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Alpha-fetoprotein and high sensitive C-reactive protein levels in Iraqi patients with liver cirrhosis

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ABSTRACT

Background: Liver-related death globally is caused mainly by cirrhosis. It is the final grade of extensive liver fibrosis, in which the hepatic architecture is modified. Cirrhosis is a common disease worldwide and can be the end stage for several reasons such as obesity, non-alcoholic fatty liver, alcoholism, viral infection such as viral hepatitis, immune disorders, bile duct obstruction, and metabolic diseases. Alpha-fetoprotein (AFP) is defined as a protein secreted by the germinal yolk sac and liver. AFP level is used as a marker to diagnose inherited disorders and chromosomal anomaly, whereas the high-sensitivity C-reactive protein (hs-CRP) has a separate correlation with NAFLD. Therefore, hs-CRP can be used as a beneficial marker for identifying liver defects.

Subjects and Methods: Thirty participants with liver cirrhosis and 30 healthy participants as control (male and female) were enrolled. The participants from Baghdad, Iraq, were enrolled in this study. Blood and serum samples were obtained for the estimation of hemoglobin, serum AFP, and hs-CRP levels.

Results: The pooled data of participants showed that hs-CRP and alpha-fetoprotein levels in the participants with cirrhosis were significantly higher than in the control group, $P<0.0001$. There were no significant differences in the sexes while considering alpha-fetoprotein, whereas hs-CRP levels were higher in males compared with females.

Conclusion: This research shows a significantly high level of hs-CRP and alpha-fetoprotein in patients with liver cirrhosis compared with the control participants. There were non-significant gender differences concerning alpha-fetoprotein with significantly high level of hs-CRP in males compared with females.

Keywords: *Liver cirrhosis, alpha-fetoprotein, hs-CRP.*

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INTRODUCTION

Liver-related death globally is caused mainly by cirrhosis.[1] It is the final grade of extensive liver fibrosis, in which the hepatic architecture is altered.[2]

Cirrhosis is a common disease globally and can be the end stage for several reasons such as obesity, non-alcoholic fatty liver disease, alcoholism, viral infection such as viral hepatitis, immune disorders, bile duct obstruction, and metabolic diseases. Cirrhosis occurs after a continued period of inflammation, which leads to the restoration of hepatocytes with fibroid tissue and reestablished buds, causing portal hypertension.[3]

Alpha-fetoprotein (AFP) is defined as a protein secreted by the germinal yolk sac and liver.[4] AFP levels used are used as a partition test for inherited disorders, chromosomal anomalies, in addition to other adult malignancies and disorders.[5] This biochemical indicator is a glycoprotein. In a growing human fetus, its level increases from the second trimester and decreases after 32 weeks of gravidity.[6] In cancer or by rejuvenated hepatocytes, the AFP level may be increased, and is also intermittently increased in chronic active hepatitis C cases. AFP can also be high in several other cases, such as a hepatitis B infection, after liver resection, or during recovery after a hepatic toxic injury.[7]

AFP rises, between 50 and 500 ng/ml, were found in 40% of patients with acute and chronic viral hepatitis.[8] and massive hepatic necrosis. Active hepatocyte generation after hepatic degeneration with AFP elevation indicates hepatocyte regeneration.[9] A diacritic type of cell damage or renovated hepatocyte modification in some patients with liver cirrhosis may be caused by viruses and certain other hepatic toxins, leading to AFP production and deliverance into the serum.[10]

C-reactive protein (CRP) is a non-restricted acute-phase protein formed by the liver as feedback to extensive and chronic inflammation, and thus equates to a molecular clue for inflammation, infection, and damage and tissue degeneration.[11] Previous studies have established that the serum CRP level can be used not only to determine the sharpness of liver damage and fibrosis in liver steatosis and chronic HCV, but additionally behaves as an autonomous marker for impecunious individuals with hepatocellular carcinoma.[12]

High-sensitive C-reactive protein (hs-CRP) is correlated with liver inflammation. In addition, the summation classification in a Japanese study concluded that hs-CRP has been considered a part of progression in non-alcoholic fatty liver disease (NAFLD).[13]

In a cohort study of the Indian community, hs-CRP has a self-supporting correlation with NAFLD. Therefore, hs-CRP may act as a good marker for liver disease determination.[14]

Recent studies indicate that a higher level of hs-CRP is correlated with NAFLD.

The foretelling of hepatitis B and its related problems can be estimated by using hs-CRP.[15]

MATERIALS AND METHODS

This study was conducted on 30 individuals with liver cirrhosis and 30 healthy individuals as control (male and female). The specimens were obtained from participants from Baghdad, Iraq, between December 2017 and June 2018. Specimens were obtained by a vein slit. The collected specimens were transferred to patent tubes and left to coagulate at room temperature (20–25°C) for 15 min. The coagulated specimens were centrifuged at 2000 rpm for 15 min; soon after, the sera were distributed into parts of 200 µl in mini tubes, which were reserved in a freezer. After procuring and gathering of all specimens, the sera were thawed to quantify the AFP and hs-CRP levels in the sera with the ELISA technique, using a kit manufactured by Ray Bio Tech Co., USA.

The participants included in this research were of different sexes, within the age range of 25–65 years, with no other conditions and they were civilians.

Statistical Analysis

SAS (2012) Statistical Analysis System program was handling to assay the alteration agents in the research criterion. A *t*-test was used to assess the cogent discrimination among means. Correlation coefficient midway factors were estimated randomly in this study.[16]

RESULTS AND DISCUSSION

High sensitive CRP level

This study indicated that hs-CRP levels in patients with liver cirrhosis were significantly higher than in control, P<0.0001 as shown in Table 1, C-reactive protein (CRP) was thought to be an indicator for acute and chronic integrated inflammation and microbial contagion, although increased values have been found in several disorders, such as acute alcoholic hepatitis, cancer (including hepatocellular carcinoma).[17]

CRP levels reflect a good indicator in patients with cirrhosis, principally in the acute liver failure. CRP is useful to diagnose individuals with cirrhosis who have a low short-term speculation.[18] Chian et al. indicate that high hs-CRP values not only correlate with liver disease determinants, but also with cardiovascular risk.[19] In another case-controlled study, proinflammatory cytokines like IL-6 and TNF-α, and hs-CRP levels were higher in the patients with cirrhosis than in healthy individuals.[20]

Alpha-fetoprotein level

In this study, it was shown that AFP levels in patients with liver cirrhosis was significantly higher than in the control group, 9.75 ± 0.63 ng/ml and 5.32 ± 0.26 ng/ml, respectively, P<0.0001 as illustrated in Table 1. There are articles of altitude of up to 1000 ng/mL and straight over this amount in individuals with chronic hepatitis and cirrhosis.[21–24]

Horváth and coworkers[25] demonstrated that AFP levels might exceed the normal value with no HCC. The reason for the increased AFP levels found in cirrhosis could be due to high liver regeneration following HCV produced cell death. Hepatocyte damage and hepatic regeneration is considered the cause for the elevation in serum AFP levels.[26] Proliferation of hepatocytes during hepatic regeneration is also collaborated with discrimination of hepatocytes and elevated level of AFP in the liver.[27] Increased hepatocyte-hepatocyte interaction may cause the loss of normal hepatic architecture.[28]

TABLE 1. Patients high-sensitive C-reactive protein, hemoglobin, and alpha-fetoprotein levels compared with the control group.

Group	Mean ± SE		
	Hb (g/dL)	AFP (ng/ml)	hs-CRP (mg/ml)
Patients	8.58 ± 0.18	9.75 ± 0.63	3.39 ± 0.35
Control	12.67 ± 0.11	5.32 ± 0.26	0.443 ± 0.04
t-test	0.432**	1.372**	0.716**
P-value	0.0001	0.0001	0.0001

**P<0.05; **P<0.01.*

Hemoglobin level

In this study, hemoglobin level in patients with cirrhosis was indicatively lower than in the control group, 8.58 ± 0.18 g/dl and 12.67 ± 0.11 g/dl, respectively, P<0.01, as shown in Table 1.

Anemia is the most common symptom of liver cirrhosis and is present in 75% of the cases.[29] The cause of anemia in liver cirrhosis is complicated. Known causes include acute and chronic blood loss, malnutrition, malabsorption vitamin B12 and folate deficiency, hypersplenism secondary to portal hypertension[30,31], bone marrow toxicity caused by alcohol. Drugs such as ribavirin and interferons may cause anemia in patients with chronic hepatitis C virus. Aplastic anemia, which is associated with individuals with hepatitis by pancytopenia and hypocellular bone marrow, appears within 6 months of infection with hepatotropic viruses such as hepatitis B, hepatitis C, and Epstein–Barr virus.[32]

In a previous study, the extent of anemia was 66% along with 7% of patients with oppressive

TABLE 2. Effect of sexes on the studied parameters.

Parameters	Mean ± SE		T-Test
	Male	Female	
hs-CRP (mg/ml)	4.33 ± 0.67	2.83 ± 0.36	1.424*
Hb (g/dL)	8.94 ± 0.27	8.38 ± 0.23	0.758 NS
AFP (ng/ml)	9.32 ± 1.17	10.00 ± 0.76	2.732 NS

NS: Non-significant.
** (P<0.05).*

anemia—these counts are equivalent to other investigations.[33,34] Anemia is firmly associated with portal hypertension and its prognosis in these patients due to hepatic decompensation and refractory ascites.[32] and in liver cirrhosis portal hypertension-induced anemia due to gastrointestinal (congestive) hemorrhage and pancytopenia as a result of hypersplenism.[33,34]

Effect of sexes on studied parameters

Alpha-fetoprotein levels showed non-significant differences between male and female sexes in this study, as shown in Table 2. Generally, the plasma AFP levels in the males are slightly higher than that in the females.[34-38]

Although the hs-CRP level in males was significantly higher than in the females in this study, as shown in Table 2, females had higher CRP levels than males, and differences in races and sexes exist in the CRP levels of the population distribution.[39]

CONCLUSIONS

This study showed a significantly high level of hs-CRP and alpha-fetoprotein in patients with liver cirrhosis compared with the control group.

There are non-significant differences in sexes concerning alpha-fetoprotein with significantly high level of hs-CRP in males compared with females.

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