## RECENT DIAGNOSTIC ADVANCEMENTS IN CHRONIC VIRAL HEPATITIS B

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## Abstract.

Chronic hepatitis B virus (HBV) infection remains a global public health problem, affecting over 250 million people worldwide and causing significant morbidity and mortality due to cirrhosis and hepatocellular carcinoma. Traditional diagnostic approaches such as HBsAg detection, HBV DNA quantification, and serological markers remain central to clinical practice. This review summarizes the latest diagnostic advancements in HBV, highlighting their relevance for global and regional practice, with particular emphasis on applicability in Central Asia.

**Keywords:** chronic hepatitis B, HBcrAg, pre-genomic RNA, biomarkers, elastography, digital PCR, artificial intelligence, Uzbekistan.

**Introduction.** Hepatitis B virus infection is a major cause of liver-related disease worldwide, particularly in regions with high prevalence such as Asia and sub-Saharan Africa. Despite widespread vaccination programs, HBV remains endemic in Central Asia, including Uzbekistan, where co-infection with hepatitis D virus further complicates clinical outcomes [1]. Traditional diagnostics, including HBsAg and HBV DNA testing, although widely used, have limitations in predicting treatment response and long-term outcomes. Recent technological

advancements aim to overcome these gaps and support personalized management [2].

However, in recent years novel diagnostic technologies have emerged, improving accuracy in evaluating viral replication, liver fibrosis, and treatment response. Among them, hepatitis B core-related antigen (HBcrAg), pre-genomic RNA (pgRNA), next-generation sequencing (NGS), and digital droplet PCR (ddPCR) have shown potential for refining disease monitoring. Non-invasive tools, including transient elastography and serum fibrosis panels, provide valuable alternatives to liver biopsy. Artificial intelligence (AI) and machine learning-based algorithms are increasingly applied for predictive modeling and interpretation of complex biomarker patterns.

Emerging biomarkers. Hepatitis B core-related antigen (HBcrAg): HBcrAg reflects transcriptional activity of covalently closed circular DNA (cccDNA), providing better insight into viral persistence. Studies have shown that HBcrAg correlates with HBV DNA and intrahepatic cccDNA levels, serving as a potential surrogate marker for monitoring disease activity and therapeutic response [3].

**Pre-genomic RNA (pgRNA):** Serum HBV pgRNA represents active transcription from cccDNA and predicts viral rebound after nucleos(t)ide analogue discontinuation. Measurement of pgRNA by sensitive PCR methods has become an important research tool with potential for clinical application [4].

**Advanced molecular diagnostics.** Digital droplet PCR (ddPCR): ddPCR offers higher sensitivity than conventional PCR, enabling precise quantification of low-level viremia and resistance mutations. This is particularly relevant for patients under long-term antiviral therapy.

**Next-generation sequencing** (NGS): NGS allows simultaneous detection of viral genotypes, mutations, and quasispecies diversity. It is essential for studying drug resistance, immune escape variants, and regional genotype distribution, including HBV genotype D, which predominates in Central Asia [5,8].

**CRISPR-based diagnostics:** Though still in development, CRISPR/Cas systems are being explored for rapid and highly specific HBV DNA detection, holding promise for point-of-care applications.

Non-invasive assessment of liver damage

Liver biopsy, once the gold standard, is increasingly being replaced by non-invasive techniques:

Transient elastography (FibroScan): widely adopted for assessing fibrosis and cirrhosis, offering real-time results.

Magnetic resonance elastography (MRE): provides highly accurate fibrosis staging, though less available in resource-limited settings.

Serum fibrosis panels (FIB-4, APRI, ELF score): validated for fibrosis prediction and used as alternatives in primary care [6,9].

Imaging and artificial intelligence. Ultrasound-based elastography combined with AI algorithms enhances diagnostic accuracy in differentiating fibrosis stages. Machine learning models using laboratory and imaging data improve prediction of disease progression and treatment response. Such approaches may be particularly useful in Uzbekistan, where access to advanced molecular tests remains limited.

Regional perspectives. In Uzbekistan and neighboring Central Asian countries, HBV remains a pressing problem. Genotype D predominates, often associated with poorer response to interferon therapy and higher risk of progression [5,10]. Local studies emphasize the need for integrating advanced diagnostics, including non-invasive fibrosis assessment and molecular biomarkers, into clinical practice. The implementation of modern technologies could improve early detection and optimize treatment strategies in Samarkand and other high-burden regions.

## Conclusion

Recent diagnostic advancements in HBV, including novel biomarkers (HBcrAg, pgRNA), molecular methods (ddPCR, NGS), non-invasive fibrosis assessment, and AI-supported imaging, provide new opportunities for precision medicine. While implementation remains limited in low-resource regions, integration of these tools into clinical practice will significantly improve disease monitoring and patient outcomes. Expanding access to advanced diagnostics in Central Asia, particularly Uzbekistan, is essential for better management of HBV and reduction of its burden.

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