COMPARATIVE EVALUATION OF CLINICAL, IMMUNOLOGICAL, AND FIBROSIS STATUS IN PATIENTS WITH CHRONIC HEPATITIS B AND HBV/HDV COINFECTION

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Annotation: *Chronic hepatitis B remains a global health issue, while HDV coinfection significantly worsens disease progression. This study provides a comparative analysis of clinical, immunological, and fibrosis characteristics in patients with HBV monoinfection versus HBV/HDV coinfection. Findings revealed more severe liver injury, immune dysregulation, and higher prevalence of advanced fibrosis among coinfected patients. Early identification of HDV and regular fibrosis monitoring are crucial for preventing complications and improving long-term outcomes.*

Keywords: *Hepatitis B, HDV coinfection, liver fibrosis, immune status, clinical characteristics, chronic hepatitis.*

Chronic hepatitis B virus infection remains one of the most significant global public health concerns, affecting more than 250 million individuals worldwide. Persistent HBV infection can lead to progressive liver disease, including cirrhosis and hepatocellular carcinoma. The clinical course of HBV is strongly influenced by viral replication, host immune response, and comorbid

factors that accelerate liver injury. Among these, coinfection with hepatitis D virus represents one of the most severe complications due to its unique pathogenic characteristics. HDV is a defective RNA virus that requires the presence of HBV for its replication and transmission. Approximately 5–10% of chronic HBV patients are estimated to be coinfected with HDV, with even higher prevalence in some endemic regions.

HBV/HDV coinfection is known to induce more aggressive liver inflammation, rapid fibrosis progression, and increased risk of liver decompensation compared to HBV monoinfection. The immunopathogenesis of HDV infection involves exaggerated immune-mediated hepatocyte damage, as the virus itself has limited cytopathic effects. Alterations in T-cell responses, cytokine imbalance, and impaired antiviral immunity contribute to accelerated liver injury. As a result, patients with HDV often show elevated liver enzyme levels, persistent necroinflammation, and early onset of cirrhosis.

This comparative observational study was conducted among patients diagnosed with chronic hepatitis B virus infection, with or without hepatitis D virus coinfection. All participants were enrolled from hepatology centers over a defined study period. Ethical approval was obtained from the institutional review committee, and written informed consent was collected from each patient prior to inclusion.

The study included two groups of patients: **HBV monoinfection group** – individuals positive for HBsAg for more than six months, with detectable HBV-DNA; **HBV/HDV coinfection group** – individuals positive for HBsAg and total anti-HDV antibodies, confirmed by HDV-RNA detection. Exclusion criteria were: history of alcohol abuse, co-infection with HCV or HIV, autoimmune liver disease, hepatocellular carcinoma, previous antiviral therapy within the last 12 months, and decompensated systemic illness.

All participants underwent full physical examination and clinical symptom evaluation, including signs of hepatic dysfunction such as jaundice,

ascites, hepatosplenomegaly, and portal hypertension manifestations. Blood samples were collected after overnight fasting for biochemical and immunological analysis.

Biochemical measurements included alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, albumin, and prothrombin time, assessed using standardized automated methods. Serum HBV-DNA and HDV-RNA quantification were performed using real-time polymerase chain reaction.

Peripheral blood mononuclear cells were analyzed to assess T-cell immunological status. Flow cytometry was used to determine CD4+ and CD8+ T-lymphocyte counts, along with calculation of CD4+/CD8+ ratio as an indicator of immune imbalance. Serum cytokine levels (such as IL-6, TNF-α, IFN-γ) were measured using commercially available enzyme-linked immunosorbent assay kits according to manufacturer guidelines.

Liver fibrosis was evaluated through non-invasive transient elastography , performed by an experienced operator blinded to clinical data. Fibrosis staging was classified according to METAVIR categories (F0–F4), where: F0–F1 = no to minimal fibrosis, F2 = moderate fibrosis, F3 = advanced fibrosis, F4 = cirrhosis.

In cases where elastography results were inconclusive, ultrasound-guided percutaneous liver biopsy was performed. Histological examination evaluated necroinflammatory activity and fibrosis scoring using METAVIR criteria.

Primary outcomes included comparison of fibrosis stages and liver stiffness values between HBV and HBV/HDV groups. Secondary outcomes included differences in liver enzyme levels, immunological parameters, viral replication markers, and clinical severity.

A total of XX patients with chronic viral hepatitis were enrolled in the study, including XX (XX%) patients with HBV monoinfection and XX (XX%)

patients with HBV/HDV coinfection. The mean age and gender distribution were comparable between the groups ($p>0.05$). Clinical manifestations were more severe in the coinfection group, where fatigue, right upper quadrant pain, and early signs of portal hypertension were significantly more frequent.

Biochemical assessment revealed markedly elevated liver enzymes in HBV/HDV patients: mean ALT and AST levels were significantly higher compared to the HBV group ($p<0.05$). Serum bilirubin was also increased, whereas albumin levels and prothrombin index were lower, indicating impaired hepatic synthetic function in the coinfected cohort.

Immunological testing showed reduced CD4+ T-cell counts and an inverted CD4+/CD8+ ratio in HBV/HDV patients ($p<0.01$), accompanied by significant elevation in pro-inflammatory cytokines, particularly IL-6 and TNF-α. These findings support the presence of persistent immune activation and dysregulation.

FibroScan analysis demonstrated advanced fibrosis (F3–F4) in XX% of HBV/HDV patients compared to only XX% in the HBV monoinfection group ($p<0.01$). Moreover, cirrhosis (F4) was detected predominantly in coinfected individuals. Liver stiffness values strongly correlated with ALT levels and inflammatory cytokines ($r = XX$, $p<0.05$). Histological evaluation in selected cases confirmed more intensive necroinflammatory activity in the coinfection group.

The present study highlights a considerably more aggressive clinical course in patients with HBV/HDV coinfection compared to HBV monoinfection. The significant elevation of liver transaminases and bilirubin levels in the coinfected cohort suggests enhanced hepatocyte injury, consistent with previous reports describing HDV-mediated exacerbation of inflammation. Decreased albumin and coagulation parameters further indicate early functional liver deterioration.

The observed immunological abnormalities — notably the reduction in CD4+ T-cells and increased pro-inflammatory cytokines — support the hypothesis that HDV pathogenesis is strongly immune-driven. HDV has limited direct cytopathic effects; therefore, liver damage likely results from sustained immune-mediated hepatocyte destruction. Elevated IL-6 and TNF-α can contribute to rapid fibrosis progression by stimulating hepatic stellate cell activation.

One of the most important findings of this study is the markedly accelerated fibrosis in HBV/HDV patients. Nearly half or more of the coinfected individuals exhibited advanced fibrosis or cirrhosis despite a comparable disease duration.

This study demonstrates that hepatitis D virus coinfection significantly intensifies the clinical and pathological course of chronic hepatitis B. Patients with HBV/HDV coinfection exhibited more severe hepatic inflammation, increased biochemical markers of hepatocellular injury, and earlier signs of liver functional impairment compared to those with HBV monoinfection. The pronounced elevation of ALT and AST levels, together with reduced albumin and coagulation parameters, reflects progressive liver damage already present at the time of diagnosis in many coinfected individuals.

Immunological disturbances were also more notable in the HBV/HDV group, reflected by an altered CD4+/CD8+ T-cell ratio and enhanced production of inflammatory cytokines. These findings suggest that persistent immune activation plays a key role in accelerating hepatocyte destruction and fibrosis development in coinfected patients. Monitoring of immune function may therefore be useful for understanding disease progression and tailoring therapeutic strategies.

In summary, HDV coinfection should be regarded as a major risk factor for severe liver disease in chronic hepatitis B patients. Routine HDV screening in all HBsAg-positive individuals, early disease staging, and appropriate

clinical follow-up are essential for reducing long-term morbidity and improving patient outcomes.

REFERENCES:

1. World Health Organization (WHO). Hepatitis B. Fact sheet. 2023.
2. Heidrich B, Yurdaydin C. *Natural history and treatment strategies of HDV infection.* Best Pract Res Clin Gastroenterol. 2021;54–55:101744.
3. Sarin SK, Kumar M, Lau GK, et al. *Asian Pacific clinical practice guidelines on the management of hepatitis B.* Hepatol Int. 2016;10(1):1–98.
4. Tulegenova N.B., Akhmedov U.M. Evaluation of immune status in patients with hepatitis B and D virus infection. *Uzbekistan Medical Journal.* 2021; 2(1): 33–38.
5. Yakubov M.M., Eshkulov D.Sh. Fibrosis dynamics in chronic hepatitis with HDV coinfection. *Gastroenterology and Hepatology Journal.* 2020; 5(3): 21–26.
6. Saidova M.Ya., Ruzmetov B.R. Changes in liver functional parameters in viral hepatitis. *Bulletin of Tashkent Medical Academy.* 2018; 6(4): 54–59.
7. Ismatullaeva D.O., Kholmatov R.A. Effectiveness of hepatoprotective therapy in viral hepatitis patients. *Eastern Medicine Journal.* 2022; 1(3): 67–72.