ETIOLOGY, EPIDEMIOLOGY AND PATHOGENESIS OF VIRAL HEPATITIS B

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Abstract. Viral hepatitis B remains one of the most significant infectious diseases worldwide, affecting more than 250 million people chronically. The etiological agent, hepatitis B virus (HBV), is a DNA virus of the Hepadnaviridae family with unique replication mechanisms involving reverse transcription. Epidemiologically, HBV is transmitted through parenteral, sexual, and perinatal routes, with prevalence varying widely across regions.

Keywords: Hepatitis B, HBV, epidemiology, etiology, pathogenesis, hepatocellular carcinoma, chronic infection.

Introduction. Hepatitis B virus (HBV) infection is a major global public health problem. According to the World Health Organization (WHO), more than 296 million people live with chronic HBV infection, causing approximately 820,000 deaths annually due to cirrhosis and hepatocellular carcinoma. Despite the availability of effective vaccines and antiviral therapies, HBV remains highly prevalent in many parts of the world.

Etiology of viral hepatitis B. The causative agent of viral hepatitis B is the hepatitis B virus (HBV), a small, enveloped virus belonging to the family Hepadnaviridae, genus Orthohepadnavirus. HBV is remarkable for its compact genome, overlapping reading frames, and unique replication cycle that involves

reverse transcription of an RNA intermediate, a feature more typical of retroviruses [5].

Viral structure and morphology. The complete infectious particle, known as the Dane particle, has a diameter of approximately 42 nm. It consists of:

Outer envelope containing the hepatitis B surface antigen (HBsAg) proteins (small, middle, and large forms). These proteins are essential for viral entry into hepatocytes and are also the major targets for neutralizing antibodies.

Inner nucleocapsid, composed of hepatitis B core antigen (HBcAg) and enclosing the partially double-stranded DNA genome together with viral polymerase. In addition to infectious particles, HBV produces large quantities of non-infectious spherical and filamentous subviral particles containing only HBsAg. These particles act as decoys for the host immune system, contributing to immune evasion [3].

Genome organization. The HBV genome is a circular DNA molecule of about 3.2 kilobases. It contains four overlapping open reading frames (ORFs):

1. S gene – encodes surface antigens (HBsAg), which exist in three forms and are essential for viral entry and vaccine development.

2. C gene – encodes the nucleocapsid protein (HBcAg) and the secreted HBeAg, which modulates immune tolerance and serves as a marker of active viral replication.

3. P gene – encodes the viral polymerase, which has reverse transcriptase, DNA polymerase, and RNase H activities. This multifunctional enzyme enables viral replication from RNA templates.

4. X gene – encodes the HBx protein, which acts as a transcriptional regulator, interferes with host signaling pathways, and contributes to viral persistence and hepatocarcinogenesis [2].

Routes of transmission. HBV is transmitted through several well-established pathways: Parenteral transmission: exposure to infected blood through transfusions, invasive medical procedures, or sharing of contaminated needles. Sexual transmission: unprotected intercourse with an infected partner, a common mode in low-prevalence countries. Vertical (perinatal) transmission: from mother to child during delivery, the predominant route in high-endemic regions. Household transmission: less common but possible through shared items (razors, toothbrushes) contaminated with blood [Lok, McMahon, 2022].

Genetic diversity.HBV exhibits extensive genetic variability, with at least 10 recognized genotypes (A–J) and multiple subgenotypes. These genotypes differ in geographical distribution, clinical presentation, and therapeutic response. For instance:

Genotype C (prevalent in East Asia) is associated with a higher risk of cirrhosis and hepatocellular carcinoma.

Genotype A (common in North America and Europe) responds better to interferon therapy.

Genotype D (frequent in the Mediterranean and Middle East)is linked with more severe liver disease and higher rates of HBeAg-negative chronic hepatitis [3].

Epidemiology. The global distribution of HBV infection is heterogeneous:

-High prevalence regions (>8%): Sub-Saharan Africa, East Asia, and the Pacific.

-Intermediate prevalence (2–7%): Mediterranean, Eastern Europe, parts of South America.

-Low prevalence (<2%): North America, Western Europe, Australia.

The main determinants of epidemiological trends include vaccination programs, socio-economic conditions, healthcare standards, and cultural practices. Perinatal transmission plays a dominant role in high-prevalence areas,

while parenteral and sexual routes are more common in low-prevalence countries.

Pathogenesis of viral hepatitis B. The pathogenesis of hepatitis B virus (HBV) infection is determined by the interaction between the virus and the host immune system. HBV itself is not directly cytopathic; instead, most of the liver injury results from immune-mediated mechanisms aimed at clearing the virus [5,6].

Acute infection and immune clearance. After entering hepatocytes and establishing covalently closed circular DNA (cccDNA) in the nucleus, HBV begins replication and expression of viral proteins. In individuals with a competent immune system, infection induces a strong adaptive immune response, especially by CD8+ cytotoxic T lymphocytes (CTLs), which recognize viral peptides presented on hepatocytes and mediate cell lysis. This immune attack is responsible for liver inflammation and elevated aminotransferases observed during acute hepatitis [5].

Chronic infection and immune tolerance. When infection occurs perinatally or in early childhood, the immature immune system often fails to mount an effective antiviral response. As a result, HBV persists and chronic infection develops [2,7]. The natural course of chronic HBV infection typically includes several phases:

1. Immune tolerance phase: High viral replication (HBeAg positive, high HBV DNA), but minimal liver damage due to weak immune activity.

2. Immune clearance phase: The immune system begins attacking infected hepatocytes, leading to hepatic necroinflammation and fluctuating liver enzyme levels.

3. Inactive carrier phase: HBV replication decreases (low or undetectable HBV DNA), inflammation subsides, but cccDNA persists in hepatocytes.

4. Reactivation phase: HBV replication may increase again due to viral mutations, immune suppression, or other triggers, causing renewed liver damage. These dynamic phases explain the variable clinical course of chronic hepatitis B [3,8].

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