

Assessment of Tissue inhibitor of metalloproteinase-1 and many biochemical parameters in patients with chronic hepatitis B in Tikrit city

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ABSTRACT: The main objective of this study to assess biomarkers associated with liver fibrosis, namely Tissue inhibitor of metalloproteinase 1 TIMP-1, alanine transaminase ALT, aspartate aminotransferase AST, and Alkaline phosphatase ALP. The study investigated 90 samples, their age (20-68). The sample collected from patients in Dialysis Unit in Tikrit Teaching Hospital from September 2022 to March 2023. The samples were divided into three groups, the first group for patients with chronic hepatitis B (G1). The second group for patients with chronic hepatitis B suffered of chronic kidney diseases (G2). The third group for healthy individual as control group (G3). Enzyme linked immunosorbent assay (ELISA) kits were employed to assess serum concentrations of (TIMP-1), Whereas used Monarch-240 to detect the activity of enzymes such as ALT, AST and ALP.

The findings of the present investigation demonstrated in chronic hepatitis patients there were significant increased ($P \leq 0.05$) in the levels of TIMP-1, and activity of ALT and ALP whereas no significant rise ($P \geq 0.05$) for activity of AST when compared with control. In patients with chronic hepatitis B (CHB) suffered of chronic kidney diseases (CKD) there were significant raised ($P < 0.05$) in the levels TIMP-1, ALT and ALP while no significant raised ($P \geq 0.05$) in levels of AST when compared with control.

Current data suggest that TIMP-1 can be a promising biomarker of active fibrogenesis, after HBV chronic infection.

Keywords: chronic hepatitis B, Tissue inhibitor of metalloproteinase 1 TIMP-1, alanine transaminase ALT, aspartate aminotransferase AST, and Alkaline phosphatase ALP.



1. INTRODUCTION

Liver fibrosis (LF) is a significant Globally public health issue linked to significant mortality and morbidity. Its incidence is increasing in both the adult and pediatric populations [1]. Drug-induced hepatotoxicity, Steatohepatitis, immunological liver disorders, chronic liver infections, alcohol dependence, and schistosomiasis are all etiological factors associated with the progression of liver fibrosis. The prevalence of liver fibrosis is primarily attributed to chronic infection with hepatitis viruses, which stands as the most prevalent identified risk factor [2]. The accumulation of extracellular matrix proteins is a consequence of chronic liver injury, leading to the degradation of the hepatic structure. Consequently, irrespective of the underlying etiology, the condition of liver fibrosis can advance to the final stage known as liver cirrhosis. (LC) [3]. The differentiation between asymptomatic liver fibrosis and cirrhosis is of critical significance in the effective management of chronic liver disease [4]. Cirrhosis is an important risk indicator for Hepatocellular carcinoma (HCC), and severe liver fibrosis is strongly linked to HCC risk [5]. A growing body of research suggests that if treated early on, liver fibrosis can be reversed. However, there is no effective and particular drug in clinical practice for the treatment of liver fibrosis[6]

The aim of the study: The purpose of the research is to Investigating the role of TIMP-1 as Indicator for liver fibrosis sand measurement of activity of some liver enzymes such as ALP, ALT and AST.

2. MATERLIAS AND METHOES

The study investigated 90 samples, their age (20-68) for both sexes. The sample collected from patients in Dialysis Unit in Tikrit Teaching Hospital from September 2022 to March 2023. The samples were divided into three groups, the first group (G1) for patients with chronic hepatitis B (n:30). The second group(G2) for patients with chronic hepatitis B suffered of chronic kidney diseases (n:30). The third group(G3) for healthy individual as control group (n:30). 4 mL of venous blood was obtained from each patient. The blood was placed in a Gel tube without any anticoagulant in order to obtain serum. Subsequently, the tube was left at room temperature (20-25°C) until coagulation occurred. The coagulated blood was thereafter subjected to centrifugation at a rotational speed of 3500 revolutions per minute for a period of 5 minutes. Following centrifugation, the serum was extracted using a micro pipette and distributed equally into two ependorf tubes that were without of coagulants. The tubes were securely sealed, and the serum was subsequently stored at -20C° temperature for future use in tests. Enzyme linked immunosorbent assay (ELISA) kites were employed to assess serum concentrations of (TIMP-1), Whereas used Monarch-240 to detect the activity of enzymes such as ALT, AST and ALP.

3. RESULTS

Table (1): The findings of the present investigation, indicate a statistically significant ($P < 0.05$) increase (483.3 ± 59.1) in the patients diagnosed with G1 and (468.2 ± 50.7) in patients with G2 in compared with G3. The findings indicated that there were notable disparities between the patient's groups and the control samples group.

Table (1) shows result of TMIP-1(Pg/ml) in study sample

Groups	N0. Individuals	TIMP-1
(G1) G1means patients with chronic hepatitis B	n=30	483.3 ± 59.1 a
(G2) G2means patients with chronic hepatitis B suffered by chronic kidney diseases	n=30	468.2 ± 50.7 a
Control	n=30	282.7 ± 47.5 b
P-value		*0.05

Table (2): The findings of the present investigation show significant ($P < 0.05$) statistical disparities in mean \pm SD of ALT between the groups that were (18.07 \pm 10.55) in G1, (8.15 \pm 5.94) in G2, (9.35 \pm 6.42) in G3. The study revealed that there is significant differences between G1 and G3, while there is no observed differences between G2 and the G3.

Whereas no statistically significant ($P \geq 0.05$) alterations in the levels of AST among G1 that were (34.59 \pm 4.51) and G2 that were (29.21 \pm 3.41), when compared to the G3.

While mean \pm SD of ALP show significant ($P < 0.05$) disparities between the groups. These results show that (311.5 \pm 20.2) in G2. The group of G1 had the lowest values (276.9 \pm 30.3) when compared to the G3. The results also indicate notable distinctions among (G1), (G2), and a G3.

Table (2) Comparison between CHB, chronic hepatitis B suffered of chronic kidney diseases, and control in regarding the mean of ALT, AST and ALP.

Groups	ALT(U/L)	AST(U/L).	ALP(U/L)
(G1)	18.07 \pm 10.55a	34.59 \pm 4.51a	276.9 \pm 30.3b
(G2)	8.15 \pm 5.94b	29.21 \pm 3.41a	311.5 \pm 20.2a
Control	9.35 \pm 6.42b	27.77 \pm 3.08a	243.8 \pm 29.2c
P-Value	0.05**	ns	0.05*

4. DISCUSSION

Liver fibrosis is a common feature in chronic active liver disease, and is characterized by an accumulation of extracellular matrix proteins. This accumulation can be the result of an increase in synthesis or a decrease in degradation or a combination of both. MMPs play an important role in the degradation of extracellular matrix proteins. The biological activity of MMPs, which are secreted in an inactive proenzyme form and activated extracellularly, is regulated mainly by the specific inhibitors secreted from the local tissue such as TIMPs [8,9]. The study shows elevated TIMP-1 in patients with CHB, and patients with CHB suffered by chronic kidney diseases. This study agrees with [10] that show high TIMP-1 levels in CHB, who suggest high TIMP-1 levels may inhibit active MMP matrix metalloproteinases (MMP-1 and MMP-3) to form tight, non-covalent 1:1 complex and thus suppress the degradation of ECM, leading to the accumulation of ECM in liver tissue and contributing to the progression of liver fibrosis in CHB patients.

Other study shows a strong correlation between the levels of TIMP-1 and the onset and progression of liver fibrosis [11,12]. Moreover, previous studies have demonstrated a correlation between TIMP-1 and the progression of cardiac fibrosis (13), renal fibrosis (14), and pulmonary fibrosis (15).

The results show high level of ALT in CHB patients that agree with [16] who founds the Patients with severe fibrosis exhibited considerably higher ALT (alanine amino transferase) level. However [17] founds that some chronic HBV carriers develop significant hepatic necroinflammation and fibrosis despite having persistently normal or slightly abnormal ALT values.

The outcomes of AST investigation agree with [18] who founds AST had predictive value for advanced liver cirrhosis but was less sensitive in identifying fibrosis stages

The present study's findings agreed with the previous study's findings of [19] who indicated that ALP is extremely important in people with liver disorders. Serum ALP activity has been reported to be elevated in certain liver ailments

and osteoblast bone diseases. Any of the liver, gall bladder, pancreas, or duodenum may be involved in biliary tract congestion or obstruction [20].

The progression of liver fibrosis causes the obstruction of bile ducts and damages the hepatocytes, particularly in CHB patients. TIMP-1 was found to be significantly correlated with the AST, but not ALT, in our patients. Given that AST is valuable biomarkers on bile duct obstruction and liver damage, the significant correlation may reflect severe fibrosis in CHB patients. This, together with the correlation between serum TIMP-1 and the grade of liver inflammation, suggests that liver inflammation accelerates the progression of liver fibrosis, leading to progressive liver damage in CHB patients [10,21,22]

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5. CONCLUSION

Current data suggest that TIMP-1 can be a promising biomarker of active fibrosis, after chronic infection with hepatitis B virus.

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