgh.2010.03.025
15. Vagu C, Sultana C, Ruta S. Serum iron markers in patients with chronic hepatitis C infection. Hepat Mon. 2013;13(10):e13136. https://doi.org/10.5812/hepatmon.13136
16. Radicheva MP, Andonova AN, Milcheva HT, Ivanova NG, Kyuchukova SG, Nikolova MS. Serum markers of iron metabolism in chronic liver diseases. Maced J Med Sci. 2018;6(6):1010–1016. https://doi.org/10.3889/oamjms.2018.251
17. Gao YH, Wang JY, Liu PY, Sun J, Wang XM, Wu RH, et al. Iron metabolism disorders in patients with hepatitis B-related liver diseases. World J Clin Cases. 2018;6(13):600–610. https://doiorg/10.12998/wjcc.v6.i13.600
18. Uchino K, Tateishi R, Nakagomi R, Fujiwara N, Minami T, Sato M, et al. Serum levels of ferritin do not affect the prognosis of patients with hepatocellular carcinoma undergoing radiofrequency ablation. PloS One. 2018;13(7):e0200943. https://doi.org/10.1371/journal.pone.0200943
19. Adams P. Management of elevated serum ferritin levels. Gastroenterol Hepatol. [Internet]. 2008 [Retrieved 2018 December 4];4(5):333. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3093720/pdf/GH-04-333.pdf
20. Umer N, Makki MU, Kiran SK, Jadoon NA. Serum ferritin as a predictor of 30 days mortality in patients of decompensated chronic liver disease. J Ayub Med Coll Abbottabad. [Internet]. 2017 [Retrieved 2018 December 4];29(3):415–418. Available from: jamc.ayubmed.edu.pk/index.php/jamc/article/download/2229/1055