Study of Physiological and Some Biochemical Parameters in Patients Infected with Chronic Hepatitis-B Virus

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Abstract
Background/Purpose: Hepatitis B is a potentially life-threatening hepatitis B virus (HBV) liver disease. It is a major health issue in the world. It may result in chronic infection and puts populations at high risks of death because of cirrhosis of the liver and liver malignancy. The objective of this study aimed to study effects of infections with Hepatitis B disease on the functions of the liver through study of some physiological, Biochemical, and hormonal variables in patients with the disease, as well as study the effect of the age and sex of patients on these variables. Methodology: The study included 30 patients infected with chronic hepatitis B for period from 1/11/2021 up to 1/2/2022. Blood tests were conducted, which included complete blood count (CBC) included: Packet cell volume (PCV), total count and differential (WBC), count of red blood corpuscles (RBC), Erythrocyte sedimentation rate (ESR), Estimation of Hemoglobin concentration (Hb) and calculate the RBCS Indices (MCH, MCV, MCHC)), Concentration of total protein (TSP), Albumin concentration (Alb) and calculate the concentration of Globulin (Glub). Assessment of renal function (estimated concentration of blood urea (BU), uric acid (U.acid) and creatinine (Cre.). assess liver function secretory: which Included assess the effectiveness of liver enzymes: The biochemical variable has included: Aminotransferase enzymes (ALT, AST), (GGT) and assess the effectiveness of the enzyme Alkaline phosphatase (ALP). Estimate concentration of Total bilirubin (TSB) and total cholesterol (T. Chol.) Triglycerides, LDL, HDL-C and VLDL. As well as have been estimated concentration of some hormones such as thyroid stimulating hormone (TSH) and thyroid hormones (T4, T3). These analytes have been examined in chronic hepatitis B(CHB) patients to compare an association between these markers with healthy controls & study. Results: Serum concentrations of Several biochemical tests were performed for patients and healthy subjects, such as ALT, AST, ALP, GGT, T.S.B, total protein (TSP), Albumin concentration (Alb) and calculate the concentration of Globulin (Glub). The results showed that the patients group had a considerable increase in the level of ALT, AST, ALP, and GGT compared to control group. Total cholesterol (T. Chol.) Triglycerides, LDL, VLDL, blood urea (BU), and creatinine (Cre.) was significantly decreased in patient with CHB. The results showed a significant increase at the level of a Platelet count. Whereas no considerable differences between groups of patients and control in Hemoglobin and the (RBC) and total count of (WBC), (PCV), lymphocytes, there has not been any significant difference between 2 groups in RBCS Indices (MCH, MCV, MCHC). Conclusion: Many biochemical parameters (aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase) have been considerably higher in CHB patients in comparison with controls; the levels of GGT were also higher than in healthy subjects; and there was no considerable difference in thyroid hormone concentrations (T3, T4) or TSH levels between controls and patients.
Keywords: Thyroid hormones, Renal function, HBV, Liver enzyme, Lipid Profile, Hematological Parameters.

1. Introduction

Viral hepatitis is a chronic infection, including the main viral replication cycle site of the liver [1]. Some viruses, such as A, B, C, D, E can cause hepatitis [2]. HBV infections remains an extensive common health issue which may result in chronic and acute hepatitis, hepatocellular carcinoma, and hepatic cirrhosis [3]. It has been estimated that 2 billion people are infected with the HBV, and that includes about 350 million chronically infected; 0.50-1.20 million deaths result from the HBV-related complications, each year [4]. Alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), Alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum albumin (ALB), and total serum bilirubin (TSB), as well as prothrombin time (PT), are currently used to diagnose and monitor liver disease in the laboratory. [5,6] Serological indices of virus B infection, like HBsAg, hepatitis B e antigen (HBeAg), HBsAb, HBcAg, HBcAb, HBeAg, and HBV-DNA, are also important for diagnosing and evaluating the infection's severity. [5] Hepatic function tests, such as ALT, AST, bilirubin, ALB, and AST/ALT ratio, have shown significant differences between infected patients, according to certain researchers. Furthermore, HBV-DNA plays a critical role in the persistence of infection. [7] As a result, the coexistence of HBV-DNA quantity as well as degree of liver damage or fibrosis severity has been established. [8, 9] Viral hepatitis is a pantropical disease with hematological symptoms. Even after

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healing from acute viral hepatitis, abnormalities in hematologic profiles could indicate patients who would have hematological problems. [10] The liver plays a significant role in thyroid hormone metabolism since it is the most significant organ in the peripheral conversion regarding tetra-iodothyronine (T4) to triiodothyronine (T3) by type I iodinase, which leads to T4 5' de-iodination. [11] It also plays a role in the circulation and conjugation of thyroid hormones through the thyroid binding proteins' synthesis. [12] There is evidence that there is a link between chronic liver disease and thyroid gland alterations. [13] In the case when cirrhotic individuals were compared to controls, they had a 17% increase in thyroid glandular volume. [14] Thyroid hormone levels as well as their binding proteins have been shown to be changed in patients who have hepatic disorders, particularly cirrhosis. [15] nonetheless, practically all of these patients are clinically thyroid. The most common change in thyroid hormone plasma levels is a drop in total T3 and free T3 concentration that has been linked to hepatic dysfunction's severity. [13]

2. Patients and Methods

A: The design of population and study

This has been a cross-sectional, observational study that took place from November 1, 2021, to February 1, 2022. Patients who have chronic HBV infections who had been diagnosed by an experienced clinician, as well as healthy subjects, took part in the study (controls). Clinically, healthy subjects were chosen based on clinical and/or laboratory indicators of hepatic disease. It was determined that none of the study subjects were on any kind of medication. All patients selected, have no clinical history of recent. The patients have been evaluated prior to initiating any treatment.

B: Sample collection

Samples were taken from patients with CHB based on their clinical stage of disease (CHB), as judged by an expert hepatologist. Patients with CHB had their samples taken when they have been in chronic hepatitis phase (infection for more than six months). In both the research patient and the healthy control, fresh blood (total, 8 mL) was taken. Complete blood counts were performed on the samples, and serum was obtained and utilized as quickly as feasible for biochemical tests.

C: Evaluation of the Hematological and Bio-chemical Parameters

Hepatic function indicators, AST, ALT, TSB, ALP, GGT, were assessed with the use of lyophilized liver function panel (MNCHIP, Tianjin, China). Total protein concentration in the sera sample was determined using a modified Biuret method. While the method of measured Albumin depends on the binding an anionic dye bromocresol green (BCG) and albumin at acid pH to form complex color, the intensity of this color is symmetrical to the Albumin concentration in the test sample. The concentration of globulin in the sera sample of healthy and patients was calculated, using the

Following equation

S. Globulin (g/dL) =T.S. P (g/dL) - S. Albumin (g/dL)

Where Estimation of cholesterol concentration in the blood serum has been determined according to the enzymatic technique, using the diagnostic kit provided by the French company Biolabo.

With the use of diagnostic kit given by Biolabo, the concentration of triglycerides in the blood serum has been determined using the enzymnatie nethod technique.

As for Estimation of HDL concentration in serum. The basic principle was the determination of the level of HDL-c in the blood serum using the diagnostic kit equipped by the French company Biolabo. To estimating the concentration of Low-Density lipoprotein concentration in serum. The concentration of the lowest density lipoproteins for cholesterol = total cholesterol concentration - (The concentration of HDL cholesterol + triglycerides/ 5) and LDL is estimated by.

LDL = Total cholesterol (HDL+ VLDL)

Whereas

VLDL = Triglycerides/5.

The level of Urea, Creatinine and Uric acid in the blood serum was determined by using the diagnostic kit equipped by the French company Biolabo.

T4, T3, TSH levels have been measured with radioimmunoiogical assay kits (Monobind, U.S.).

The total and differential leukocytes count and platelets have been performed with the use of differential hematology analyzer (SFRI Medical Diagnostics, St. Jean D'Illac, and France).

D: Statistical analyses

Statistical analysis has been conducted utilizing SPSS software (SPSS Inc., Chicago, U.S.) version 25.0 with descriptive statistical analysis, all study parameters were demonstrated as mean ± standard deviation (SD). One-way ANOVA test determined the significance of differences between individuals. Spearman has confirmed the relationship between parameter relationship analyses. P-value < 0.05 considered significant.

3. Results and Discussion

A 30 CHB patients (15 males and 15 females) and 30 (15 males, 15 females) healthy control, have been enrolled in this research.

Biochemical investigations

Liver enzymes

Table (1) lists the results that have been obtained in the present study from which we can see there was the concentration of ALT, AST, ALP, GGT were increased in patients compared to healthy control subject (35.49 ± 13.2), (35.57 ± 15.01), (163.8 ± 39.23) and (17.9 ± 6.01) respectively. The statistical analysis (Table 1), it was found that the level of T.S.B,

Total protein, Albumin, Globulin among (CHB) patients group showed no significant difference results in (CHB) patients and healthy control.

Table 1: (ALP, ALT, AST, GGT, T.S.B, Total protein, Albumin and Globulin levels for all Control and Patients groups).

Parameters		Mean ± S. D	p-value
ALP U/L	cases	163.8 ± 39.23	<0.0001
	controls	115.6 ± 11	
ALT U/L	cases	35.49 ± 13.2	<0.0001
	controls	21 ± 7.97	
AST U/L	cases	35.57 ± 15.01	0.002
	controls	25.7± 7.25	
GGT U/L	cases	17.9 ± 6.01	<0.0001
	controls	8.733± 3.68	
T.S. B mg/dL	cases	0.92 ± 0.35	0.0005
	controls	0.66± 0.16	
Total protein g/dL	cases	4.06±0.71	0.835
	controls	4.02± 0.77	
Albumin g/dL	cases	3.57 ± 0.58	0.972
	controls	3.57 ± 0.69	
Globulin g/dL	cases	0.48±0.84	0.887
	controls	0.45± 1.01	

Hepatocellular injury is strongly suggested by increases in both AST and ALT values. During liver injury, AST is released through damaged muscle tissues, hepatocytes, and red blood cells [16], and ALT is released through hepatocytes, typically reflecting the liver damage degree. The level of the ALT is frequently utilized in order to determine the severity of liver disease as well as identifying patients who need treatment. ALT, on the other hand, can be altered by a variety of variables, making it an unreliable surrogate marker. [17] In our investigation, patients with envelop antigens had high ALT and AST levels compared to those without antigens and controls, which was consistent to a prior study. [16] As the liver disease proceeds, AST and ALT values rise, most possible due to membrane leakage and direct hepatocellular damage. [18] GGT, the most accurate bio indicator for liver disease, is found mostly in kidney, liver, and intestinal cells. Hepatic GGT accounts for almost all serum-detected GGT. [19] In addition, GGT levels have been found to be considerably higher in CHB patients in comparison with healthy controls in our investigation. This finding is consistent with the findings of another research, which found that the levels of GGT in sera from hepatitis B patients are significantly higher than in controls. [20] In hepatitis B patients, high serum GGT levels indicate advanced fibrosis. [21] Increased levels of ALP have been linked to a variety of liver parenchymal disorders, such as hepatitis. [16] ALP levels have been substantially greater in HBV patients compared with healthy persons in this work. Prior research of CHB patients' serum revealed a comparable outcome. [20] ALP is found in cell membranes related to hepatic sinusoids as well as biliary canaliculi in liver. As a result, when there is extrahepatic and intrahepatic biliary obstruction, as well as sinusoidal obstruction, as in infiltrative liver disease, levels rise. [22] Since such enzymes are contained in hepatocytes, if the hepatocytes are damaged, they could "leak" into the bloodstream. [23]

Levels of Lipid Profile

Table (2), lists the results that have been obtained in the present study from which we can see there was the concentration of total cholesterol (T. Chol.) Triglycerides (TG), LDL and VLDL were decreased in patients compared to healthy control subject (137.4 ± 43.61), (96.62± 18.03), (78.98± 46.29) and (19.32± 3.607) respectively. The statistical analysis (Table 2), it was found that the level of HDL-C among (CHB) patients group has been higher compared to the healthy control 39.07± 6.938).

Table 2 (total cholesterol (T. Chol.) Triglycerides (TG), LDL, HDL-C and VLDL levels for all Control and Patients groups).

Parameters		Mean ± S. D	p-value
TC mg/dL	cases	137.4 ± 43.61	<0.0240
	controls	165.8 ± 51.1	
TG mg/dL	cases	96.62± 18.03	<0.7831
	controls	97.89 ± 17.54	
HDL-C mg/dL	cases	39.07± 6.938	0.0002
	controls	32.07± 7.25	
LDL-C mg/dL	cases	78.98± 46.29	0.0525
	controls	102.5± 45.69	
VLDL mg/dL	cases	19.32± 3.607	0.7831
	controls	19.58± 3.508	

It is estimated that the liver removes around half of the insulin secreted through the pancreas by first-pass extraction. Insulin inhibits glycogen breakdown in the liver (glycogenolysis) and promotes glycogen synthesis (glycogenesis). It stimulates the development of very low-density lipoprotein cholesterol and promotes cholesterol, protein, and triglyceride synthesis. Glucagon increases gluconeogenesis, glycogenolysis, and ketogenesis in the liver, which is its primary target organ [24]. Low levels of cholesterol (total, HDL, and LDL) were identified in the two groups of hepatitis patients in our investigation, which corresponded with the findings of another research. [25]. this also agrees with the findings of a research conducted by (26). HBSAG-seropositive participants had low total cholesterol, triglyceride, and HDL cholesterol levels in comparison with seronegative (control) group, according to our findings. HBV infection was inversely linked with high triglycerides in both women and men after adjusting for several variables. Actually, there is mounting evidence of a negative relation between HBV infection status and all lipid profiles, including glycerides, cholesterol, HDL cholesterol, and LDL cholesterol (LDL-C). In addition, HBSAG seropositivity was found to be inversely linked with hypertriglyceridemia in a study including 17,030 Taiwanese residents. [27]. The authors used a structural equation model to show that HBV infection had a significant negative impact on hypertriglyceridemia in this work [27]. A large-scale cohort investigation indicated that HBV

seropositivity was related with a decreased prevalence of both hypercholesterolemia and hypertriglyceridemia [28], which was comparable to our findings. HBV infection has a negative relation with lipid profiles.

S. Urea, S. Creatinine and S.Uric acid

Table (3), shows the distribution of biochemical tests of (CHB) patients and healthy control, and the comparison between them. It was found that the level of S. Urea among (CHB) patients group was less than the healthy control with the mean for the first was (56.77± 12.82) and (63.47± 5.077) respectively and the difference was (P = 0.0100). The level of Creatinine among (CHB) patients group was less than the healthy control with the mean for the first was (1.393± 0.3973) and (1.6± 0.2493) respectively and the difference was (P = 0.0205).

Regarding Uric acid levels showed no significant difference results in each (CHB) and and healthy control.

Table 3: (Urea, Creatinine and Uric acid levels for all Control and Patients groups).

Parameters		Mean ± S. D	p-value
Urea (mg/dL)	cases	56.77± 12.82	0.0100
	controls	63.47± 5.077	
Creatinine (mg/dL)	cases	1.393± 0.3973	0.0205
	controls	1.6± 0.2493	
Uric acid (mg/dL)	cases	5.933± 1.66	0.9301
	controls	5.9± 1.242	

The previous study also demonstrated that a group of (CHB) patients and a group of healthy control, there has been a significant reduction in the rate of urea concentration in the blood of patients experiencing CHB in comparison with healthy controls. Also, it was found that there was a decrease in the concentration of creatinine, while there has been a significant increase in the Uric acid concentration in (CHB) patients, compared to its concentration in the healthy control. [25]

T3, T4, TSH Levels

Hormonal changes: The results of the current study showed that no significant differences between control group and patients in a thyroid hormone concentration (T3, T4) and Thyroid stimulating hormone TSH with the mean for the first was (0.8536±2.955), (83.03±10.94) and (3.989±0.9929).

Table 4: (T3, T4 and TSH levels for all Control and Patients groups).

Parameters		Mean ± S. D	p-value
T3 (nmol/L)	cases	2.955±0.8536	0.9746
	controls	2.949±0.7581	
T4 (nmol/L)	cases	83.03±10.94	0.9555
	controls	82.89±6.87	
TSH (μiu/mL)	cases	3.989±0.9929	0.8545
	controls	4.032±0.79	

These results do not agree with the results of previous research, which reported a significant reduction in the concentration of T3, T4 hormones in patients experiencing hepatitis B virus type compared to its concentration in the control group, when the concentration of TSH was within the normal limits. [29]. The process of metabolism of thyroid hormones is concentrated in the liver cells, in a number of regular and sequential steps, which eventually leads to the regulation of the level of hormones in the blood by converting T4 to T3. Damage to liver cells. The findings of this work reported that the process of regulating the level of these hormones in liver cells was not affected, which indicates that the extent of damage in the liver cells was simple and did not affect the concentration of thyroid hormones in the blood, meaning that the disease is in the initial stages. [30].

Hematological Parameters

Hematological changes: The results showed a significant increase at the level of probability (P=0.2597) between the patients and the control group in the value of a Platelet count (360.4±63.86). whereas no significant differences between groups of patients and control in Hemoglobin and the (RBC) and total count of (WBC), (PCV), lymphocytes with the mean for the first was (12.66± 2.465), (4.989± 1.057), (11.22± 2.981), (41.05±8.116), (12.7± 2.705), there was no significant differences between two groups in RBCS Indices (MCH, MCV, MCHC) with the mean for the first was (82.8± 3.354), (28.53±3.649), (34.51±5.048).

Table 1: (PLT, RBC, WBC, PCV, lymphocytes and MCH, MCV, MCHC levels for all Control and Patients groups).

Table 5: (PLT, RBC, WBC, HCT,Hb, LYM, MCV,MCH and MCHC] levels for all Control and Patients groups).

Parameters		Mean ± S. D	p-value
PLT*10^3	cases	360.4±63.86	0.2597
	controls	346.4± 44.35	
RBCs x 106/μL	cases	4.989± 1.057	0.0001
	controls	4.058± 0.6625	
WBCs x 103/μL	cases	11.22± 2.981	0.7621
	controls	11.03± 1.555	
HCT (PCV) %	cases	41.05±8.116	0.2439
	controls	40.99 ± 4.098	
Hb g/dL	cases	12.66± 2.465	0.9564
	controls	12.7± 2.705	
LYM %	cases	32.85±6.154	0.8987
	controls	32.71± 5.599	
MCV (fl)	cases	82.8± 3.354	0.6144
	controls	82.69± 3.407	
MCH (pg)	cases	28.53±3.649	0.4009
	controls	28.37± 3.633	
MCHC (g/dl)	cases	34.51±5.048	0.1248
	controls	34.88± 5.519	

Hematological parameters present information on the hemolysis and activity regarding the bone marrow. [31] Hepatic parenchymal cells synthesize the majority of anticoagulant proteins, coagulation factors, and components related to the fibrinolytic system, hence they play an important role in hemostasis. [32] In addition, WBC counts are typically high as a result of the infectious disease as well as inflammation that follows. [33] The WBC

counts indicated no significant differences between healthy controls and patients with HBV infections in this work. Because another research [34] found clear similarity between healthy controls and patients with HBV infections, the outcome was uncertain. Depending on current researches which show that presence of hematological cytopenias is connected to poor prognoses in the cirrhosis, many factors have a role in the "incidence of atypical hematology results". [35]

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