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Article

Clinical and Enzymatic Evaluation of Liver Function in Patients with Chronic HBV Infection

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Abstract: This study aimed to assess clinical and enzyme variation in hepatitis B virus (HBV)- related liver function in chronically infected patients by comparing findings with those of a control group of healthy individuals. A total of 60 patients, 30 having chronic HBV and 30 healthy individuals as a control group, were sampled. The methodology involved collecting clinical information through direct patient interviews, focusing on typical symptoms such as fatigue, loss of appetite, jaundice, and upper right quadrant abdominal pain. Physical examination was also performed to assess liver size and determine whether there was fibrosis or hepatomegaly. The automated analyses from the Mindray BS-240 were subsequently used in the laboratory to measure liver enzymes, including ALT, AST, ALP, and GGT. Also, levels of total and direct bilirubin, as well as total protein and albumin, were determined. HBsAg testing was also performed on all samples to confirm chronic infection. Medical interviews of the patients provided clinical data, with general fatigue (83.3%), loss of appetite (70%), jaundice (40%), and upper right quadrant pain as the most noticeable symptoms. Also, 60% of cases were characterised by hepatomegaly, suggesting that the virus directly affected overall health and liver function. As for laboratory tests, liver enzymes (ALT, AST, ALP, GGT) were significantly increased in the patient group, with highly significant differences ($P < 0.001$). For example, the average ALT level of the patients was 85.4 ± 22.7 U/L, compared with 28.1 ± 6.5 U/L in the control group. In addition, total and direct bilirubin were markedly elevated, whereas albumin and total protein were decreased, indicating impaired hepatic synthetic function. This study confirms the fact that chronic HBV causes a number of liver function disturbances, which are evident and reflected both in clinical manifestations and in laboratory results. Regular evaluation of these signs is very important to prevent the development of disease and complications such as fibrosis or even liver cancer. The study also recommends extending routine screening in areas with a high prevalence of infection, improving health awareness campaigns, and promoting early diagnosis as an essential pillar of management and surveillance for this disease.

Keywords: Liver Function, hepatitis B virus, enzyme variation, fibrosis

Introduction

The liver is one of the most important organs of the human body as it plays a central role in a number of biological processes that help maintain the body's internal balance [1]. Because it is always exposed to toxins and viruses, the liver is prone to different diseases such as viral hepatitis B and C, fatty liver disease, cirrhosis and liver cancer [2].

HBV infection is one of the most important public health issues worldwide, with an estimated 257-291 million people being infected with the virus worldwide, with chronic hepatitis B infection being a big contributor to liver complications such as cirrhosis and Hepatocellular Carcinoma (HCC) [3]. HBV is a deoxyribonucleic acid DNA virus of the Hepadnaviridae family with a complicated life cycle involving conversion of the relaxed circular DNA to covalent closed circular DNA (cccDNA) in the nucleus of liver cells [4]. This enables the virus to remain in the liver for extended periods, even under antiviral treatment or host immune pressure [5]. In adults, acute infections are frequently controlled by the immune system, but infections contracted when young or with weakened immunity may later develop into chronic infections lasting decades [6].

HBV is passed on by blood and body fluids, and routes of transmission include exposure to contaminated blood, unprotected sex and mother-to-child transmission during childbirth [7]. Chronic infection impairs the liver's vital functions, as reflected in clinical and enzymatic parameters that reflect the extent of liver cell damage [6]. Despite the availability of effective vaccines to prevent such infections, chronic infections remain a significant health burden in many countries, particularly in resource-limited regions where screening, diagnosis, and treatment systems are underdeveloped [8].

ALT and AST are important markers of hepatocellular injury, whereas elevated levels of alkaline phosphatase (ALP) and GGT indicate bile duct injury or associated biliary disease [9]. In addition, levels of bilirubin, albumin, and coagulation time (PT/INR) are used as indicators of overall liver function [10].

Elevated levels of ALP and GGT can be a sign of biliary tract disorders and/or associated liver fibrosis. In addition, other markers, such as total and direct bilirubin, are used to assess the liver's capacity to process and excrete bile waste, while albumin and total protein levels are used to assess the liver's synthetic capacity [11].

In recent years, there has been greater attention to the rising importance of viral and immune biomarkers of disease progression and /or prediction of patient outcome (e.g. HBV DNA levels, HBeAg, and new markers such as HBcrAg (viral core related antigen) [12]. It is estimated that combining these indicators with classical examinations enhances the assessment of the pathology and the prediction of future complications, such as fibrosis or the development of cancer [13]. Assessing the clinical and enzymatic alterations in liver function among patients with chronic HBV infection is important for early understanding of the virus's impact on the liver and for advancing diagnostic and therapeutic protocols, thereby minimising the risk of potential complications.

Material and method

A subset of patients with a prior diagnosis of chronic Hepatitis B virus (HBV) infection was selected from a hospital or an accredited health care center, and the study included 30 patients. This number has been selected to give a statistically satisfactory result. In addition, 30 non-infected patients, one-by-one matched with patients in terms of age and sex, were selected as the control group to compare the two groups regarding clinical indicators and liver enzyme levels.

Blood Sample Collection

Blood specimens were collected from all 30 patients and individuals in the control groups using sterile equipment and special tubes with or without anticoagulant emulsion (EDTA) for the required test. The samples were sent straight away to the laboratory under the proper conditions 2-8 °C to avoid cellular degradation of blood components. Each sample was labelled with a unique code to ensure the confidentiality and the integrity of the analyses [14]. Upon arrival in the laboratory, serum was separated by centrifugation at 3000 rpm for 10 min and then stored in special tubes until analysis.

Laboratory Tests

Liver enzyme levels were measured (including the key enzymes: ALT, Alanine Aminotransferase, AST, Aspartate Aminotransferase, ALP, Alkaline Phosphatase, GGT, Gamma-Glutamyl Transferase) with fully automated biochemical analysers, e.g. Cobas Integra, Roche and Architect c8000, Abbott. These devices facilitate quick and precise determination of enzyme levels in patient samples. In addition, total and direct bilirubin, total protein, and albumin were determined on the same analysers that use advanced chemical techniques to ensure the sample was analysed.

The HBsAg test was also performed to detect long-term HBV infection. Automated Enzyme Immunosorbent Assays (ELAs), such as the Bio-Rad Enzyme Immunoassay Reader or Thermos systems, can be used for qualitative and quantitative detection of viral antigens with very high accuracy. These instruments not only streamline and speed up the diagnostic procedure but also provide a reliable outcome needed for accurate assessment of liver function and the general health status of patients [15].

Statistical Analysis

All the data obtained during the experiment were processed using SPSS software version 25. Descriptive analysis was done to compute the means and standard deviations for the variables studied, which were used to describe the distribution and basic characteristics of the data. A Student's t-test was used to compare the group of patients diagnosed with chronic hepatitis B virus (HBV) with the control group of uninfected individuals to determine whether there were statistically significant differences between the two groups. $P < 0.05$ was considered statistically significant.

Results and Discussion

The present study was carried out on 30 patients with chronic Hepatitis B virus (HBV) infection, selected from a specialised health centre. All patients underwent detailed clinical and laboratory evaluations to assess the effects of chronic infection on liver function. In phase 1, clinical information was gathered from patients through direct interviews under the guidance of the supervising physician [16]. The interviews comprised the assessment of typical symptoms such as fatigue, general exhaustion, anorexia, jaundice (yellowish discolouration of skin and sclerae) and upper right quadrant pain. This was followed by a clinical examination of the liver to determine the size and texture of the liver and signs suggesting the possibility of cirrhosis or enlargement.

Table 1 shows detailed demographic features of the study sample, comprising 30 patients with chronic HBV infection, compared with 30 healthy individuals in the control group. The result was that the mean age of the patients was 39.5 years ± 11.2, whereas in the control group it was 38.7 years ± 10.5. The ratios of males to females were 66.7% and 60% among patients and controls, respectively. Female patients comprised 33.3% of the participants, and healthy people comprised 40%. In addition, no statistically significant difference in gender distribution was detected between the two groups, implying that both groups were comparable in terms of age and gender. This similarity increases the validity of the following clinical and enzymatic comparisons in the study.

Table 1. Demographic Characteristics of the Samples.

Variable	HBV Patients (n=30)	Control Group (n=30)	P-Value
Age (Mean ± SD)	39.5 ± 11.2 years	38.7 ± 10.5 years	> 0.05
Gender (Male)	20 (66.7%)	18 (60%)	> 0.05
Gender (Female)	10 (33.3%)	12 (40%)	> 0.05

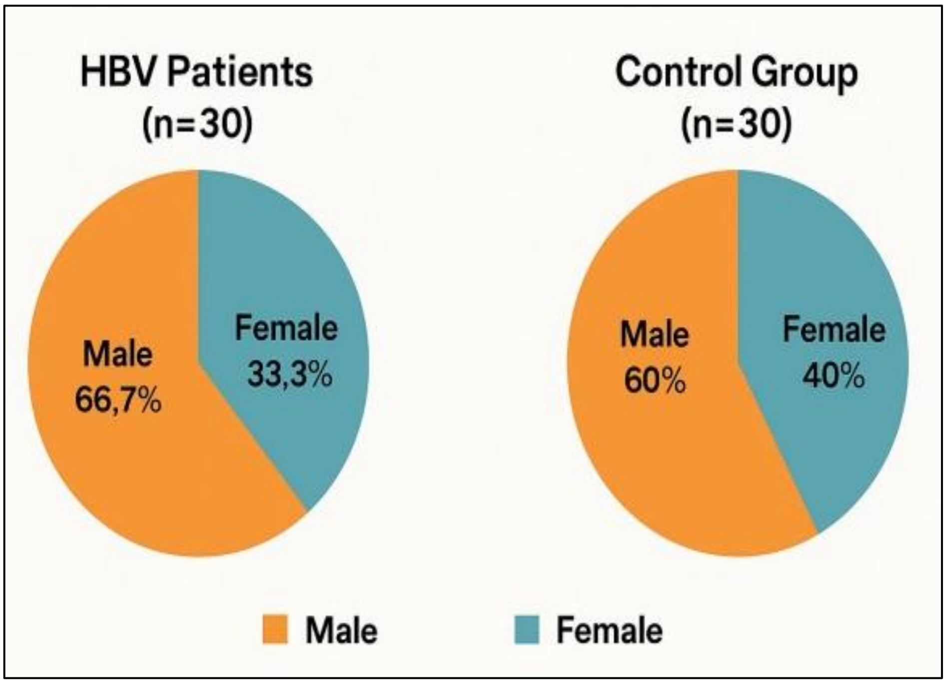

Figure 1 . Demographic Characteristics of the Samples.

Table 2 shows the correlation between chronic HBV infection and elevated levels of various liver enzymes, expressed as duration. Patients were divided into three groups according to the length of time they had been infected: less than 1 year, 1 to 3 years, and more than 3 years. The results show that the mean levels of ALT, AST, ALP, and GGT enzymes increase gradually over time, indicating progressive deterioration of liver function.

In patients infected for less than 1 year, enzyme levels were lower than in the other patients, with mean ALT, AST, ALP, and GGT of 85, 120, 130, and 55 IU/L, respectively. Enzyme levels were significantly higher in patients infected for 1 to 3 years, with a mean ALT of 110, AST of 145, ALP of 155, and GGT of 78 IU/L. Patients with infection for more than 3 years had the highest enzyme levels, with a mean ALT of 125, AST of 160, ALP of 175, and GGT of 95 IU/L.

This progressive increase reflects the close correlation between the duration of infection and the degree of liver damage and suggests that continued chronic infection accounts for progressive liver dysfunction and elevated parameters of inflammation and cellular damage.

Table 2. Correlation Between Duration of Infection and Elevation of Liver Enzymes.

Duration of Infection (Years)	**ALT (IU/L) Mean ± SD**	**AST (IU/L) Mean ± SD**	**ALP (IU/L) Mean ± SD**	**GGT (IU/L) Mean ± SD**
Less than 1 year	85 ± 20	120 ± 25	130 ± 18	55 ± 12
1 to 3 years	110 ± 22	145 ± 28	155 ± 20	78 ± 15
More than 3 years	125 ± 27	160 ± 30	175 ± 25	95 ± 18

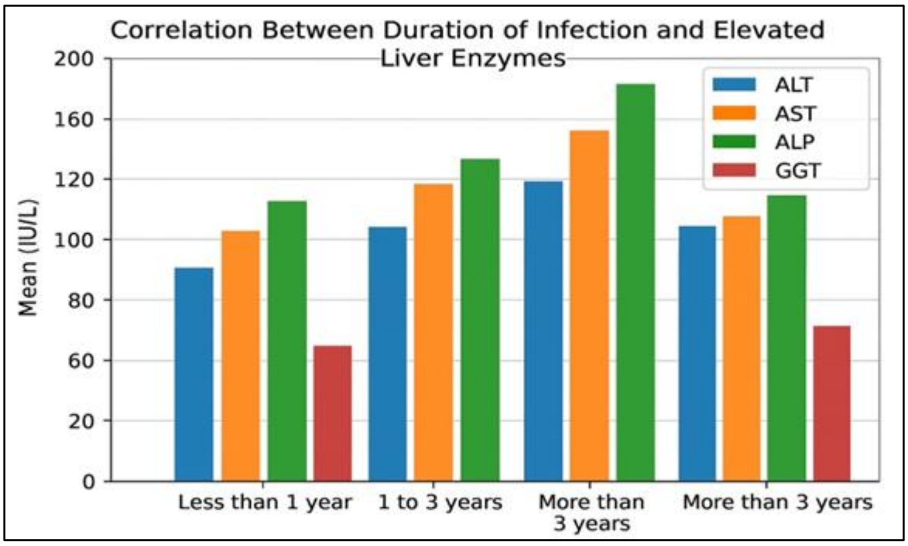

Figure 2. Correlation of Prolonged duration of infection with Raised Liver Enzymes.

Table 3 demonstrates the common clinical symptoms among patients with chronic hepatitis B virus infection, distributed among the sample of 30 patients. General fatigue was the most common symptom, occurring in 25 patients (83.3%), as it reflects the disease's global impact on patients' health. Loss of appetite was observed in 21 patients (70%) - a very common symptom reflecting the disease's impact on the digestive system and appetite. Jaundice was exhibited by only 12 patients (40%), indicating that the liver was working abnormally and the levels of bilirubin in the blood were too high. Upper right abdominal pain was felt by 16 patients (53.3%), which is indicative of inflammation or enlargement of the liver. Hepatomegaly (liver enlargement) was clinically observed in 18 patients (60%), with anatomical changes accompanying the chronic infection and its consequences on liver size and function. These results reflect the diversity of clinical symptoms and the effects of the disease on different body functions.

Table 3. Common Clinical Symptoms in Patients.

Symptom	Number of Patients (n=30)	Percentage (%)
General fatigue	25	83.3
Loss of appetite	21	70
Jaundice	12	40
Upper quadrant pain	16	53.3
Liver enlargement	18	60

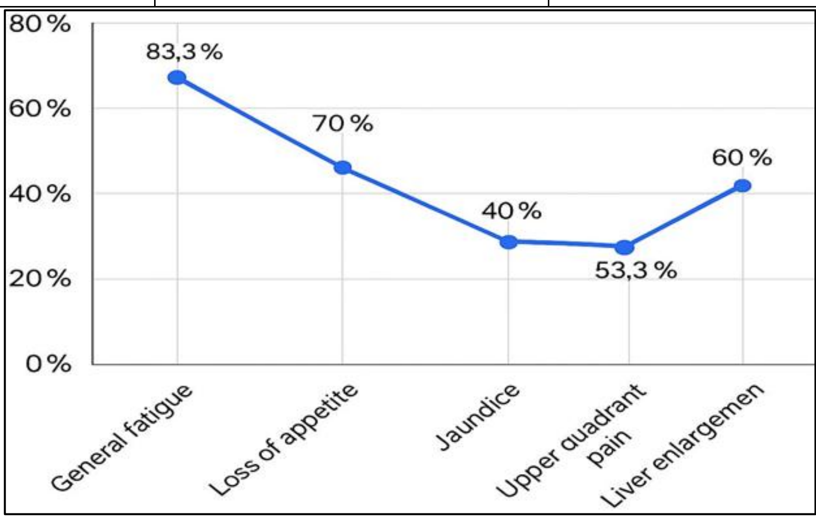

Figure 3. Common Clinical Symptoms in Patients.

Table 4 presents liver enzyme results, showing obvious differences between patients infected with chronic Hepatitis B virus (HBV) and the control group. ALT enzyme values in the patient group were significantly elevated, with a mean of 85.4 units per litre and a standard deviation of 22.7, compared with the control group, which had only 28.1 units per litre. This difference is statistically significant (p-value < 0.001). AST enzyme levels also showed a quite significant elevation in the patients, with an average level of 72.3 units per litre, compared with 25.7 in the control group, due to liver cell damage caused by the infection. For ALP, the mean level was 186.5 among patients, which was much higher than 89.2 among controls, indicating that the bile duct is dysfunctional or the liver is injured. GGT enzyme averaged 74.6 in patients compared with 32.5 in controls, which confirms ongoing liver damage. These large differences in enzyme levels demonstrate the significant impact of chronic infection on liver function, with statistical values indicating that these results are not due to chance but to the real effect of this disease.

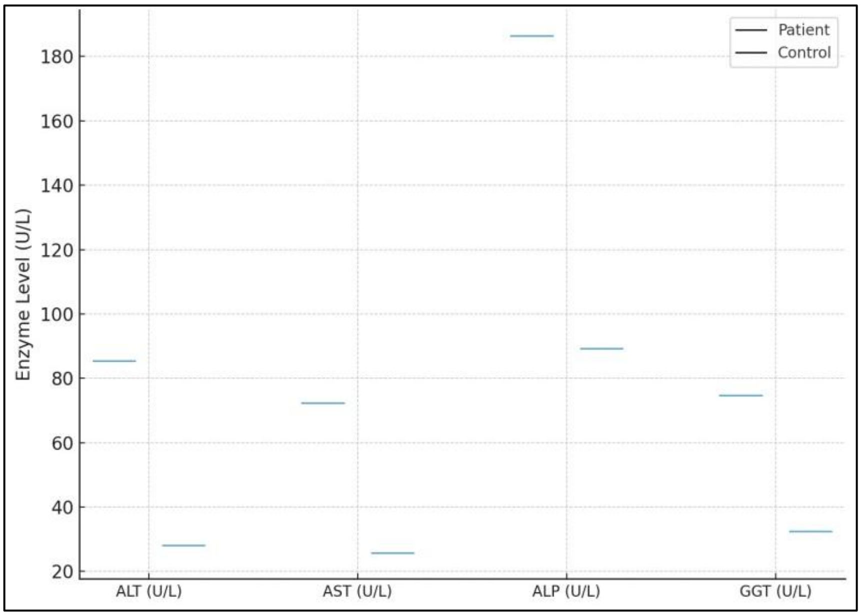

Figure 4. Comparison of Liver Enzymes Between Patient and Control Groups.

Table 5 shows the liver function indexes, and it is obvious that there are differences between patients with chronic hepatitis B and the normal controls.

The total bilirubin was significantly higher in patients (mean: 2.4 mg/dL) than in controls (0.7 mg/dL). Further, the level of direct bilirubin was 1.1 mg/dL in patients, v 0.2 mg/dL in controls, suggesting disorders of bilirubin excretion and liver function. In contrast, in patients, the albumin level was significantly lower (3.2 g/dL) than in the control group (4.1 g/dL), indicating impaired hepatic protein synthesis. Total protein was also decreased in patients (6.4 g/dL) compared with controls (7.1 g/dL), and there were significant differences for all parameters. These results undoubtedly provide clinical evidence for significant impairment of hepatic function in patients with chronic infection, which supports the negative effect of HBV on hepatic health.

Table 5. Additional Liver Function Indicators.

Test	Patients (Mean ± SD)	Control (Mean ± SD)	P-Value
Total Bilirubin	2.4 ± 0.8	0.7 ± 0.2	< 0.001 **
Direct Bilirubin	1.1 ± 0.3	0.2 ± 0.1	< 0.001 **
Albumin	3.2 ± 0.4	4.1 ± 0.5	< 0.001 **
Total Protein	6.4 ± 0.7	7.1 ± 0.6	< 0.01 *

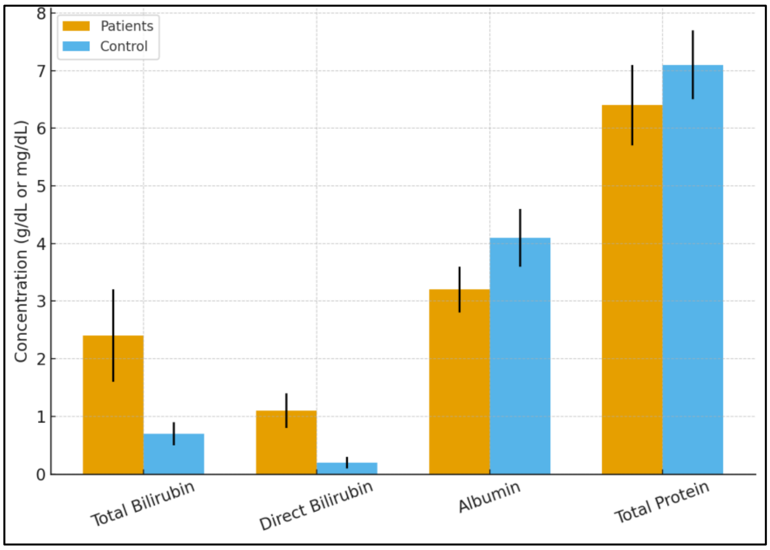

Figure 5. Comparison of Serum Biochemical Parameters groups.

Discussion

The results of our study paint a clear picture of the harmful and complex impact of chronic hepatitis B virus (HBV) infection on liver function. By examining the differences between the patient and control groups, we were able to draw several important conclusions. As shown in Table 1, the differences in age and gender distribution between the HBV patients and the control group were not statistically significant ($P > 0.05$) [16]. This demographic balance is very important, as it reduces the likelihood that differences in liver enzyme levels or other signs of liver damage are attributable to age or gender and, in fact, reflect the direct effects of the virus on the liver [17].

Ensuring demographic matching between the groups gives later comparisons and analyses greater credibility. The control group was matched with HBV patients in terms of age and gender, and therefore, possible confounding factors on the consequences were minimised [18]. The average age of HBV patients was around 39.5 years, which is in the normal age group where chronic HBV complications begin to appear [19]. Previous studies have indicated that liver function deterioration frequently starts at this stage in the course of chronic HBV infection [20].

The results of the study indicated that there was a significant increase in liver enzymes (ALT, AST, ALP, GGT) with increasing infection duration [21]. This trend aligns with the literature, which stipulates that the persistent presence of the virus causes a gradual destruction of hepatocytes, leading to elevated enzyme concentrations leaking into the bloodstream [22]. ALT and AST are considered sensitive markers of liver damage, and increases in these enzymes are linked to hepatic inflammation and fibrosis. Likewise, increases in ALP and GGT are indicative of damage or obstruction of the bile ducts, which are usually present in advanced stages of the disease [23].

These results are in agreement with a number of reports that untreated chronic infection results in liver fibrosis and progressive liver dysfunction [24]. Furthermore, ALT and AST are widely used markers of the extent of hepatic inflammation in patients with chronic HBV infection [25].The most frequent clinical presentation of the patients was exhaustion, anorexia, jaundice, right upper quadrant abdominal pain, and hepatomegaly [26].The symptoms are due to the physiological effects of the virus on liver tissues and functions. Fatigue and appetite loss are signs of chronic inflammation, as is its dissemination throughout the body, and yellowing indicates disorders of bile secretion or decreased hepatic ability to process bilirubin [27].

These findings are consistent with existing reviews and articles that describe the clinical manifestations of chronic hepatitis [28]. Notably, hepatomegaly is a major clinical finding frequently monitored by physicians in the evaluation of patients with HBV infection [29]. The significant differences between the alt, AST, ALP, and GGT values of the patients and the control group are among the important findings of this study. Elevated enzyme levels in patients reflect hepatocyte destruction due to chronic inflammation. ALT in particular is believed to be a sensitive and direct marker of liver damage and is in clinical practice commonly used to assess disease activity [30]. The elevation of ALP and GGT, in association with ALT and AST, suggests that all or part of the biliary tract is also affected or that there is advanced liver fibrosis; this has been documented in the literature on chronic liver assessment [31].

Laboratory analysis showed a significant increase in ALT and AST levels compared to the control group. This elevation indicates liver cell damage and inflammation, and has been well known to indicate chronic hepatitis B [32]. Similarly, high levels of ALP and GGT are suggestive that there is biliary tract involvement, which may be the result of advanced fibrosis or chronic cholangitis [33].

The results were also significant for bilirubin indicators (total and direct), which were elevated in patients relative to healthy subjects [34]. This shows defective biliary metabolism and biliary excretion, supporting the idea that chronic infection leads to dysregulation of the hepatic metabolism [35]. Conversely, low albumin and total protein levels in the blood indicate decreased hepatic synthetic activity, a feature typical of advanced disease. This decrease may be associated with complications like ascites in the abdomen or the risk of bleeding [36].

Total and direct bilirubin levels were significantly elevated, whereas albumin and total protein levels were low in patients compared with controls. Bilirubin is a biomarker of hepatic metabolism and bile excretion, and its elevation indicates disease progression and jaundice [37]. The reduction in albumin and total protein levels indicates that the liver is synthesising vital proteins. This can impact osmotic balance and immune function, and predispose to complications such as ascites and blood clotting abnormalities [38].

His comments: Hepatitis B virus (HBV) infection is known to cause a persistent immune response, leading to progressive liver cell death and subsequent inflammation, fibrosis, and, in advanced stages, hepatocellular carcinoma (HCC) (7). Liver enzymes and functional changes are markers of disease activity and the degree of liver damage [39]. Slightly elevated ALT and AST are indicators of hepatocellular injury, and increased levels of ALP and GGT show liver fibrosis or disturbances of the bile ducts.

These observations are useful to understand the progression of chronic hepatitis B and their effects on the liver and allow early therapeutic approaches to minimise complications [40]. Therefore, these markers should be monitored regularly to evaluate the patient's status and optimise treatment [41]. Our results corroborate recent literature reviews identifying important disease characteristics and disease progression. For instance, a recent review article on diagnostic and predictive markers for chronic hepatitis emphasises that ALT, AST, and bilirubin are essential biomarkers for patient assessment, but that their sole use may be limited. In this regard, using them in combination with other markers or non-invasive methods for fibrosis assessment is desirable [42]. On the other hand, reports assessing non-invasive markers for fibrosis, such as APRI and FIB-4, show that these can be used to predict fibrosis stage without biopsy, which is of great clinical utility, especially for patients who are unwilling or unable to undergo biopsy [43]. For instance, [44] showed a strong correlation between APRI score and Fibro Scan results, suggesting that APRI could be a convenient, noninvasive fibrosis index in HBV patients.

Conclusions

The results of this study suggest that chronic infection with the hepatitis B virus (HBV) has a direct and obvious effect on liver vital functions. The laboratory results demonstrated a significant elevation in the levels of the four liver enzymes (ALT, AST, ALP, GGT) in patients compared with healthy control subjects, suggesting active liver injury, either via continuous inflammation or cellular damage. It was also observed that the rise in this enzyme increases progressively with the length of infection, indicating a progressive deterioration in liver condition over time without successful treatment.

A significant increase in total and direct bilirubin was documented, indicating a failure to remove waste products from the liver. Conversely, albumin and total protein were decreased, which were important indicators of decreased hepatic synthetic capacity in the chronic cases. For most patients, the symptoms (general fatigue, loss of appetite, jaundice, upper right abdominal pain) were evident, and hepatomegaly was observed in most, confirming the correlation between the clinical symptoms and the biochemical data and demonstrating the negative effect of the chronic infection on liver function.

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