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Circulatory Levels Of Ferritin And High-Sensitivity C-Reactive Protein In Alcoholic Liver Disease

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Abstract

Introduction: India is observing tremendous increase in the population with chronic alcohol consumption which are suffering from alcoholic liver diseases. Iron overload is an important factor which plays a crucial role in disease progression. Inflammation is also a crucial factor and the objective of the study is to evaluate the serum ferritin and hsCRP levels in alcoholic liver disease.

Materials and methods: The present included 160 alcoholic liver disease cases and 160 healthy controls. The study estimated the circulatory levels of serum ferritin and high-sensitivity C-reactive protein in both study groups. An increased levels of serum ferritin and high-sensitivity C-reactive protein were observed in ALD group than healthy controls (701 ± 226.8/ 86.3 ± 25.7) and (4.6 ± 1.54/ 2.4± 0.63) respectively.

Results: It was observed that serum iron, ferritin, and hsCRP were significantly increased in alcoholic liver disease patients compared to controls. The study observed that serum ferritin and hsCRP have shown a very significant increase in alcoholic liver disease cases as compared to controls.

Conclusion: The present study concluded that serum ferritin and hsCRP were elevated in alcoholic liver diseases which indicate the role of oxidative stress and inflammation in ALD.

Keywords: Alcoholic liver diseases, Ferritin, hsCRP

Introduction

Alcoholic liver disease (ALD) is becoming more common in India due to high degree of alcohol consumption. According to a recent study, alcohol consumption is the main factor contributing to liver cirrhosis and fibrosis (1). Previous research has revealed that despite abstinence, 5–15% of patients with asymptomatic alcoholic fatty liver may advance to fibrosis and cirrhosis. It has also suggested that oxidative stress and inflammation may be factors in the development of cirrhosis (2,3). Iron is thought to be a risk factor in the development of numerous liver conditions (4,5). It is well recognized that iron and ferritin are critical factors for initiation and progression of of ALD (5). Hepatic iron overload and increased serum iron indices have been linked to ALD. According to a recent study, Iron overload has been shown in earlier studies to be a predictor of death in alcoholic cirrhosis patients (7). Previous research have looked into the role ferritin plays in the fibrogenesis of the liver parenchyma in patients with ALD. Ferritin has been demonstrated to be an indicator of iron accumulation in ALD patients' liver parenchyma (5).

An inflammatory measure called C-reactive protein (CRP) has been observed to rise in a number of diseases, including alcoholic liver disease. Serum C-reactive protein measurement has been demonstrated in earlier research to be helpful also in determining the risk of non-alcoholic steatohepatitis (8). Additionally, research has shown that CRP is a useful predictor of the outcome for alcoholic cirrhosis and hepatitis (9).

While a few research articles provided an important information on iron overload in alcohol-related liver disease, and also the relationship between blood iron indices, C-reactive protein, and the severity of the disease in the Indian population; our study also evaluated this correlation in ALD patients. The purpose of the current study was to examine serum iron, ferritin, and CRP levels and their relationship to the severity of the ALD.

Materials And Methods

This study was a prospective case control study conducted at D Y Patil Medical College and Hospital in Navi Mumbai. The institutional ethics committees for human studies at D Y Patil Medical College and Hospital accepted the study. For every subject, written informed permission was acquired. After fulfilling the inclusion and exclusion criteria, 160 consecutive patients with alcohol-related liver disease were chosen for the study. The 160 male healthy volunteers who made up the controls ranged in age from 35 to 65.

Inclusion/ Exclusion Criteria

Males aged 35–65 years who were diagnosed as alcoholic liver disease based on clinical and ultrasound findings were included in the study. As most of the patients presented with the signs and symptoms of hepatitis and cirrhosis, the study included only these two groups in the study.

Patients with history of diabetes mellitus, pre-existing renal failure, ischemic heart disease, GI bleeding within the past 3 months, co-existent chronic viral hepatitis, those who are on supplements with iron and active infection at any site such as peritonitis, urinary tract infections or pneumonia within the past 2 weeks were excluded. The other causes of liver disease due to viral infection, drugs, malignancies and metabolic disorders like Wilson disease were also excluded from the study.

Methodology:

Fasting venous blood were drawn from each participant. After separating the serum, the parameters of the liver function test were promptly estimated. The leftover sample was kept at -80°C and utilized to examine the test parameters.

Using commercially available kit method serum ferritin was evaluated in a clinical chemistry analyzer. The liver function test parameters were routine parameters analyzed for patient care services. HsCRP was analyzed using ELISA where quality control was done with regents provided with the kits.

Statistical Analysis:

Statistical analysis was done on version 23.0 of the SPSS program (IBM SPSS Statistics,). The findings were presented as median (range) and mean ± S.D. The "t" test was used to compare the data between the cases and controls. A significant p-value was defined as one less than 0.01.

Results

The study included 160 controls and 160 patients with ALD. In patients with ALD, it was observed that the serum albumin levels were significantly lower than in controls, while serum bilirubin, aspartate transaminase, alanine transaminase, alkaline phosphatase, Gamma glutamyl transferase and prothrombin time were significantly higher in ALD patients. An increased levels of serum ferritin and high-sensitivity C-reactive protein were observed in ALD group than healthy controls (701 ± 226.8/ 86.3 ± 25.7) and (4.6 ± 1.54/ 2.4± 0.63) respectively.

Discussion

The present investigated the relationship between iron excess and inflammation and the severity of alcohol-related liver damage in the current study. Our study's main conclusions are that alcoholic liver disease patients have higher levels of serum ferritin, and C-reactive protein than control subjects.

There are reports of a correlation between iron overload, liver illness, and alcohol usage. It has been demonstrated that alcoholic liver disease and chronic alcohol use raise the incidence of iron overload. Husić-Selimović et al. found that patients with alcoholic liver disease had higher serum iron, transferrin saturation, and total iron binding capacity

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than controls, but there was no discernible difference in ferritin levels between the two groups (5).

When compared to controls, previous researchers have found that individuals with alcoholic liver disease had much lower iron and greater ferritin levels (12). Patients with ALD showed significantly higher serum iron, ferritin, and transferrin saturation in their studies. Amino transferases and gamma glutamyl transferase have been demonstrated in earlier research to function as important indicators of liver fibrosis (13). In individuals with ALD, gamma glutamyl transferase and alanine transaminase showed a substantial correlation with iron and ferritin. These results are consistent with previous studies that showed elevated ferritin and hsCRP in ALD participants, and it suggests that iron excess is linked to alcoholic liver disease (6).

Alcohol's impact on hepcidin has been linked by several researchers to improved iron absorption and storage (14). Although the mechanism underlying iron overload in alcoholic liver disease, experimental research has shown that alcohol decreases the expression of hepcidin in the liver, which in turn causes the expression of iron transport proteins to be elevated in the intestine, increasing the absorption and storage of iron (15, 16).

C-reactive protein (CRP), an acute phase protein is widely studied as a marker of low grade inflammation (17). Apart from cardiovascular diseases elevated hsCRP levels have been documented in patients with liver disease. Previous studies have indicated that CRP can be used as a prominent marker of alcoholic hepatitis in heavy drinkers (9). Ciećko-Michalska et al. have reported high hsCRP levels in alcoholic liver disease patients and demonstrated that hsCRP is associated with poor prognosis in these patients (18). In the current study hsCRP levels were significantly elevated in alcoholic liver disease patients compared to non alcoholic subjects without any liver disease. These findings were supported by earlier studies which hypothesized that hsCRP can be used as a predictor of short term mortality in ALD patients.

Acute phase protein C-reactive protein (CRP) is extensively researched as a marker of low grade inflammation (17). Patients with liver illness have been reported to have increased hsCRP levels in addition to cardiovascular disorders. Prior research has demonstrated that CRP is a noninvasive marker. A shared pathway including oxidative stress and inflammation has been identified as the connection between alcohol-induced iron overload and liver disease. Being a pro-oxidant, iron overload has been shown to produce harmful free radicals through the Fenton reaction, which in turn causes damage to cellular lipids, proteins, and nucleic acids. According to reports, free radicals contribute to the activation and maturation of pro-inflammatory cytokines, which in turn cause inflammation (20, 21). The results of our study suggest that iron overload linked to inflammation may cause liver injury, which in turn increases the severity of the disease and may be connected to complications related to alcoholic liver disease, even though the presence of inflammation is well established in alcoholic liver disease.

This study will provide a supportive evidence to the previously published studies on Indian population to investigate the relationship between inflammation and iron excess and the severity of alcohol-related liver damage. The study's primary limitations are its small sample size and the absence of a second control group with non-alcoholic liver disease, which would have allowed researchers to link the variations in parameters to alcoholic liver disease. The hepcidin levels were not estimated in the present study.

Conclusion:

In individuals with alcoholic liver disease, the current investigation observed elevated levels of serum ferritin, and hsCRP, indicating iron overload and increased inflammation. To learn more about the mechanism underlying iron overload in individuals with alcohol-related liver disorders, more research is required to examine the expression of iron storage proteins. It will be necessary to conduct more clinical trials to determine whether reducing inflammation and oxidative stress can lessen the severity of alcohol-related liver damage.

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"Table 1: Comparison of biochemical findings between ALD and controls"

Parameters	***Controls (n = 160)***	***Alcoholic liver disease (n = 160)***	***p value***
Age (years)	52.7 ± 7.2	54.4 ± 7.1	0.114
Blood glucose (mg/dL)	88.3 ± 8.4	90.7 ± 17.3	0.136
Blood urea (mg/dL)	22.4 ± 4.6	43.9 ± 22.4	<0.01
Serum creatinine (mg/dL)	0.8 ± 0.21	1.9 ± 1.2	<0.01
Total bilirubin (mg/dL)	0.9 ± 0.20	7.6 ± 6.5	<0.01
Direct bilirubin (mg/dL)	0.31 ± 0.13	4.1 ± 3.7	<0.01
Aspartate aminotransferase (IU/L)	28 ± 4.6	134.6 ± 72.4	<0.01
Alanine aminotransferase (IU/L)	30.3 ± 7.3	74.3 ± 35.3	<0.01
Alkaline phosphatase (IU/L)	72.3 ± 16.3	152.3 ± 86.4	<0.01
Gamma glutamyl transferase (IU/L)	26.2 ± 11.3	110 ± 22.3	<0.01
Total Protein (g/dL)	7.3 ± 0.42	6.3 ± 1.2	<0.01
Albumin (g/dL)	4.5 ± 0.31	2.6 ± 0.48	<0.01
Ferritin (ng/mL)	86.3 ± 25.7	701 ± 226.8	<0.01
hsCRP(ng/mL)	2.4± 0.63	4.6 ± 1.54	<0.01

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