

Study of Key Immunological and Hepatic Indicators in Patients with Hepatitis B Virus Attending and Admitted to Merjan Teaching Hospital in Babylon Province

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ABSTRACT

Objective: This cross-sectional study aimed to evaluate key hepatic cellular markers and systemic inflammatory responses among HBV-infected patients attending outpatient clinics and admitted to inpatient wards at Merjan Teaching Hospital in Babylon Province, Iraq. **Method:** Serum levels of liver transaminases – alanine aminotransferase (ALT) and aspartate aminotransferase (AST) – were quantitatively measured alongside pro-inflammatory cytokines, specifically Interleukin-6 (IL-6) and Tumor Necrosis Factor-alpha (TNF- α), using Enzyme-Linked Immunosorbent Assay (ELISA) techniques, and compared against healthy controls. **Results:** Statistically significant elevations ($p \leq 0.01$ for liver enzymes; $p \leq 0.001$ for cytokines) were observed in HBV patients compared to the control group. **Novelty:** These findings demonstrate that continuous immune-mediated hepatocyte destruction and cytokine dysregulation drive the pathogenesis of HBV, underlining the clinical relevance of incorporating cytokine profiling alongside standard liver function tests for improved diagnostic and prognostic monitoring.

INTRODUCTION

Hepatitis B Virus (HBV) is an enveloped, partially double-stranded DNA virus belonging to the Hepadnaviridae family [1]. The HBV genome consists of a relaxed circular DNA (rcDNA) of approximately 3.2 kb, which is converted inside the host cell nucleus into covalently closed circular DNA (cccDNA), forming a persistent transcriptional template responsible for chronic infection and disease recurrence [2], [3]. According to recent World Health Organization (WHO) estimates, over 250 million people worldwide live with chronic HBV infection, putting them at high risk for developing end-stage liver complications such as cirrhosis and hepatocellular carcinoma (HCC) [4], [5].

The pathogenesis of HBV-induced liver damage is predominantly immunopathological rather than directly cytopathic [6]. The host's immune response plays a dual role: while cellular immunity mediated by CD8⁺ cytotoxic T lymphocytes (CTLs) is vital for viral clearance, it simultaneously causes massive hepatocyte necrosis through the destruction of infected liver cells [7], [8]. Furthermore, activation of the innate immune system and resident liver macrophages (Kupffer cells) triggers an overproduction of pro-inflammatory cytokines, particularly Interleukin-6 (IL-6) and Tumor Necrosis Factor-alpha (TNF- α) [9].

In clinical settings, serum transaminases – Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) – serve as standard biomarkers reflecting active liver parenchymal damage [10]. However, these enzymes do not fully capture the complex immunological activity occurring within the liver microenvironment. Given the significant burden of viral hepatitis in Iraq and the critical role of specialized regional medical centers such as Merjan Teaching Hospital in Babylon Province, this study was designed to systematically assess both functional hepatic enzymes and key pro-inflammatory cytokines in local HBV patients to provide a clearer immunopathological baseline.

Aims of the Study

1. To quantitatively evaluate serum levels of key functional liver enzymes (ALT and AST) in HBV-infected patients compared to healthy control individuals.
2. To quantify serum concentrations of key pro-inflammatory and immunomodulatory cytokines (IL-6 and TNF- α) in HBV patients.
3. To examine the correlation between immunological cytokine elevation and the severity/duration of infection among outpatient and inpatient populations at Merjan Teaching Hospital.
4. To establish baseline diagnostic and immunological reference data tailored to the patient demographic in Babylon Province.

RESEARCH METHOD

Study Design and Setting

This observational cross-sectional study was conducted between October 2025 and April 2026. Samples were collected from outpatient clinics and inpatient wards at Merjan Teaching Hospital, a major tertiary referral center in Babylon Province, Iraq. Laboratory analyses were carried out at the Department of Clinical Analyses and Advanced Microbiology Laboratories.

Study Population and Criteria

A total of 80 human subjects were enrolled in this study, divided into two distinct groups:

1. Patient Group (n = 50): Confirmed HBV-infected individuals who tested positive for Hepatitis B surface Antigen (HBsAg) using standard screening and ELISA confirmation. Patients with co-infections (HCV, HIV, HDV), systemic autoimmune diseases, alcohol-induced liver diseases, or acute non-hepatic systemic inflammation were excluded.
2. Control Group (n = 30): Age- and gender-matched apparently healthy individuals with no prior history of liver disease, negative HBsAg test results, and normal biochemical profiles.

Sample Collection and Processing

Approximately 5 mL of peripheral venous blood was drawn from each participant under aseptic conditions using sterile plain vacutainer tubes. The blood was allowed to

clot at room temperature for 20 minutes and subsequently centrifuged at 3,000 rpm for 10 minutes to obtain clear serum. Serum aliquots were immediately stored in sterile microcentrifuge tubes at -20°C until biochemical and immunological assays were performed.

Laboratory Procedures

1. Liver Function Assays: Serum levels of ALT and AST were measured using automated spectrophotometric kinetic enzymatic methods according to standard manufacturer guidelines.
2. Immunological Assays: Serum concentrations of Interleukin-6 (IL-6) and Tumor Necrosis Factor-alpha (TNF- α) were measured using commercial high-sensitivity Enzyme-Linked Immunosorbent Assay (ELISA) kits following the manufacturers' specific protocols. Optical densities were measured at 450 nm using a microplate reader.

Statistical Analysis

Data were processed and analyzed using the Statistical Package for the Social Sciences (SPSS, Version 27.0). Continuous variables were expressed as Mean $\pm$ Standard Deviation (SD). Student's t-test was used to compare differences between groups. A p-value of ≤ 0.05 was considered statistically significant, and $p \leq 0.01$ or $p \leq 0.001$ was considered highly significant.

RESULT AND DISCUSSION

Results

Table 1. Demographic Distribution of the Study Groups

Parameter	Patient Group (n = 50)	Control Group (n = 30)	p-value
Male, n (%)	32 (64.0%)	18 (60.0%)	> 0.05 (NS)
Female, n (%)	18 (36.0%)	12 (40.0%)	> 0.05 (NS)
Mean Age (Years $\pm$ SD)	42.5 $\pm$ 8.4	40.1 $\pm$ 7.9	> 0.05 (NS)

Table 2. Comparison of Liver Transaminase Levels (ALT and AST)

Biomarker	Patient Group (Mean $\pm$ SD)	Control Group (Mean $\pm$ SD)	p-value	Significance
ALT (U/L)	78.4 $\pm$ 15.2	24.1 $\pm$ 5.3	$p \leq 0.01$	Highly Significant
AST (U/L)	65.9 $\pm$ 12.8	22.8 $\pm$ 4.6	$p \leq 0.01$	Highly Significant

Table 3. Serum Pro-inflammatory Cytokine Levels (IL-6 and TNF- α)

Immunological Marker	Patient Group (Mean $\pm$ SD)	Control Group (Mean $\pm$ SD)	p-value	Significance
IL-6 (pg/mL)	45.6 $\pm$ 9.1	12.3 $\pm$ 3.2	p $\leq$ 0.001	Extremely Significant
TNF- α (pg/mL)	38.2 $\pm$ 7.4	8.9 $\pm$ 2.1	p $\leq$ 0.001	Extremely Significant

Discussion

The physiological integrity of the liver is heavily dependent on a balance between localized immune tolerance and protective antiviral responses. In the present study, the quantitative analysis of serum ALT and AST revealed a marked, statistically significant elevation in HBV patients compared to healthy controls (78.4 $\pm$ 15.2 U/L vs. 24.1 $\pm$ 5.3 U/L for ALT; 65.9 $\pm$ 12.8 U/L vs. 22.8 $\pm$ 4.6 U/L for AST; p $\leq$ 0.01). Intracellularly, ALT is predominantly localized in hepatocyte cytoplasm, making it a highly specific biomarker for liver membrane leakage and parenchymal cell injury [11]. AST, although present in cardiac and skeletal muscle tissue as well, resides in both mitochondrial and cytosolic compartments of hepatocytes [12]. The concurrent elevation of both enzymes directly reflects active structural disintegration of liver cellular membranes triggered by virus-induced immunopathogenesis [13].

From an immunological perspective, the significant surge in serum IL-6 (45.6 $\pm$ 9.1 pg/mL) and TNF- α (38.2 $\pm$ 7.4 pg/mL) in HBV patients (p $\leq$ 0.001) underscores the central role of cytokine dysregulation in viral hepatitis. TNF- α is a master pro-inflammatory cytokine primarily secreted by activated Kupffer cells and infiltrating CD8⁺ T cells [14]. It acts via binding to TNFR1 and TNFR2 receptors on hepatocytes, inducing caspase activation and apoptosis, while simultaneously amplifying local cellular recruitment [15].

Similarly, Interleukin-6 (IL-6) serves as a key mediator of the acute-phase response. While transient IL-6 elevation promotes hepatocyte regeneration and tissue repair, sustained high levels—as observed in this cohort—drive chronic inflammation, stimulate hepatic stellate cells (HSCs), and facilitate fibrogenesis [16], [17]. These findings strongly align with recent regional and international literature highlighting that elevated systemic cytokine storms correlate with higher HBV viral DNA loads, increased histological activity index (HAI), and accelerated progression toward hepatic fibrosis and cirrhosis [18], [19].

CONCLUSION

Fundamental Finding: Infection with Hepatitis B Virus leads to substantial hepatocellular dysfunction, demonstrated by highly significant elevations in serum ALT and AST transaminases. The immunopathogenesis of HBV in local Iraqi patients is

characterized by severe systemic inflammation, marked by dramatic increases in pro-inflammatory cytokines IL-6 and TNF- α . **Implication:** Combining functional liver enzymes with inflammatory cytokine profiling provides a comprehensive diagnostic framework for assessing disease severity and active hepatic damage in clinical settings such as Merjan Teaching Hospital. Serum IL-6 and TNF- α measurements should be incorporated into routine diagnostic and prognostic panels for HBV patients in Iraqi teaching hospitals. Regional vaccination programs should be expanded, mandatory pre-marital and blood donor screening should be implemented, and public health awareness regarding HBV transmission routes should be promoted to reduce the burden on public healthcare facilities. **Limitation:** The provided text does not contain a specific limitation statement. **Future Research:** Larger multi-center longitudinal studies incorporating HBV DNA viral load quantification (qPCR) and HBV genotyping should be conducted to correlate viral variations with cytokine profiles in Babylon Province. Future studies should also evaluate correlations between these immunological biomarkers and non-invasive liver fibrosis scoring tools, such as FibroScan or the APRI index.

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