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Study of serum cholinesterase as a biomarker in a sample of patients with viral hepatitis B or hepatitis C in Baghdad

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***Abstract*---**The most prevalent illnesses that affect the liver are viral infections; when the liver cell is destroyed by viruses, it loses its function and most of the body's processes are compromised. The liver is the primary source of serum cholinesterase. Therefore, serum cholinesterase can be used as a predictive biomarker for the liver's synthetic capability. This study aims to evaluate serum cholinesterase as a biomarker in patients with hepatitis B virus (HBV) or hepatitis C virus (HCV). The study was conducted at the Gastroenterology and Hepatology Teaching Hospital and Poisoning Consultation Center in Baghdad during the interval from November 2021 to March 2022. The liver function tests and serum cholinesterase were measured in one hundred fifty samples. Fifty patients with HBV and fifty patients with HCV were compared with fifty healthy individuals as a control group. The mean serum cholinesterase in the HBV and HCV patient groups (8528.76±2000.45 U/L and 7494.12± 2586.30 U/L, respectively) was lower than in the control group (9380.12±1848.96 U/L), and the difference was statistically significant ($P < 0.05$). The mean serum cholinesterase in the HCV patient group (7494.12±2586.30 U/L) was significantly lower ($P < 0.05$) than in the HBV patient group (8528.76 ±2000.45 U/L). In conclusion, serum cholinesterase test can be used to monitor liver function in patients with HBV or HCV.

***Keywords*---**HBV, HCV, serum cholinesterase.

Introduction

Hepatitis is characterized by liver inflammation. Although inflammation can occur concurrently or by cause of both alcoholic and non-alcoholic steatosis, liver inflammation can occur as a result of viral infection only (1). Viral hepatitis B is a contagious illness that leads to a variety of conditions, ranging from mild hepatitis to serious disorders like fulminant hepatitis or chronic hepatitis marked by persistent inflammation that may lead to liver cirrhosis or liver cell cancer (2). HCV infection can result in both acute and chronic hepatitis. It is uncommon for an acute infection to heal on its own; between 75% and 85% will progress to a chronic infection. Asymptomatic people will make up 50–85% of those infected with the virus. Chronic hepatitis C is a slow-progressing illness that produces continuous inflammation; 20% of patients will progress to cirrhosis within 20 to 30 years (3).

Tests that evaluate liver function are elevated in non-liver disease. For example, transaminase levels in heart disease, alkaline phosphatase levels in bone disease, and so on. Therefore, a more precise and sensitive test for diagnosing liver disease is needed (4). Cholinesterases are a class of enzymes that catalyze the breakdown of the neurotransmitter acetylcholine, producing choline and acetic acid, a necessary process for cholinergic neurotransmission to be restored (5). Cholinesterases are classified into two types: acetylcholinesterase (AChE) and butyryl cholinesterase (BChE). AChE (true cholinesterase) is found in the central nervous system, platelets, and erythrocyte membrane, whereas BChE is more frequent in serum and is made in the liver (6). BChE is also known as serum cholinesterase, nonspecific cholinesterase, or pseudocholinesterase (7). Because BChE is mostly made in the liver and is primarily found (about one-third) in serum, liver pathologies such as acute hepatitis, chronic liver disorders, hepatocellular carcinoma, and liver cirrhosis may reduce BChE levels in serum (8,9).

Materials and Methods

This study was conducted at the Gastroenterology and Hepatology Teaching Hospital and Poisoning Consultation Center in Baghdad during the interval from November 2021 to March 2022. A total of 150 blood samples were collected from 100 patients with viral hepatitis (50 with HBV and 50 with HCV) and 50 apparently healthy individuals as a control group. Inclusion criteria were patients with chronic hepatitis B or hepatitis C, with the exclusion of patients with hemolytic anemia, hemophilia, cancer, other chronic diseases, and organophosphorus poisoning, as well as pregnant women and female patients taking oral contraceptive pills. The patients were diagnosed by a specialist physician.

All patients and controls who gave their consent to be sampled were investigated for alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), total serum bilirubin (TSB), direct bilirubin (DBIL), total protein (TP), serum albumin (ALB) and serum cholinesterase (CHE) using an autoanalyzer (Cobas c311 analyzer, Roche Diagnostic Company).

Statistical analysis

The Statistical Package for Social Sciences version 26 (SPSS-26) was used to analyze the data. The qualitative data was presented as frequency and percentage, while the quantitative data was presented as mean ± standard deviation (SD). The significance of the difference between the two means was determined using an independent sample t-test and a paired sample t-test. Statistical significance was considered when the p-value was equal to or less than 0.05. When the p-value was equal to or less than 0.01, the difference was considered highly significant.

Results

From 100 viral hepatitis patients, 51 (51%) were females and 49 (49%) were males. In the control group, 25 (50%) were females and 25 (50%) were males. The age range was (20-29), (30-39), (40-49), (50-59), and (60-69) years with (30%), (22%), (17%), (19%), and (12%) respectively in the patient group, while in the control group it was with (32%), (24%), (18%), (20%), and (6%) respectively, as shown in the table (1).

Table (1): Gender and age distribution of study groups

Gender		Study groups	
		Patients	Control
Female	No.	51	25
	%	51.0%	50.0%
Male	No.	49	25
	%	49.0%	50.0%
Total	No.	100	50
	%	100.0%	100.0%
Age groups (years)			
(20-29)	No.	30	16
	%	30.0%	32.0%
(30-39)	No.	22	12
	%	22.0%	24.0%
(40-49)	No.	17	9
	%	17.0%	18.0%
(50-59)	No.	19	10
	%	19.0%	20.0%
(60-69)	No.	12	3
	%	12.0%	6.0%
Total	No.	100	50
	%	100.0%	100.0%

Data in table (2) demonstrates that the mean value of the body mass index (BMI) in patients (28.48±4.90) was slightly higher than in controls (26.97±4.00), but the difference was not significant statistically (P = 0.061). It is also demonstrated that there was no statistically significant difference between the studied groups

according to ALT, AST, ALP, TSB, and DBIL (P = 0.058), (P = 0.662), (P = 0.434), (P = 0.092), and (P = 0.858), respectively. In contrast, there was a highly significant difference between the studied groups according to TP and ALB (P = 0.000).

Table (2): Comparison of the BMI, ALT, AST, ALP, TSB, DBIL, TP, and ALB levels between patients (HBV & HCV) and control groups.

	Study groups	Mean ±Std.	P-Value
Body Mass Index (Kg/m^2) (BMI)	Patients	28.48±4.90	P=.061 (NS)
	Control	26.97 ±4.00	
Alanine transaminase (U/L) (ALT)	Patients	14.85±12.08	P=.058 (NS)
	Control	11.46 ±4.76	
Aspartate transaminase (U/L) (AST)	Patients	18.48±7.26	P=.662 (NS)
	Control	18.97±4.74	
Alkaline phosphatase (U/L) (ALP)	Patients	77.07±21.21	P=.434 (NS)
	Control	79.95±21.03	
Total serum bilirubin (mg/dl) (TSB)	Patients	0.52 ±0.34	P=.092 (NS)
	Control	0.60±0.15	
Direct bilirubin (mg/dl) (DBIL)	Patients	0.21±0.12	P=.858 (NS)
	Control	0.21 ±0.04	
Total protein (g/dl) (TP)	Patients	7.00 ±0.42	P=.000 (HS)
	Control	7.18 ±0.37	
Albumin (g/dl) (ALB)	Patients	4.12 ±0.30	P=.000 (HS)
	Control	4.45±0.30	

NS = Non-significant (p > 0.05), HS = Highly significant (P < 0.01).

Table (3) shows that the mean serum cholinesterase in the HBV and HCV patient groups (8528.76±2000.45 U/L and 7494.12± 2586.30 U/L, respectively) was lower than in the control group (9380.12±1848.96 U/L), and the difference was statistically significant (P < 0.05).

Table (3): Comparison between serum cholinesterase levels of the HBV and HCV patient groups with the control group

	Mean ±Std.		
	HBV	Control	HCV
Serum cholinesterase (U/L)	8528.76 ±2000.45	9380.12±1848.96	7494.12 ±2586.30
	P =.029 (S)		P =.000 (HS)

S = significant (P < 0.05), HS = Highly significant (P < 0.01).

Table (4) demonstrates that the mean serum cholinesterase in the HCV patient group (7494.12±2586.30 U/L) was significantly lower (P = 0.028) than in the HBV patient group (8528.76 ±2000.45 U/L).

Table (4): Comparison between HBV and HCV patient groups according to serum cholinesterase

	Studied groups	Mean ±Std.	P-Value
Serum cholinesterase (U/L)	HBV	8528.76 ±2000.45	P=.028 (S)
	HCV	7494.12 ±2586.30	

S = significant (P < 0.05).

Discussion

Viral hepatitis can affect both males and females of all ages. Our study found that males and females were affected nearly equally (male 49%, female 51%), with the highest percentage of the infections (30%) being among the younger ages (20–29 years). This study differs from another study done in Dhi-Qar province that showed that most patients with HAV, HBV, and HCV are males. However, it agrees with our study in that the majority of patients with viral hepatitis (29%) are young, between 18 and 29 years of age (10). Another study done in Misan province found that males were the most affected gender by HAV, HBV, and HCV infections. It also shows that HBV and HCV most affect the age group (25–50 years) (11). These differences may be due to the differences in the sample sizes of these studies.

Alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP) are indicators of liver damage rather than liver function and should be referred to as liver chemistries or liver testing (12). In the current study, there was no significant difference in the ALT, AST, ALP, TSB, and DBIL levels between patients and healthy controls. Normal transaminase activities do not rule out pathological signs of chronic hepatitis, especially in the case of chronic viral hepatitis or nonalcoholic steatohepatitis. In general, total bilirubin, direct bilirubin, and alkaline phosphatase levels are usually normal in chronic viral hepatitis patients (13).

Albumin is a major protein component of the blood, accounting for 50–60% of the protein content in serum. Because albumin is synthesized in the liver, it is considered a biomarker for the synthetic function of the liver. However, other factors can affect albumin levels, including systemic inflammation, protein malnutrition, nephropathy, fluid overload, and protein-losing enteropathy (14). Our study showed that the TP and ALB concentrations in viral hepatitis patients were lower than in controls, and it agrees with another study that found a significant decrease ($p < 0.05$) in the TP and ALB concentrations in viral hepatitis patients (15).

Serum cholinesterase is primarily synthesized in the liver and delivered into the bloodstream. Serum cholinesterase activity is decreased in hepatic insufficiency due to decreased synthesis (16). The present study showed that there was a significant decrease in the serum cholinesterase levels in HBV and HCV patients when compared to apparently healthy controls.

Hassan *et al.* found that all patients with chronic liver diseases had a significantly lower level of serum cholinesterase than the control group, and they concluded that serum cholinesterase is a preferred diagnostic and prognostic biomarker over traditional liver function tests, which are elevated in other diseases (17).

Salama *et al.'s* study showed that the sensitivity of serum cholinesterase, its specificity, and its accuracy are all 100% in predicting liver damage in individuals with chronic hepatitis C (18). Roshankumar Jha and Mahajan found that the cholinesterase levels are closely related to the severity of liver cell damage (19).

To the best of our knowledge, no study compared serum cholinesterase levels between HBV and HCV patients. HBV and HCV share several important similarities, including considerable diffusion worldwide, the modes of transmission, hepato-tropism, and the capacity to induce a chronic infection that may lead to cirrhosis and hepatocellular carcinoma (HCC) development. However, HBV and HCV are biologically very different from each other (20). Both HBV and HCV are known to promote inflammatory reactions and oxidative stress in the liver, though HCV is thought to contribute to greater oxidative DNA damage than HBV (21). Under these conditions, liver damage occurs and is sequentially followed by fibrosis, cirrhosis, and HCC. HCV patients have significantly more evidence of liver dysfunction as opposed to their HBV counterparts (22). Wong *et al.*'s study found that HCV patients, compared to HBV patients, have significantly greater rates of cirrhosis and worse liver function on presentation (23).

Conclusion

Patients with HBV or HCV have lower serum cholinesterase levels compared to healthy controls, and this test can be used to monitor liver function in those patients.

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