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# Association between Hepatitis B Viral Load and Liver Function Biomarkers in Patients with Chronic Hepatitis B

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## Abstract

General Background Chronic hepatitis B virus infection remains a major global public health challenge leading to progressive liver damage. Specific Background Evaluating viral replication alongside liver biochemistry is essential for accurate disease staging and clinical management. Knowledge Gap However, data regarding the precise correlation between viral load and liver function parameters in Iraqi chronic hepatitis B cohorts remain limited. Aims This study investigates the correlation between HBV DNA viral load and biochemical liver parameters in chronic hepatitis B patients. Results Significant positive correlations emerged between viral load and alanine aminotransferase ($r = 0.68, p < 0.001$), aspartate aminotransferase ($r = 0.62, p < 0.001$), alkaline phosphatase ($r = 0.49, p = 0.003$), and total bilirubin ($r = 0.45, p = 0.002$). Conversely, serum albumin showed a significant negative correlation ($r = -0.51, p = 0.001$). Novelty This study validates localized clinical relationships between molecular viral replication and liver synthetic impairment. Implications Combining molecular quantification with routine biochemical testing optimizes clinical assessment and therapeutic decision-making in resource-limited settings.

**Key Findings Highlights**

High viral loads correlate directly with elevated serum transaminases and total bilirubin levels.

Serum albumin concentrations decline significantly in patients experiencing active viral replication.

Joint molecular and biochemical evaluation improves disease monitoring and clinical risk assessment.

**Keywords**: Hepatitis B, Viral Load, Liver Function, Transaminase Levels, Serum Albumin

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## Introduction

Hepatitis B virus (HBV) infection is one of the most serious infectious-diseases affecting millions of people worldwide [1]. Though considerable progress is made in vaccination and treatment regimens HBV still remains the serious contributor to chronic liver disease and deaths related to liver especially in developing countries [2]. Infection with HBV is linked with progressive liver damage resulting in liver fibrosis, cirrhosis, liver failure and even hepatocellular carcinoma. Because of its long-term complications and silent clinical progression in many patients therefore HBV infection still represents major challenge for healthcare systems-globally [3].

HBV is a hepatotropic DNA virus belonging to the Hepadnaviridae family and is transmitted through exposure to infected blood or body fluids [4]. The virus can spread through several routes which including vertical transmission from mother to child, unsafe blood transfusion, needle sharing and unprotected sexual contact. After entering the body HBV targets hepatocytes where viral replication occurs. The clinical results of infection varies widely depending on several factors such as age at infection, immune status, viral replication activity and host immune response [5]. While some individuals successfully clear the virus during the acute phase the others develop chronic infection characterized by persistent hepatitis B surface antigen (HBsAg) positivity for more than six months [6]. Progression of the course of chronic-infection with HBV varies greatly from person to another. Some people stay symptom-free with little injury to their livers while other get active-hepatitis which is characterized by progressive liver inflammation and fibrosis [7]. Injury to the liver in cases of chronic HBV infection depends mostly on viral-replication and immune-mediated-damage. HBV does not cause direct cytotoxicity of liver cells. Damage to the liver is mostly mediated through the body's immune-response to the virus present in liver-cells. Cytotoxic T lymphocytes and inflammatory-cytokines showed important role in the destruction of infected hepatocytes and leading to chronic-inflammation and tissue-injury [8]. Persistent immune-activation for long time contributes to fibrosis and structural changes in the liver.

One of the important indicators for evaluating chronic hepatitis B virus infection is the determination of the viral-load. Quantification assessment of HBV-DNA by using real-time polymerase-chain-reaction (RT-PCR) provide direct test of viral-replication activity. An increase in viral load often reflects the infectivity of the virus, inflammatory-activity within the liver, and disease progression. Viral load quantification is critical and important in the diagnosis and treatment of HBV infection as it assists in staging the disease, assessing the outlook, and determining anti-viral therapy [9]. Individuals with high viral loads have a higher likelihood of developing cirrhosis and hepatocellular carcinoma than individuals with low viral loads.

Biochemical liver function tests are critical assessment in the diagnosis of HBV-infection. Liver enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are broadly indicators of hepatocellular-injury [10]. Raised levels of these biochemical-markers indicated cellular injury to the cell membrane of the hepatocytes which subsequently results in the leakage of the intracellular enzymes contents to blood stream. ALT is regarded as more specific indicator of hepatocellular injury compared to AST although AST could increase due to tissue damage elsewhere in the body. [11]. There are other biochemical tests that can help in get information about the condition and healthy status of the liver. Alkaline phosphatase (ALP) help in determining if there is any bile duct damage. "Serum bilirubin level shows the liver capacity to metabolize the bile-pigment". High serum bilirubin levels may be indicator of poor hepatic function and liver-damage [12]. Raised bilirubin in the blood may indicate impaired in the hepatic function or advanced liver-injury. Serum albumin which is synthesized exclusively by hepatocytes is considered an important marker of hepatic synthetic capacity. Reduced albumin levels are often associated with chronic liver dysfunction and advanced hepatic disease [13]. Therefore combined evaluation of liver enzymes and other biochemical indictors which provide extensive understanding of hepatic status in patients with chronic HBV-infection.

Different studies have examined the relationship between HBV viral-load and liver biochemical tests but the results remain unpredictable in the different populations and some studies reported strong positive-correlations between HBV-DNA levels and serum ALT and AST values which showed that increased viral replication is associated with larger hepatocellular-injury [14] [15]. some studies show poor correlation and variable-associations especially in in cases with inactive carriers or during immune-tolerant phases of infection [16]. These differences may be related to variations in patient-populations, viral genotypes, disease stages, host immune responses and environmental-factors. Consequently further studies are still needed in order to gain more insight into the interplay between viral-replication and biochemical liver damage. In Middle Eastern countries such as Iraq the chronic-HBV infection continues to be major public-health problem even though there have been significant advances in the coverage of hepatitis B virus vaccines. Most patients present in the later-stage of the disease since there is poor awareness between the population, poor screening rates and also lack of access to molecular diagnostics in certain medical facilities. The early detection of patient with ongoing viral replication and liver damage is essential in reduce risks and achieving favorable results [17]. The detetmine of the relationship between HBV viral load and liver biochemical tests can help to identify high-risk patients and optimize disease monitoring-strategies.

The understanding of the relationship between the viral load and biochemical value of liver is also highly important from a clinical perspective. Several medical facilities find that liver function tests are easier to conduct and are cheaper compared to molecular-based tests. If there is evident correlation between biochemical parameters and viral-replication and this can serve as additional information on disease activity particularly in low-income areas [18]. Furthermore, assessment of these parameters may assist physicians in monitoring treatment response and predicting disease progression during follow-up. Although numerous international studies have examined HBV-associated liver dysfunction the data from Iraqi populations remain relatively limited. Regional studies are important because disease patterns, healthcare access, viral characteristics and environmental influences may differ between populations [19]. Therefore evaluating HBV viral load and its association with liver biochemical parameters in Iraqi patients may provide valuable information relevant to local clinical practice and

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disease management. Based on these considerations the present study was designed to investigate the correlation between HBV viral loads and liver function biochemical parameters including ALT, AST, ALP, bilirubin and albumin, in patients with chronic hepatitis B infection. The results of this study may contribute to a better understanding of disease activity and support the use of combined molecular and biochemical assessment in the clinical management of chronic HBV infection.

## Materials and Method

This cross-sectional hospital-based study was conducted between January 2025 and March 2025 at the Gastroenterology and Hepatology special clinics in Iraq. A total of 120 patients with confirmed chronic HBV infection were enrolled in the study. Patients were recruited during their routine clinical follow-up visits to the hepatology outpatient clinic.

### 2.1. Inclusion and Exclusion Criteria

Participants were included in the study according to the following criteria: Positive hepatitis B surface antigen (HBsAg) for more than six months, age ≥18 years, both males and females and diagnosed with chronic hepatitis B infection based on clinical and laboratory results. Whereas exclusion criteria including patients they met any of the following conditions: Co-infection with Hepatitis C virus (HCV), Hepatitis D virus (HDV), or Human Immunodeficiency Virus (HIV) also including history of alcoholic liver disease, autoimmune hepatitis or other chronic liver diseases, current or recent antiviral therapy within the previous three months, hepatocellular carcinoma, Severe renal disease or systemic inflammatory disorders and use of hepatotoxic medications. Clinical assessment and detailed demographic and clinical data were collected from all participants using a standardized questionnaire and medical record review. Information included:

Age

Gender

Duration of HBV infection

Clinical symptoms

Medical history

Previous treatment history

A physical examination was performed for all patients by specialized clinicians.

### 2.2. Sample Collection

Approximately 10 mL of venous blood was collected from each participant under aseptic conditions. Blood samples were divided into two portions when EDTA tubes for molecular analysis (HBV DNA quantification) and Plain tubes for serum separation and biochemical analysis. Serum samples were separated by centrifugation at 3000 rpm for 10 minutes and stored at −20°C until laboratory analysis [20].

### 2.3. Laboratory Investigations

Serological-testing of HBsAg positivity was confirmed using enzyme-linked immunosorbent assay (ELISA) kits according to the Fortress Diagnostics (USA) instructions [21].

### 2.4. Quantification of HBV Viral Load

HBV DNA viral load was measured using real-time polymerase chain reaction (RT-PCR). Procedure including viral DNA extracted from plasma samples using a (Roche Diagnostics, USA) viral DNA extraction kit [22]. Amplification and quantification were performed using a real-time PCR thermal cycler. Results were expressed as International Units per milliliter (IU/mL).

### 2.5. Viral Load Classification

Patients were categorized into three groups according to HBV DNA levels when first group as low viral load ($<10^3$ IU/mL), second group as moderate viral load ($10^3$–$10^6$ IU/mL) and last groups as high viral load ($>10^6$ IU/mL).

### 2.6. Biochemical Analysis

Liver function biochemical parameters were analyzed using an automated biochemical analyzer (The Biolyzer® 300, China) [23]. The following parameters were measured: Alanine aminotransferase (ALT) and expressed as U/L, aspartate aminotransferase (AST) expressed as U/L, alkaline phosphatase (ALP) and expressed as U/L, total bilirubin expressed as mg/dL and S. albumin expressed as g/dL. All laboratory analyses were performed according to standard operating procedures. The internal-quality control serum was used daily in order to guarantee the precision and correctness of the biochemical and molecular-tests. All samples were examined duplicate in order to decrease any possible technical mistakes.

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### 2.7 Statistical Analysis

Data of this study were analyzed using “GaphPad-prism software version 8.0”. Continuous-variables were determined and expressed as mean± standard deviation (SD). Categorical-variables were dtetemine as frequencies and percentages. One-way analysis of variance (ANOVA) was used to compare biochemical-parameters among viral load groups [24]. Pearson correlation coefficient was used to assess the relationship between HBV viral load and biochemical parameters. Chi-square test was used for categorical variables where appropriate. A p-value ≤0.05 was considered statistically significant.

## Results and Discussion

A total of 120 patients with chronic hepatitis B infection were included in the present study. The mean age of participants was 39.8 ± 11.6 years, with an age range of 18–67 years. Male patients represented 58.3% (n = 70) of the study population, while females accounted for 41.7% (n = 50). The predominance of males may reflect the higher exposure risk and greater prevalence of HBV infection among males reported in several regional studies. The majority of patients were within the age group of 31–50 years (48.3%), followed by 18–30 years (29.2%), while patients older than 50 years represented 22.5% of the cohort.

Patients were classified into three groups according to HBV DNA viral load levels. Moderate viral load was the most common category representing 41.7% of patients followed by low viral load (30.8%) and high viral load (27.5%) as in Table 1.

**Table 1. Distribution of Patients According to HBV Viral Load Levels**

| Viral Load Group | HBV DNA Level (IU/mL) | Number of Patients (%) |
|---|---|---|
| Low viral load | $<10^3$ | 37 (30.8%) |
| Moderate viral load | $10^3$–$10^6$ | 50 (41.7%) |
| High viral load | $>10^6$ | 33 (27.5%) |

Table 1.
The results of the present study demonstrated that the majority of patients belonged to the moderate viral load category indicating ongoing viral replication in considerable proportion of chronic HBV-infected individuals. Patients with moderate and high HBV DNA levels together represented more than two-thirds of the study-population which proposing active disease status and an increased likelihood of progressive hepatic-injury.

High HBV viral load is considered one of the most important predictors of disease progression in chronic hepatitis B infection [25]. Persistent viral replication contributes to continuous immune-mediated hepatocellular damage which may eventually lead to liver-fibrosis, cirrhosis and hepatocellular-carcinoma [26]. Patients with elevated HBV DNA levels are therefore more likely to experience progressive-deterioration of liver function compared to patients with low viral replication.

The predominance of moderate viral load cases observed in this study may indicate that many patients were in the immune-active phase of chronic HBV infection which is characterized by detectable viral-replication accompanied by varying degrees of hepatic inflammation. This results showed the importance of regular monitoring of HBV DNA levels in chronic HBV patients to evaluate disease activity and determine the need for antiviral-therapy. Additionally the relatively high percentage of patients with high viral load levels reflects insufficient viral suppression and may be associated with delayed diagnosis, poor treatment adherence or lack of early therapeutic-intervention [27]. In developing countries the limited access to routine molecular testing and specialized-hepatology tests may contribute to persistence of active viral replication among patients.

The current results are consistent with several previous studies that reported a positive association between elevated HBV DNA levels and increased risk of liver disease progression [28]. Previous-studies have shown that patients who showed high levels of viral replication are more exposure to develop severe liver inflammation and associated complications and therefore the importance of assessing viral-load in chronic hepatitis B cannot be overstated [29].

In addition the lowest percentage of the patients had low viral-loads which could be comparable to inactive-hepatitis B virus carriers or people with partially suppressed viral replication [30]. Despite their favorable clinical results and monitoring is crucial since there is a possibility that viral reactivation during the progression of chronic hepatitis B.

The significant differences were shown in liver biochemical tests between the different viral-load groups. Patients with high HBV-DNA level showed significant elevated in liver enzymes and impaired liver function compared to patients with lower viral loads as shown in Table 2.

**Table 2. Comparison of Liver Function Parameters among HBV Viral Load Groups**

| Parameter | Low Viral Load | Moderate Viral Load | High Viral Load | *p*- value |
|---|---|---|---|---|
| ALT (U/L) | 32 ± 10 | 68 ± 18 | 145 ± 35 | <0.001 |
| AST (U/L) | 30 ± 9 | 62 ± 15 | 138 ± 30 | <0.001 |
| ALP (U/L) | 98 ± 22 | 120 ± 30 | 165 ± 40 | 0.002 |
| Total Bilirubin (mg/dL) | 0.9 ± 0.3 | 1.6 ± 0.5 | 2.8 ± 0.9 | 0.001 |

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| | | | | |
|---|---|---|---|---|
| Albumin (g/dL) | 4.1 ± 0.5 | 3.6 ± 0.4 | 3.0 ± 0.6 | <0.001 |

Table 2.

As in the Table 3 there is evident that both ALT and AST were found to progressively increase with an increasing level of viral-load. Those patients with high viral-load were found to have significantly high levels of ALT and AST than those patients with low viral-loads (p<0.001). This results showed that there was increased hepatocellular-injury due to viral replication activity. Transaminases elevation is often associated with inflammatory destruction of the liver cells due to infection. Similarly ALP level and bilirubin levels were significantly higher in patients with high HBV-DNA level which showed progressive hepatic-dysfunction and possible cholestatic involvement in advanced disease states as in Figure 3. In contrast the total bilirubin vlaue and serum albumin level showed a significant decreasing in patients with high viral-load which indicating impaired hepatic synthetic capacity as showed in Figure 4 and Figure 5 respectively.

These results agree with the concept that increasing HBV replication contributes directly or indirectly to liver injury and deterioration of hepatic function [31].

**Table 3. Pearson Correlation Analysis between HBV DNA Viral Load and Liver Biochemical Parameters**

| Parameter | Correlation Coefficient (r) | *p*- value |
|---|---|---|
| ALT | 0.68 | <0.001 |
| AST | 0.62 | <0.001 |
| ALP | 0.49 | 0.003 |
| Total Bilirubin | 0.45 | 0.002 |
| Albumin | -0.51 | 0.001 |

Table 3.

A strong positive correlation was observed between HBV viral load and ALT levels (r = 0.68, p < 0.001) as showed in Figure 1, as well as AST levels (r = 0.62, p < 0.001) as showed in Figure 2. These results indicate that higher viral replication is associated with greater hepatocellular-injury.

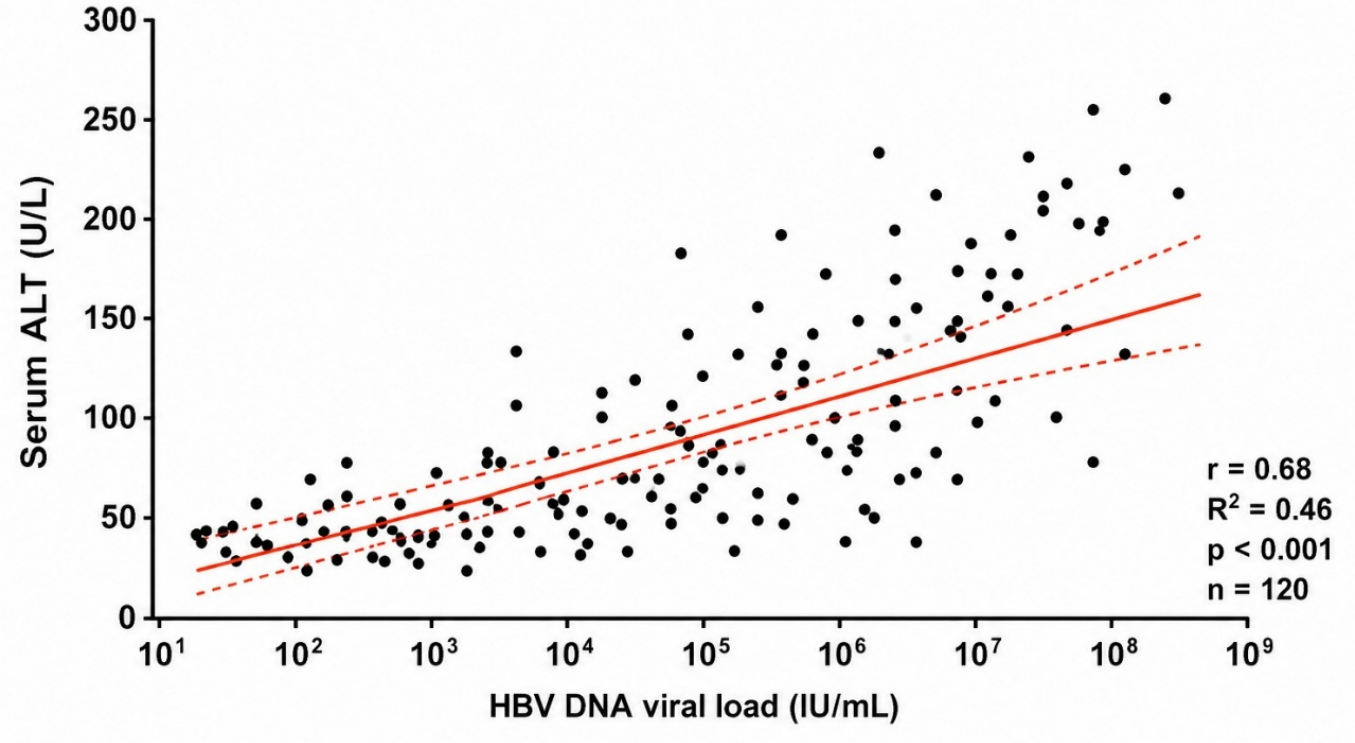


Figure 1.

**Figure1. Correlation between HBV DNA viral load and serum ALT levels in chronic hepatitis B patients.**

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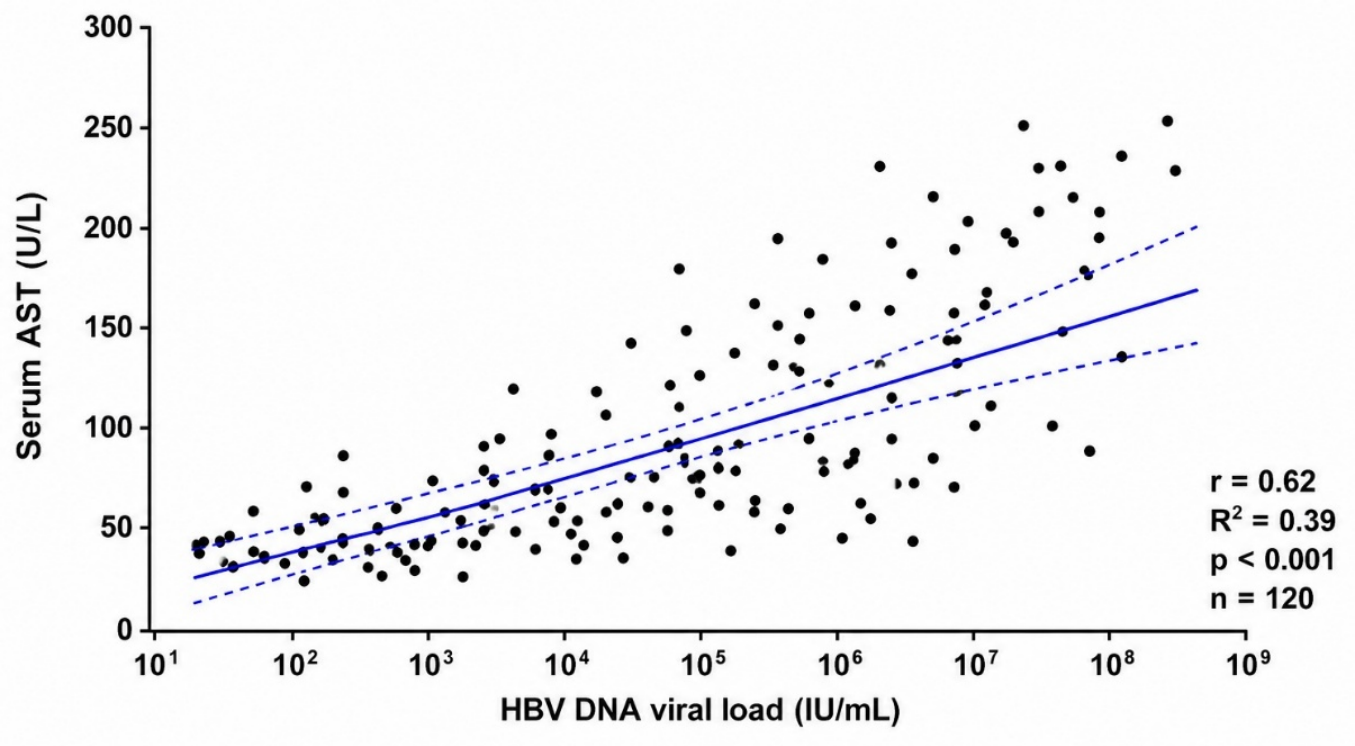


Figure 2.

**Figure 2. Correlation between HBV DNA viral load and serum AST levels in chronic hepatitis B patients.**

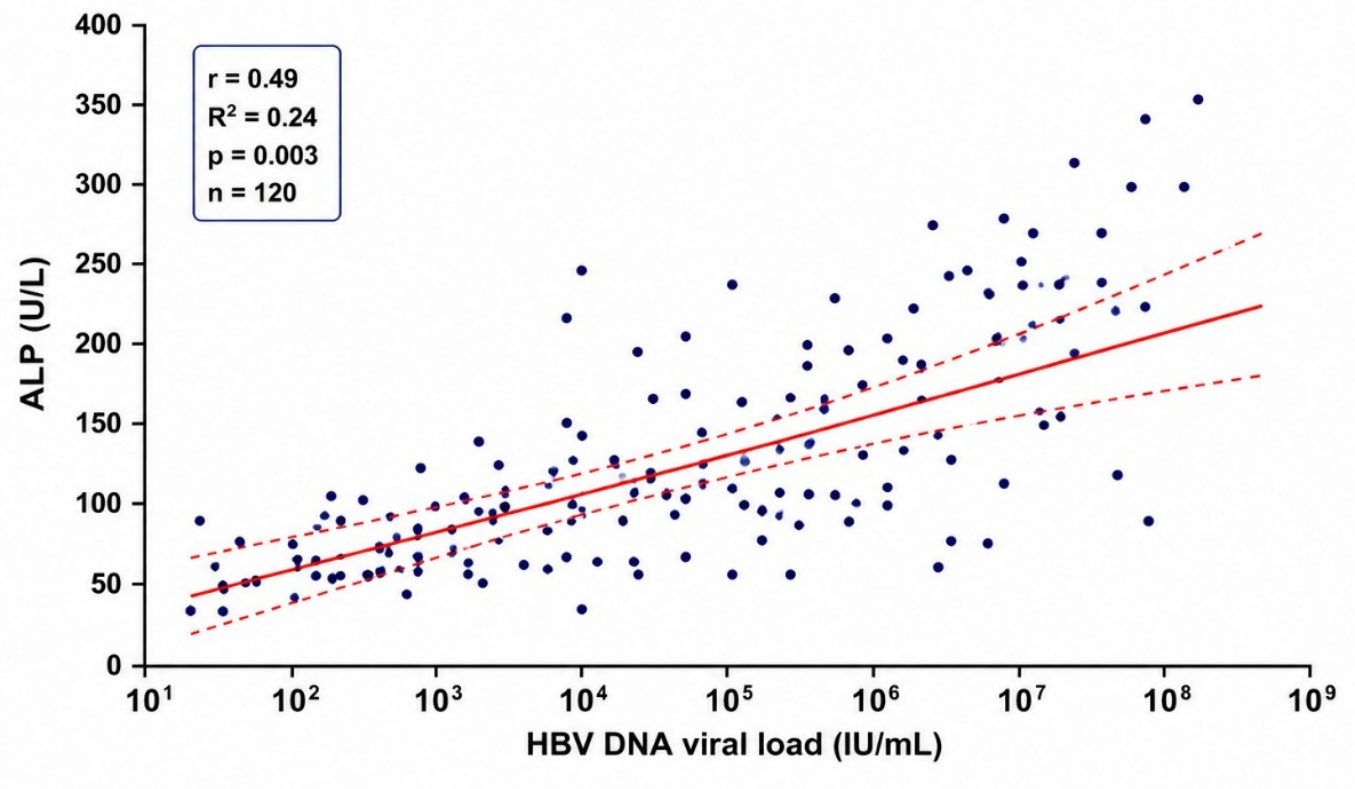


Figure 3.

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**Figure3. Correlation between HBV DNA viral load and serum ALP levels in patients with chronic hepatitis B infection.**

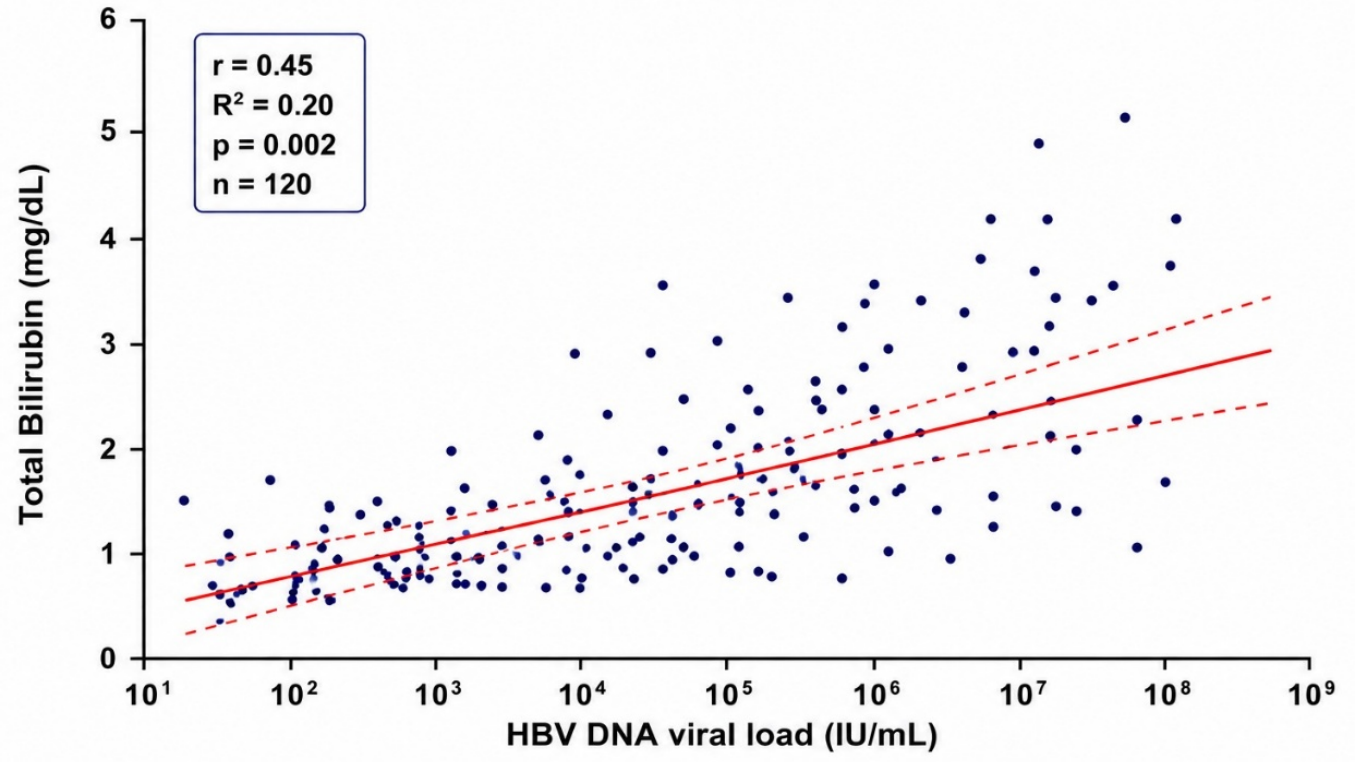


Figure 4.

**Figure 4. Correlation between HBV DNA viral load and serum T. bilirubin levels in patients with chronic hepatitis B infection.**

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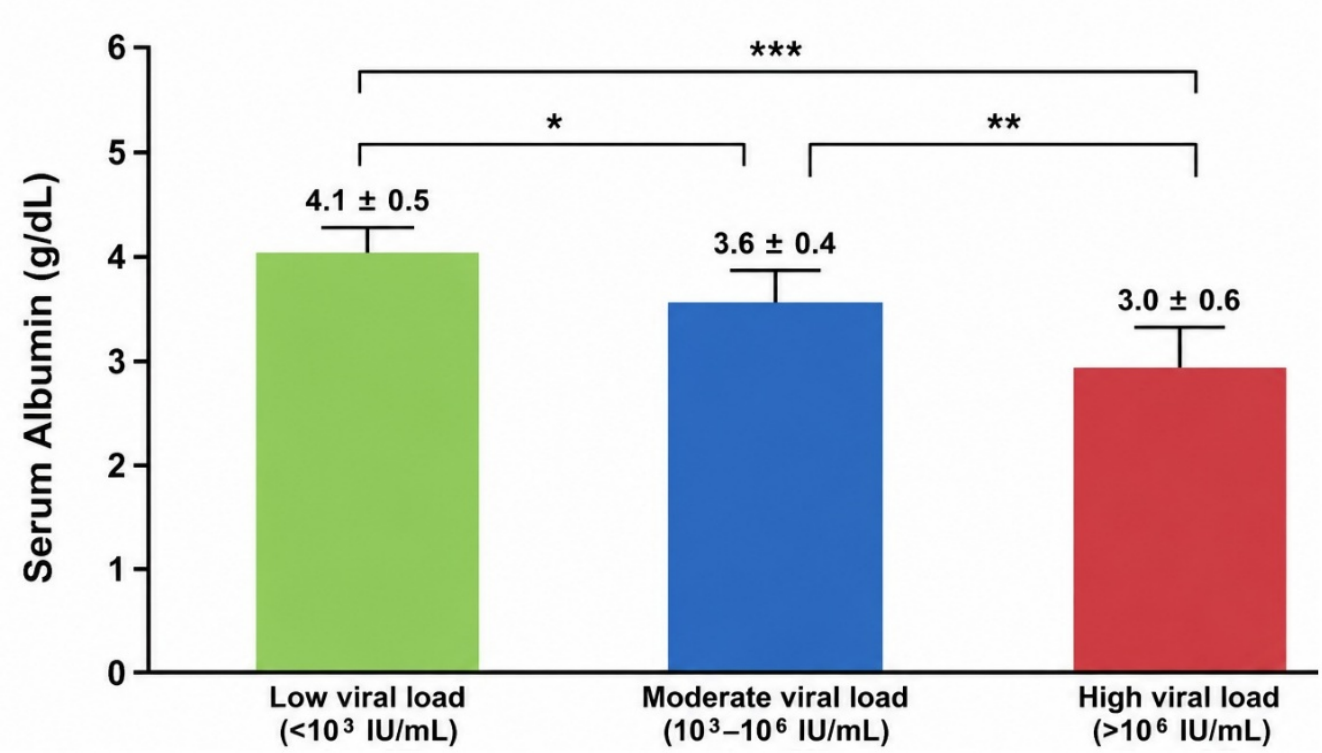


Figure 5.

**Figure 5. Comparison of serum albumin levels among different HBV viral load groups.**

The positive correlation between HBV DNA and bilirubin levels suggests worsening liver excretory function with increased viral activity [32]. Meanwhile, the negative correlation between viral load and serum albumin indicates progressive impairment of liver synthetic function in patients with active infection [33]. The above results are agree with the pathology associated with chronic HBV infection which involves inflammation and destruction of the liver cells due to constant viral-replication. In addition the most of the patients with high viral load showed symptoms such as fatigue, right upper abdominal pain, hepatomegaly and increasing in liver enzyme levels. Furthermore some patients also showed signs of chronic liver failure which included jaundice and low serum albumin levels. [34].

The observed biochemical change are reflect the progressive nature of the chronic HBV infection. Raised ALT and AST value are markers of hepatocyte membrane damage and inflammatory activity whereas reduced albumin levels may indicate-chronic liver insufficiency

## Conclusion

The present study demonstrates that HBV viral-load is strongly associated with liver biochemical abnormalities in patients with chronic hepatitis B infection. Patients with high HBV DNA levels showed significantly increased liver enzyme values and impaired liver synthetic function compared to patients with lower viral replication. These results give emphasis to the clinical-value of HBV DNA quantification as the important marker of disease activity and progression. Combined evaluation of viral load and liver biochemical-parameters may improve disease monitoring, therapeutic decision-making and prediction of hepatic complications.

**Conflict of interest:**

Author confirm there is no conflict of interest.

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