ORIGINAL ARTICLE

ANNALS OF PUNJAB MEDICAL COLLEGE

Assessment of Serum Iron Indices and Levels of C-Reactive Protein in Patients of Alcoholic Liver Disease and Their Relationship with Severity of Disease

Ali Chand[1], Farah Naz Tahir[2], Rabia Shahbaz[3], Roma Salman[4], Sana Umar[5], Hassan Burair Abbas[6]

1 *Medical Officer, Shaikh Zayed Hospital, Lahore Pakistan*
Compiled the paper

2 *Assistant Professor, Department of Biochemistry, Central Park Medical College, Lahore Pakistan*
Data collection, Perform experimental work, Paper writing

3 *Women Medical Officer, Suryia Azeem Hospital, Lahore Pakistan*
Data collection & Result analysis

4 *Lecturer, Department of Community Medicine, HITEC, Institute of Medical Sciences, Taxila Cantt Pakistan*
Data analysis & Review the paper

5 *Lecturer, Department of Biochemistry, HITEC, Institute of Medical Sciences, Taxila Cantt Pakistan*
Literature review

6 *Associate Professor, Department of Medicine, HITEC, Institute of Medical Sciences, Taxila Cantt Pakistan*
Contribution in the study

CORRESPONDING AUTHOR
Dr. Farah Naz Tahir
Assistant Professor, Department of Biochemistry, Central Park Medical College, Lahore Pakistan
Email: tahirnazfarah@gmail.com

Submitted for Publication: 23-02-2023
Accepted for Publication 30-03-2023

How to Cite: Chand A, Tahir FN, Shahbaz R, Salman R, Umar S, Abbas HB. Assessment of Serum Iron Indices and Levels of C-Reactive Protein in Patients of Alcoholic Liver Disease and Their Relationship with Severity of Disease. APMC 2023;17(1):106-111. **DOI: 10.29054/APMC/2023.1277**

ABSTRACT

Background: Diagnosing ALD presents a number of difficulties including early-stage ALD is often symptom-free, and there is currently no confirmed etiological laboratory biomarker or diagnostic test. There have been a few studies on the effects of iron excess on alcohol-related liver disease, but none have examined the correlation between blood iron indices and C-reactive protein or disease severity in the Pakistani population. **Objective:** Therefore, the objective of the study is to assess the serum iron indices and levels of c-reactive protein in patients of alcoholic liver disease and their relationship with severity of disease. **Study Design:** Case control study. **Settings:** This study was conducted in Biochemistry Department of Central Park Medical College, Lahore Pakistan. **Duration:** Six months from January 2022 to June 2022. **Methods:** In this study the demographic details were recorded on a questionnaire. This questionnaire was made to describe the demographic variables age, weight and height for BMI. After taking consents from ALD and healthy individuals the blood was drawn for biochemical analysis. All parameters underwent low and high-level internal quality check before analysis. After ensuring that the standard deviation of the internal quality control was less than one standard deviation. A total of 55 patients of ALD and 55 as healthy control enrolled in this study. The statistical analysis was done by using SPSS version 20. **Results:** The mean age of control group is 42.3 ± 5.0 years and 39.2 ± 4.2 years of ALD patients in case group. The albumin levels were significantly lower in patients with ALD compared to controls ($p<0.001$), while serum iron, ferritin, high-sensitivity C-reactive protein, bilirubin, aspartate transaminase, alanine transaminase, alkaline phosphatase, and prothrombin time were all significantly elevated. The transferrin saturation is increased in ALD group but not significant. The model for end stage liver disease score is a measure of the severity of alcoholic liver disease, and it was shown to be positively connected with iron ($r = 0.345$, $p = 0.014$) and ferritin ($r = 0.456$, $p = 0.012$). Iron ($r = 0.931$, $p <0.001$), ferritin ($r = 0.964$, $p <0.001$) were all significantly correlated with high-sensitivity C-reactive protein in alcoholic liver disease patients. **Conclusion:** Alcohol's effects on iron and proteins in iron metabolism. The effects of alcohol on ferritin and serum iron levels are uncertain and may be either beneficial or detrimental. In this research, patients with alcoholic liver disease had higher levels of serum iron, ferritin, and C-reactive protein, all of which are indicative of iron overload and inflammation. Iron, ferritin, and C-reactive protein levels correlated significantly with the MELD score, indicating that iron excess and inflammation may contribute to the severity of ALD in these patients.

Keywords: *ALD, CLD, Iron indices, CRP, MELD.*

INTRODUCTION

One of the leading causes of the worldwide rise in chronic liver disease (CLD) is alcohol-associated liver disease (ALD)[1]. Because alcohol intake is a cofactor in the pathologies of other CLDs such iron overload hemochromatosis and chronic viral hepatitis. Hepatocellular carcinoma is more likely to occur in those who have a history of heavy alcohol use[2]. Incidence rates of alcoholic liver disease (ALD) are rising in countries like Pakistan. Recent research has linked alcohol use to liver scarring and cirrhosis revealed that 5-15% of individuals with asymptomatic alcoholic fatty liver may develop fibrosis and cirrhosis despite abstinence, and that inflammation and oxidative stress may play a role in this process[3]. Diagnosing ALD presents a number of difficulties including early-stage ALD is often symptom-free, and there is currently no confirmed etiological laboratory biomarker or diagnostic test[4]. In addition, many of these patients fail to accurately disclose their alcohol use. Problems with total abstinence, disease reversal in late stages, and high expenses of ALD therapy are only a few of the obstacles in disease management and medicines[5]. Due to iron loan, the physiology of mesenchymal stem cells is altered, which may have an effect on liver function in pathological situations, and it may also increase hepatic fibrosis, carcinogenesis, and metastasis[6]. Alcohol use, whether short-term or long-term, may interfere with iron homeostasis by decreasing hepcidin production, the iron-hormone released by the liver that controls overall iron levels in the body[7]. Recent research on the effects of moderate alcohol use found that those who drank more than 88 grams per week had elevated iron in the liver, while those who drank more than 56 grams per week had elevated iron in the brain, both of which were linked to worse cognitive performance[8]. In addition, elevated amounts of reactive oxygen species (ROS) are produced during alcohol metabolism and may contribute to oxidative damage, and their combined effects can accelerate the progression of cirrhosis[9]. Cirrhosis from hepatic iron excess is a known risk factor for high sensitivity of C-reactive protein. In addition, alcohol use is a common factor in inhibiting erythropoiesis, which may lead to anemia. Patients with ALD have been studied for the potential ferritin involvement in liver parenchyma fibrogenesis[10]. Patients with ALD had elevated ferritin levels, suggesting that the liver parenchyma contained iron. Five illnesses, including alcoholic liver disease, are associated with elevated levels of the inflammatory marker C-reactive protein (CRP). Serum C-reactive protein levels is elevated to be an effective risk factor predictor for non-alcoholic steatohepatitis[11]. Also, the CRP's is the predictive value in the prognosis of alcoholic hepatitis and alcoholic cirrhosis[12].

There have been a few studies on the effects of iron excess on alcohol-related liver disease, but none have examined the correlation between blood iron indices and C-reactive protein or disease severity in the Pakistani population[13]. The purpose of this research was to examine the relationship between blood iron, ferritin, and CRP levels in individuals with alcoholic liver disease. Therefore, the objective of the study is to determine the association of severity serum iron indices and high-sensitivity C-reactive protein with disease severity in men with alcoholic liver disease.

METHODS

This case control study was completed in the Biochemistry Department of Central Park Medical College, Lahore between January 2022 to June 2022. This study was approved by the Ethical review committee. In this study the demographic details were recorded on a questionnaire. This questionnaire was made to describe the demographic variables age, weight and height for BMI and the history of any disease. After taking consents from ALD and healthy individuals the blood was drawn for biochemical analysis.

Clinical and ultrasonography results were used to identify alcoholic liver disease in males aged 18-65 (n = 55). Since hepatitis and cirrhosis were the most common diagnosis, only those individuals with these conditions were included in the analysis.

Patients with a history of diabetes mellitus, chronic renal failure, ischemic heart disease, gastrointestinal (GI) bleeding within the past three months, concomitant chronic viral hepatitis, use of iron supplements, or an active infection at any site (including peritonitis, urinary tract infections, or pneumonia) within the past two weeks were not eligible to participate. Wilson disease and other metabolic diseases and viral hepatitis were not included since they are not the primary causes of liver damage.

On the WHO sample size calculator, a total of 60 participants were chosen in this study based on a prevalence of 15%[3] of liver cirrhosis prevalence with 95% confidence interval and margin of error was 5%.

A total of 55 patients of ALD and 55 as healthy control enrolled in this study. Participants' venous blood was drawn at a volume of 10 mL. 2 ml in EDTA for the plasma, 2ml in anticoagulant 2 mL for serum collection, 2 ml in fluoride tube for glucose estimation and the remaining 2ml of sample was placed in tubes containing sodium citrate, and the prothrombin time was calculated from this. Liver function test parameters were quickly assessed after the separation of serum. The rest of the sample was frozen at -80 degrees Celsius and analyzed for further test parameters.

Using a clinical chemistry analyzer (name of the analyzer) and reagent kits from (name of company) were used to determine the concentrations of iron and TIBC in the serum. Siemens reagent kits employing the chemiluminescence technique (machine name) were used to calculate ferritin concentrations. Quantitative ELISA kits (kit name) were used to determine serum hs-CRP concentrations. Transferrin saturation (TS (%) = Serum iron 100/TIBC) was determined as the ratio of serum iron to total iron binding capacity. Normal measures for patient management included serum iron, ferritin, and liver function tests were done on clinical chemistry analyzer (name of the analyzer). All parameters underwent low and high-level internal quality check before analysis. After ensuring that the standard deviation of the internal quality control was less than one standard deviation, the samples were evaluated. Quality control for the hs-CRP ELISA was performed using the supplied regents.

The data analysis for this study was carried out using version 20.0 of the IBM-SPSS. Descriptive analysis was performed on demographic factors. The independent t test was used to check the sensitivity and specificity of the assay for the comparison between healthy controls and ALD. For the association the Pearson's correlation was used. If the p-value was lower than 0.05, the data were statistically significant.

RESULTS

Fifty-five male ALD patients and healthy individuals enrolled as case and controls respectively. The mean age of control group is 42.3 ± 5.0 years and 39.2 ± 4.2 years of ALD patients in case group. However, the mean BMI of control group is 18.9 ± 1.2 Kg/m^2 and 23.7 ± 0.7 is significantly increased in ALD patients. The Albumin levels were significantly lower in patients with ALD compared to controls (Table I), while serum iron, ferritin, high-sensitivity C-reactive protein, bilirubin, aspartate transaminase, alanine transaminase, alkaline phosphatase, and prothrombin time were all significantly elevated. The transferrin saturation is increased in the ALD group but not significant.

In Table II, we see that hs-C-reactive protein, the MELD score, and liver function test parameters are all correlated with iron and ferritin levels. The model for end stage liver disease score is a measure of the severity of alcoholic liver disease, and it was shown to be positively connected with iron (r = 0.345, p = 0.014) and ferritin (r = 0.456, p = 0.012). Iron (r = 0.931, p <0.001), ferritin (r = 0.964, p <0.001) were all significantly correlated with high-sensitivity C-reactive protein in alcoholic liver disease patients. Both total bilirubin and albumin were positively linked with iron in alcoholic liver disease individuals (r = 0.94, p<0.001) and (r=0.91, p<0.001). Ferritin is also positively correlated with total bilirubin but negative correlate with albumin.

Table 1: Comparison of biochemical parameters between case and control

Biochemical Parameters		Mean	Std. Deviation	P value
Glucose (mg/dl)	Control	83.5	7.7	0.53
	Case	85.1	8.0	
Urea (mg/dl)	Control	20.7	1.5	.27
	Case	41.3	1.6	
Serum Creatinine (mg/dl)	Control	0.7	0.1	<0.001
	Case	1.7	0.1	
Total bilirubin (mg/dl)	Control	0.8	0.1	<0.001
	Case	7.3	0.1	
Direct bilirubin (mg/dl)	Control	0.3	0.0	<0.001
	Case	3.2	0.1	
Aspartate aminotransferase (IU/L)	Control	26.2	1.0	<0.001
	Case	129.2	6.4	
Alanine aminotransferase (IU/L)	Control	27.3	2.7	<0.001
	Case	66.5	4.8	
Alkaline phosphatase (IU/L)	Control	70.7	2.2	<0.001
	Case	151.8	5.8	
Gamma glutamyl transferase (IU/L)	Control	26.2	1.1	<0.001
	Case	112.7	2.6	
Total Protein (g/dL)	Control	7.3	0.1	.081
	Case	5.8	0.1	
Albumin (g/dL)	Control	4.2	0.1	.016
	Case	2.6	0.2	
Prothrombin time (seconds)	Control	14.3	0.1	<0.001
	Case	25.4	0.4	
INR	Control	1.2	0.1	<0.001
	Case	2.1	0.0	
Iron (µg/dL)	Control	83.7	4.6	<0.001
	Case	156.9	18.7	
Total iron binding capacity (µg/dL)	Control	471.7	26.1	0.141
	Case	466.6	33.7	
Transferrin saturation (%)	Control	25.1	2.6	0.137
	Case	42.6	3.2	
Ferritin (ng/mL)	Control	61.6	5.5	<0.001
	Case	653.5	61.8	
C-reactive protein (ng/mL)	Control	830.3	33.8	<0.001
	Case	8543.9	323.0	

The data are presented as mean and standard deviation (SD). The result was analyzed by using an independent t-test.

Table 2: Association of serum iron indices and high-sensitivity c-reactive protein

Parameters	Iron		Ferritin	
	r	P value	r	P value
Serum Creatinine	0.931	<0.001	0.964	<0.001
MELD Score	0.345	0.014	0.456	0.012
Total bilirubin	0.94	<0.001	0.989	<0.001
Albumin	0.91	<0.001	-0.974	<0.001

The result was analyzed by using a Pearson's correlation.

DISCUSSION

While heavy drinking increases the risk of anemia, the findings show that heavy drinkers are less likely to have iron deficient anemia but increase the iron load on liver[14, 15]. The purpose of this study is the association of severity serum iron indices and high-sensitivity c-reactive protein with disease severity in men with alcoholic liver disease. The body uses iron scavenging mechanisms in the early stages of illness or inflammation to deprive the microorganisms of iron and so prevent the spread of infection[16]. However, within 7-10 days, iron levels are back to normal. Iron was shown to be independently related to infection within 90 days in a study of individuals with alcoholic hepatitis, and a 4.2% reduction in infection risk was seen for every 1 mol/L rise in iron[17]. Therefore, it was proposed that iron deficiency in ALD patients may be utilized to predict infection risk. The need for iron in boosting immunity is borne up by studies showing a decreased risk of infection in correlation with increased iron intake[18]. In fact, the ideas of iron-mediated facilitation of infection and infection control through iron-scavenging mechanisms are showing an increase in iron reduces the risk of infection in previous studies[19, 20]. About half of ALD patients have an increase in hepatic iron storage, which may be caused in part by the alcohol-induced loss of hepcidin, which elevates blood iron levels[21]. There is an increase of serum ferritin in our study may be a result of compensating for rising iron levels in the blood, the result of alcohol's direct stimulation of de novo ferritin synthesis via some as yet unidentified mechanism, or the result of alcohol's induction of inflammation in the body, which is common in ALD, suggested by J Kosha et al[2]. Serum ferritin may be increased by acute liver damage, inflammation, infection, and malignant illness[22]. Ferritin was associated with inflammatory cytokines IL6 and IL8 but not with liver function impairment in heavy drinkers. Thus, serum ferritin concentrations mirror whole body iron storage in both healthy persons and alcoholics with mild liver damage[22]. In the previous study done by Buzzetti E et al., ferritin is employed to diagnose iron insufficiency due to its correlation with iron depletion. However, serum ferritin levels may not represent whole body iron reserves in alcoholics with severe liver damage. There is no correlation between serum ferritin and liver iron reserves in alcoholic liver injury because elevated serum ferritin reflects hepatic inflammation and necrosis. Repeating the impact of alcohol on ferritin, serum ferritin declined in some alcoholics after 1.5 to 6 weeks of sobriety[23]. We hypothesized that a correlation between iron excess and inflammation and the severity of alcoholic liver disease. Serum iron, ferritin, and C-reactive protein were all found to be higher in those with alcoholic liver disease compared to controls, which was the study's most important result. However, transferrin saturation was also elevated in ALD patients but showed no significance. In individuals with alcoholic liver disease, there is a strong correlation between C-reactive protein and the MELD score with ferritin and iron in this study, similarly in Ertan et al[24]. There seems to be a connection between heavy drinking, liver illness, and an excess of iron in the body. Iron overload is more common in those with a history of heavy drinking and alcoholic liver disease[25]. Patients with alcoholic liver disease have been shown to have lower iron and greater ferritin levels compared to controls, according to previous research done by Hakan and Nimet[26]. Patients with ALD were shown to have elevated levels of serum iron, transferrin saturation, and ferritin similarly showed in the study Penkova et al[27]. Amino transferases and gamma glutamyl transferase have been demonstrated to be noninvasive indicators for liver fibrosis in previous research of Laurent et al[28]. Significant correlations were found between iron levels and alanine transaminase and gamma glutamyl transferase in individuals with ALD in the present investigation. These results corroborated previous studies that found elevated serum iron indices in people with alcoholic liver disease (ALD), suggesting that ALD is linked to iron overload[29]. Total iron binding capacity was not significantly different between the two groups, contrary to the results of the aforementioned investigations. Alcohol's influence on hepcidin has been documented by several researchers to improve iron absorption and storage[13].

Our results did not provide a definitive answer to the question of how iron overload contributes to alcoholic liver disease; however, previous experimental research has shown that alcohol decreases hepcidin expression in the liver, which in turn increases the expression of iron transport proteins in the intestine, resulting in greater iron absorption and storage[2, 8]. C-reactive protein (CRP) has been extensively researched as a measure of subacute inflammation since it is an acute phase protein[17]. Patients with liver illness, in addition to those with cardiovascular disease, have been shown to have increased hs-CRP levels. In heavy drinkers, CRP has been shown in previous research to serve as a noninvasive marker of

alcoholic hepatitis. High levels of high-sensitivity C-reactive protein (hs-CRP) have been recorded in patients with alcoholic liver disease, and Chen Q et al. have shown that hs-CRP is related with a poor prognosis in these individuals[30]. Patients with alcoholic liver disease had considerably higher hs-CRP levels than those with no liver disease in the present research. Previous research suggested that hs-CRP might be utilized as a predictor of short-term mortality in alcoholic liver disease patients, and our results corroborate that hypothesis[31]. Liver disease and alcohol-induced iron overload have a comparable mechanism that includes oxidative damage and inflammation. Overloading on iron, which is a pro-oxidant, has been shown to cause the production of harmful free radicals through the Fenton reaction, which may harm proteins, lipids, and nucleic acids directly inside cells. There is evidence that free radicals contribute to the development and release of inflammatory cytokines. C-reactive protein and the model for end-stage liver disease (MELD) score, both indicators of disease severity in alcoholic liver disease patients, were positively linked with iron and ferritin in the current research[23, 32].

This research is the first to examine how alcohol liver damage is linked to iron excess and inflammation in Pakistani population. Our study's strength lies in the fact that we included new instances of alcoholic liver disease prior to any treatment, and we excluded smokers since tobacco use is known to influence several of the test values. Due to the high death rate (1%), liver biopsies were not performed to diagnose coexisting hepatitis and cirrhosis in these patients. The participants' hepcidin levels were not measured. We may have linked alcohol use to iron overload by checking hepcidin levels. Therefore, the lack of hepcidin measurement might be seen as a drawback of the research.

CONCLUSION

The impact of alcohol on iron and proteins involved in iron metabolism. Alcohol consumption may have a positive or negative impact on hemoglobin and serum iron levels, or it may have no effect on these parameters at all. Serum iron, ferritin, and C-reactive protein were all found to be elevated in this study's alcoholic liver disease patients, pointing to iron overload and inflammation. In these individuals, there was a statistically significant correlation between iron, ferritin, and C-reactive protein levels and the MELD score, suggesting that iron overload and inflammation may contribute to the severity of ALD. To learn more about the mechanism of iron overload in alcoholics, researchers need to examine the expression of hepcidin in liver tissues taken from these individuals..

LIMITATIONS

The short sample size with non-alcoholic liver illness makes it difficult to draw firm conclusions about the role of alcohol in the observed variations in research parameters.

SUGGESTIONS / RECOMMENDATIONS

Clinical studies should be conducted to determine whether alcohol liver damage may be mitigated by reducing iron and inflammation.

CONFLICT OF INTEREST / DISCLOSURE

Nil declared by the authors.

ACKNOWLEDGEMENTS

None.

REFERENCES

1. Paik JM, Golabi P, Younossi Y, Mishra A, Younossi ZM. Changes in the global burden of chronic liver diseases from 2012 to 2017: the growing impact of NAFLD. Hepatology. 2020;72(5):1605-16.
2. Mehta KJ, Farnaud SJ, Sharp PA. Iron and liver fibrosis: Mechanistic and clinical aspects. World journal of gastroenterology. 2019;25(5):521.
3. Ballestri S, Mantovani A, Di Girolamo M, Baldelli E, Capitelli M, Lonardo A. Liver fibrosis in nonalcoholic fatty liver disease patients: Noninvasive evaluation and correlation with cardiovascular disease and mortality. Metabolism and Target Organ Damage. 2023;3(1):1.
4. Crabb DW, Im GY, Szabo G, Mellinger JL, Lucey MR. Diagnosis and treatment of alcohol-associated liver diseases: 2019 practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2020;71(1):306-33.
5. Mellinger JL, Winder GS, DeJonckheere M, Fontana RJ, Volk ML, Lok AS, et al. Misconceptions, preferences and barriers to alcohol use disorder treatment in alcohol-related cirrhosis. Journal of substance abuse treatment. 2018;91:20-7.
6. Boey A, Ho HK. All roads lead to the liver: metal nanoparticles and their implications for liver health. Small. 2020;16(21):2000153.
7. Hilton C, Sabaratnam R, Drakesmith H, Karpe F. Iron, glucose and fat metabolism and obesity: an intertwined relationship. International Journal of Obesity. 2023:1-10.
8. Koch M, Fitzpatrick AL, Rapp SR, Nahin RL, Williamson JD, Lopez OL, et al. Alcohol consumption and risk of dementia and cognitive decline among older adults with or without mild cognitive impairment. JAMA Network Open. 2019;2(9):e1910319-e.
9. Karkucinska-Wieckowska A, Simoes IC, Kalinowski P, Lebiedzinska-Arciszewska M, Zieniewicz K, Milkiewicz P, et al. Mitochondria, oxidative stress and nonalcoholic fatty liver disease: A complex relationship. European journal of clinical investigation. 2022;52(3):e13622.
10. Nemeth E, Ganz T. Hepcidin and iron in health and disease. Annual review of medicine. 2023;74:261-77.
11. Kumar R, Porwal Y, Dev N, Kumar P, Chakravarthy S, Kumawat A. Association of high-sensitivity C-reactive protein (hs-CRP) with non-alcoholic fatty liver disease (NAFLD) in Asian Indians: A cross-sectional study. Journal of Family Medicine and Primary Care. 2020;9(1):390.
12. Jeong JH, Lee SB, Sung A, Shin H, Kim DH. Factors predicting mortality in patients with alcoholic liver cirrhosis visiting the emergency department. Medicine. 2023;102(8):e33074-e.
13. Iqbal T, Diab A, Ward DG, Brookes MJ, Tselepis C, Murray J, et al. Is iron overload in alcohol-related cirrhosis mediated by hepcidin? World journal of gastroenterology: WJG. 2009;15(46):5864.

14. Ballard HS. The hematological complications of alcoholism. Alcohol health and research world. 1997;21(1):42.
15. Mueller S, Chen C, Mueller J, Wang S. Novel insights into alcoholic liver disease: Iron overload, iron sensing and hemolysis. Journal of Translational Internal Medicine. 2022;10(2):92-124.
16. Nairz M, Weiss G. Iron in infection and immunity. Molecular Aspects of Medicine. 2020;75:100864.
17. Kong L-Z, Chandimali N, Han Y-H, Lee D-H, Kim J-S, Kim S-U, et al. Pathogenesis, early diagnosis, and therapeutic management of alcoholic liver disease. International Journal of Molecular Sciences. 2019;20(11):2712.
18. Donker AE, van der Staaij H, Swinkels DW. The critical roles of iron during the journey from fetus to adolescent: Developmental aspects of iron homeostasis. Blood Reviews. 2021;50:100866.
19. Weber JJ. Biochemical properties and physiological functions of extracellular iron-binding proteins: Kansas State University; 2021.
20. Wunderer F, Traeger L, Sigurslid HH, Meybohm P, Bloch DB, Malhotra R. The role of hepcidin and iron homeostasis in atherosclerosis. Pharmacological research. 2020;153:104664.
21. Ali N, Ferrao K, Mehta KJ. Liver Iron Loading in Alcohol-Associated Liver Disease. The American Journal of Pathology. 2022.
22. Cullis JO, Fitzsimons EJ, Griffiths WJ, Tsochatzis E, Thomas DW, Haematology BSf. Investigation and management of a raised serum ferritin. British journal of haematology. 2018;181(3):331-40.
23. Buzzetti E, Petta S, Manuguerra R, Luong TV, Cabibi D, Corradini E, et al. Evaluating the association of serum ferritin and hepatic iron with disease severity in non-alcoholic fatty liver disease. Liver International. 2019;39(7):1325-34.
24. Sal E, Yenicesu I, Celik N, Pasaoglu H, Celik B, Pasaoglu OT, et al. Relationship between obesity and iron deficiency anemia: is there a role of hepcidin? Hematology. 2018;23(8):542-8.
25. Gao Y-H, Wang J-Y, Liu P-Y, Sun J, Wang X-M, Wu R-H, et al. Iron metabolism disorders in patients with hepatitis B-related liver diseases. World journal of clinical cases. 2018;6(13):600.
26. Çam H, Yılmaz N. Serum hepcidin levels are related to serum markers for iron metabolism and fibrosis stage in patients with chronic hepatitis B: A cross-sectional study. Arab Journal of Gastroenterology. 2020;21(2):85-90.
27. Radicheva MP, Andonova AN, Milcheva HT, Ivanova NG, Kyuchukova SG, Nikolova MS. Serum markers of iron metabolism in chronic liver diseases. Open Access Macedonian Journal of Medical Sciences. 2018;6(6):1010.
28. Castera L, Friedrich-Rust M, Loomba R. Noninvasive assessment of liver disease in patients with nonalcoholic fatty liver disease. Gastroenterology. 2019;156(5):1264-81. e4.
29. Wu X, Wang Y, Jia R, Fang F, Liu Y, Cui W. Computational and biological investigation of the soybean lecithin–gallic acid complex for ameliorating alcoholic liver disease in mice with iron overload. Food & function. 2019;10(8):5203-14.
30. Chen Q, Li Q, Li D, Chen X, Liu Z, Hu G, et al. Association between liver fibrosis scores and the risk of mortality among patients with coronary artery disease. Atherosclerosis. 2020;299:45-52.
31. Mikolasevic I, Pavic T, Filipec Kanizaj T, Bender DV, Domislovic V, Krznaric Z. Nonalcoholic fatty liver disease and sarcopenia: where do we stand? Canadian Journal of Gastroenterology and Hepatology. 2020;2020.
32. Starlinger P, Ahn JC, Mullan A, Gyoeri GP, Pereyra D, Alva-Ruiz R, et al. The addition of C-reactive protein and von Willebrand factor to Model for End-Stage Liver Disease-Sodium improves prediction of waitlist mortality. Hepatology. 2021;74(3):1533-45.