

VIRAL HEPATITIS B, PREVALENCE, DIAGNOSIS, CLINICAL SIGNIFICANCE OF QUANTITATIVE DETERMINATION OF HBsAg AND ITS CORRELATION WITH GENOTYPES AND VARIANTS

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Abstract

Viral hepatitis B (HBV) is a viral anthroponotic infectious disease with a hemocontact mechanism of transmission. The disease is characterized by cyclical hepatitis, accompanied in some cases by jaundice and possible chronicity.

The prevalence of hepatitis B virus (HBV) infection in the world is very high. According to the World Health Organization (WHO) in 2022, almost every third person in the world is infected with the hepatitis B virus, and 254 million people are affected by this chronic infection.

Keywords: Viral hepatitis B, aspartate aminotransferase, prothrombin index, HBsAg , alpha-fetoprotein , anti-HBcIgG , PCR, hepatocellular carcinoma.

Introduction

WHO experts have shown that the prevalence of HBV infection in a given territory depends on the age at which the population becomes infected. A high prevalence of HBV infection (up to 8%) is observed in countries where infection occurs in the perinatal period or in early childhood (Southeast Asia, sub-Saharan Africa), with 70–90% of the population of these countries showing serological signs of past HBV infection. Uzbekistan is among the countries with an average prevalence of HBV infection of 2–7%. Such fluctuations in the level of infection are observed in countries with a mixed nature of infection (newborns, young children, and adults). Serological signs of past HBV infection in these territories are found in 10–60% of the population.

The only source of HBV is a person with various forms of the disease. The virus is found in almost all biological environments of the body - in blood, sperm, saliva, urine, bile, breast milk, vaginal secretions, cerebrospinal fluid, synovial fluid, tears. The main pathogenic factor in the transmission of the virus is blood. 0.0005 ml of infected blood is enough for HBV infection to occur. The hemocontact mechanism of infection with hepatitis B can be realized in various ways. There are natural and artificial routes of transmission. Natural routes are sexual, vertical and contact-household. According to the reference center for hepatitis surveillance, the share of natural routes of virus transmission in 2016 was 30.4%. Contact-household transmission is more often observed among children in families of patients with chronic hepatitis B when using common personal hygiene items. The proportion of vertical infection from all routes of transmission of the hepatitis B pathogen was about 0.7% in 2016. Vertical infection mainly occurs during childbirth



from mothers who are HBsAg carriers, and the risk of infection increases if the mother has active replication of the virus. The risk of infection is approximately 70–90%.

Artificial routes of transmission of hepatitis B are realized with non-medical intravenous administration of psychoactive substances (drugs), as well as during cosmetic procedures (manicure, pedicure), piercing and other manipulations, including medical ones, accompanied by damage to the skin and mucous membranes. In the structure of routes of transmission of acute hepatitis B in 2016, the share of infection through the use of injectable psychoactive drugs was 12.6%, and the share of infection through various medical manipulations was about 4.9%.

Diagnostics of viral hepatitis B. Standard laboratory tests performed on a patient with suspected acute viral hepatitis B are the same for all acute viral hepatitis. Standard laboratory examination includes a clinical blood test with determination of platelets; general urine analysis and determination of bile pigments in urine. During a biochemical blood test, the bilirubin level, alanine aminotransferase (ALT) activity, aspartate aminotransferase (AST) activity, thymol test, and prothrombin index are examined. An immunological test for all types of acute hepatitis is mandatory: anti-HAVIgM, HBsAg, anti-HBcIgM, anti-HCV.

If acute viral hepatitis is excluded, but HBsAg results are positive, the family doctor should conduct a comprehensive clinical, laboratory and instrumental examination of the patient to exclude chronic hepatitis B.

Comprehensive laboratory and instrumental examination includes:

- clinical blood and urine tests;
- biochemical blood test: bilirubin and its fractions, ALT activity, AST, alkaline phosphatase, GGT, total protein, albumin, thymol test, prothrombin index, alpha-fetoprotein, immunoglobulins;
- Ultrasound of abdominal organs;
- blood test for hepatitis B markers using the ELISA method: anti-HBcIgM, anti-HBcIgG, HBeAg, anti-HBe IgM, anti-HDV IgG;
- blood test for HBV DNA using the qualitative PCR method.

Recently, quantitative hepatitis B surface antigen (qHBsAg) has been increasingly recognized as a promising biomarker for predicting both favorable and unfavorable outcomes in hepatitis B virus carriers (Tsenget et al., 2011a, 2012a, b, 2013; Lin and Kao, 2013a). An Italian study showed that the combination of qHBsAg <1000 IU/mL and serum HBV DNA level <2000 IU/mL could predict inactive HBV carrier state in patients with genotype D (Brunetto et al., 2010). Our recent study also showed that low serum HBsAg levels (<100 IU/mL) 1 year after HBeAg seroconversion may indicate HBsAg loss in patients with HBV genotypes B or C infection (Tsenget al., 2011a). Furthermore, qHBsAg level was better than serum HBV DNA level in predicting spontaneous HBsAg loss in HBeAg-negative carriers with low viral load (<2000 IU/mL). Low serum HBsAg level was the strongest predictor of spontaneous HBsAg seroconversion in patients with low viral load (Tsenget al., 2012b; Liu et al., 2013b). In a recent update of the REVEAL - HBV study, which included over 3000 HCV carriers, qHBsAg, HCV DNA levels, and HCV genotype C were independent predictors of HCC development. Of particular note, qHBsAg was significantly associated with cirrhosis and HCC in a dose-dependent manner (P for trend < 0.001) in HBeAg-negative patients with low serum HBV DNA levels (< 200,000 IU/mL) (Lee et al., 2013). Our hospital-based cohort study, ERADICATION-B, also showed similar results. A total of 2688 Taiwanese patients with chronic hepatitis B without cirrhosis were followed for a median of 14.7 years. The risk of developing HCC was increased when patients had elevated HBV DNA levels



(OR: 4.7; 95% CI: 2.2–10.0), elevated qHBsAg (OR: 7.2; 95% CI: 1.8–28.6), and elevated ALT (OR: 6.6; 95% CI: 2.2–19.8). Furthermore, in patients with low serum HBV DNA levels (<2000 IU/mL), qHBsAg \geq 1000 IU/mL was an independent risk factor for developing HCC (OR: 13.7; 95% CI: 4.8–39.3) (Tsengetal ., 2012a). A recent study assessed the correlation between HCV DNA and HBsAg levels according to HCV genotype. These researchers found that serum HBsAg levels generally correlated with HBV DNA levels for genotype A , but did not reach a significant significance for genotype D (Tuailleone et al ., 2012). Recently, in a Chinese follow-up of 247 patients with chronic HBV infection over 8 years, inactive carriers were found to have significantly lower qHBsAg levels at baseline and during follow-up compared with patients with elevated serum HBV DNA levels. However, the longitudinal change in qHBsAg was not affected by genotypes B or C , the most common genotypes in Taiwan (Sue et al ., 2013). Certainly, further studies are needed to clarify the relationship between HBV genotype and qHBsAg levels in different clinical situations and in other geographic regions.

Also, signs indicating the possibility of chronic hepatitis according to ultrasound examination of the abdominal organs are: changes in the echogenicity of the liver parenchyma, narrowing of the hepatic veins, compaction and thickening of their walls, signs of concomitant cholecystitis and pancreatitis, expansion of the portal and splenic veins, splenomegaly, enlargement of the abdominal lymph nodes in the porta hepatis and spleen. One of the most important criteria for confirming the diagnosis of chronic viral hepatitis is the presence of liver fibrosis. In outpatient settings, the liver elastography method using the Fibroscan device is used to detect the presence of fibrosis. After receiving all the examination results, a consultation with an infectious disease specialist or gastroenterologist is indicated for final confirmation of the diagnosis.

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