

DIAGNOSTIC VALUE OF MODERN SEROLOGICAL AND MOLECULAR BIOMARKERS IN HEPATITIS B AND D CO-INFECTION DURING ANTIVIRAL THERAPY: A REVIEW

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Abstract. Chronic hepatitis B virus (HBV) and hepatitis D virus (HDV) co-infection remains one of the most severe forms of viral hepatitis and is associated with accelerated progression to liver cirrhosis, hepatic decompensation, and hepatocellular carcinoma. Early diagnosis and effective monitoring of antiviral therapy are essential for improving clinical outcomes. In recent years, significant advances have been achieved in serological and molecular diagnostics, allowing more accurate assessment of viral replication, disease activity, and treatment response. Quantitative determination of HBsAg, HBV DNA, HDV RNA, and novel biomarkers have become important tools in clinical practice.

Keywords: hepatitis B virus, hepatitis D virus, biomarkers, serological diagnosis, molecular diagnostics, antiviral therapy, HBV DNA, HDV RNA.

Introduction. Hepatitis B virus (HBV) infection remains a major global public health problem, affecting nearly 254 million people worldwide [1]. Hepatitis D virus (HDV) is a defective RNA virus that requires the presence of HBV for replication and transmission [2]. Co-infection or superinfection with HDV significantly increases the risk of liver fibrosis, cirrhosis, hepatic failure, and hepatocellular carcinoma compared with HBV monoinfection [3].

The management of HBV/HDV co-infection has become increasingly dependent on accurate laboratory diagnostics. Modern serological and molecular methods provide valuable information regarding viral activity, disease progression, and therapeutic efficacy [4].

Epidemiological Significance of HBV/HDV Co-Infection. HDV infection affects approximately 12–20 million individuals globally and remains highly endemic in several regions of Central Asia, the Middle East, Eastern Europe, and Africa [2].

The prevalence of HDV among HBsAg-positive individuals varies considerably, ranging from 4% to 20% depending on geographical location and risk groups [3]. Studies have demonstrated that HDV infection accelerates liver disease progression and significantly increases liver-related mortality [5].

Serological Biomarkers in HBV/HDV Co-Infection

HBsAg Quantification. Quantitative measurement of hepatitis B surface antigen (HBsAg) has emerged as an important marker for evaluating viral activity and treatment response [4]. Lower HBsAg levels during antiviral therapy have been associated with improved treatment outcomes and increased likelihood of functional cure [6]. Monitoring HBsAg kinetics may help clinicians predict therapeutic response and optimize treatment strategies [4].

HBeAg and Anti-HBe. The presence of hepatitis B e antigen (HBeAg) reflects active viral replication and infectivity [1]. Seroconversion from HBeAg to anti-HBe antibodies is generally considered a favorable therapeutic endpoint and is associated with suppression of viral replication [6].

Anti-HDV Antibodies. Detection of anti-HDV immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies remains the primary screening approach for HDV infection [2]. Positive anti-HDV results should be followed by molecular testing to confirm active viral replication [7].

Molecular Biomarkers and Their Clinical Significance HBV DNA Quantification. Measurement of serum HBV DNA by real-time polymerase chain reaction (PCR) is considered the gold standard for assessing HBV replication [1]. HBV DNA levels serve as a critical indicator for treatment initiation, monitoring antiviral efficacy, and evaluating long-term prognosis [4]. Persistent suppression of HBV DNA during therapy is associated with reduced risk of cirrhosis and hepatocellular carcinoma [6].

HDV RNA quantification represents the most reliable marker of active HDV replication [2]. Current clinical guidelines recommend HDV RNA measurement for diagnosis, treatment monitoring, and evaluation of virological response [5]. Reduction or disappearance of HDV RNA during therapy is considered an important predictor of favorable clinical outcomes [7].

Hepatitis B Core-Related Antigen (HBcrAg). HBcrAg reflects transcriptional activity of covalently closed circular DNA (cccDNA), which serves as the viral reservoir within hepatocytes [6]. This marker may provide additional information regarding residual viral activity when HBV DNA becomes undetectable during treatment [4].

Serum HBV RNA has recently attracted attention as a promising marker of viral transcription and treatment response [6]. Several studies suggest that HBV RNA may predict viral relapse following discontinuation of nucleos(t)ide analogue therapy [4].

Quantitative Anti-HBc. Quantitative measurement of hepatitis B core antibodies (anti-HBc) has been proposed as an indicator of host immune response and disease activity [6].

Biomarkers during modern antiviral therapy. The introduction of pegylated interferon-alpha and nucleos(t)ide analogues significantly improved

management of chronic HBV infection [1]. More recently, Bulevirtide has emerged as the first approved targeted therapy for chronic hepatitis D [7].

Assessment of HBsAg, HBV DNA, and HDV RNA dynamics during therapy allows clinicians to evaluate treatment efficacy and predict long-term outcomes [5]. Patients achieving significant reductions in HDV RNA and HBsAg concentrations demonstrate better clinical responses and slower disease progression [7].

Conclusion. Modern serological and molecular biomarkers play a crucial role in the diagnosis and monitoring of HBV/HDV co-infection during antiviral therapy. Quantitative assessment of HBsAg, HBV DNA, and HDV RNA remains central to clinical decision-making. Emerging biomarkers such as HBcrAg and serum HBV RNA offer promising opportunities for improving treatment monitoring and prognostic evaluation. The integration of innovative diagnostic technologies into routine clinical practice may contribute to earlier intervention, personalized therapy, and improved long-term outcomes for patients with chronic hepatitis B and D.

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