Research Article

Hepatitis B Vaccination Status: A Review

Mokhalad Gh. Azzawi[1], Zainalabdeen Abdulabbas Noman Al Taee[2], Zaid Shakir Abed[3], Ali Saleh Hatem[4], Husam Abdulabbas Mutasher[5], Mohammed Ali Yahya[6]

[1]M. B. Ch. B - F. I. C. M. S Lecturer Doctor Al Kut University College of dentistry,Wasit,52001,Iraq. dr.mokhalad85@gmail.com mukhlid.matar@uokut.edu.iq
[2]M.Sc. Pediatric dentistry, Lecturer, college of dentistry, University of Kut, Wasit,52001, Iraq. altaeezain8@gmail.com
[3]B.D.S, M.Sc., Periodontics Lecturer Department of Periodontics, College of Dentistry, Al Kut university, Wasit,52001, Iraq Zaid.Shakir@uokut.edu.iq nenonqutbi92@gmail.com
[4]B.D.S., M.Sc. Lecturer Al Kut University College of Dentistry Wasit, 52001, Iraq ali.saleh@uokut.edu.iq
[5]B.D.S, M.Sc., Oral and Maxillofacial Surgery Lecturer Department of Oral & Maxillofacial Surgery, College of Dentistry, Al Kut university, Wasit,52001, Iraq husam.mohammed@uokut.edu.iq
[6]M.Sc. Medical Physics Lecturer Al Kut University College of Dentistry Wasit, 52001, Iraq Mohammedalmayahy7@gmail.com

Abstract

Hepatitis B viral infection is a serious global healthcare problem. It is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). It is often transmitted via body fluids like blood, semen, and vaginal secretions. The majority (more than 95%) of immunocompetent adults infected with HBV can clear the infection spontaneously

Introduction

Patients infected with HBV could be asymptomatic initially and, depending on the particular genotype, might not be symptomatic throughout the infected state. In these particular cases, careful history taking is important to establish a diagnosis(1) However, when symptomatic from acute HBV infection, patients can present with serum sickness-like syndrome manifested as fever, skin rash, arthralgia, and arthritis. This syndrome usually subsides with the onset of jaundice. Patients may also have fatigue, abdominal pain, nausea, and anorexia.History taking should emphasize the social history, including sexual practices (e.g., unprotected, same-sex, etc.), illicit drug use, profession (e.g., healthcare worker, sex worker), and living arrangements (i.e., within the same household as a patient with HBV infection) (2).

Etiology

Transmission of hepatitis B involves the transfer of the virus from infected people to non-immune people in various ways. Major modes of transmission for hepatitis B are as follows:

1. **Horizontal transmission:** It involves the transmission of hepatitis B through sexual contact or mucosal surface contact. Unprotected sex and injection drug use are major modes of transmission in low to intermediate prevalence areas.[3]

2. **Vertical transmission:** Vertical transmission involves the maternal-to-newborn perinatal transmission of the virus.[4] It is the predominant mode of transmission in high-prevalence areas.

Sexual contact includes unprotected intercourse (vaginal, oral, or anal) and mucosal contact involves any contact involving an infected patient's saliva, vaginal secretion, semen, and blood.

Prevalence areas are based on the percentage of the population with hepatitis B surface antigen (HBsAg) positivity with greater than or equal to 8% representing high prevalence areas, 2-7% representing low to intermediate prevalence areas, and less than 2% representing low prevalence areas.[5]

Epidemiology

HBV infection has the potential for progression to a chronic state and thus presents as a global public health threat for its associated morbidity and mortality. While hepatitis B vaccines are available, limited access to healthcare and lack of proper health education contributes to the increasing global prevalence of hepatitis B. Lower incidence of hepatitis B in the United States compared to Asia and Africa is due to better access to healthcare and better use of vaccinations and other preventive measures.

- **U.S. Statistics**

Around 60,000 new cases of HBV infection annually[6]

2 million or more people with chronic hepatitis B infection

Prevalence is higher in black, Hispanic, and Asian populations compared to whites[7]

Prevalence is lower in people less than 12 years of age born in the U.S.
Accounts for 5% to 10% of chronic end-stage liver disease, and 10% to 15% of cases of hepatocellular cancer
Causes 5000 deaths annually

❖ **Worldwide Statistics**

350-400 million of the world population has chronic hepatitis B.[8]
The following population is known to have a higher prevalence: Asian Pacific Islanders, Alaskan Eskimos, and Australian aborigines.
The following geographic regions have higher prevalence: the Indian sub-continent, sub-Saharan Africa, and central Asia.
The prevalence of hepatitis B is reduced after the initiation of the hepatitis B vaccination program.
10 genotypes (A-J) of hepatitis B have been identified.[9]
High-risk groups for HBV infection include intravenous drug users, infants born to infected mothers, males who have sexual intercourse with other males, hemodialysis patients (and workers), healthcare workers, household contacts of known patients with chronic HBV. A majority of the global HBV disease burden is primarily through vertical transmission.

❖ **Hepatitis B in the Middle East**

In the Middle East, hepatitis B is considered an endemic disease in many countries, with varying rates of prevalence. For instance, countries like Saudi Arabia, Egypt, and Iran report higher rates of hepatitis B infection, often associated with unsafe medical practices such as the reuse of needles and unsterilized equipment in healthcare settings. Additionally, there are regions in the Middle East where successful vaccination programs have been implemented, leading to a decline in new infections, particularly among younger populations (Al-Tawfiq & Memish, 2015).
Egypt, in particular, has a high prevalence of hepatitis B, with studies indicating that chronic infection rates can reach 10-15% in some age groups (El-Sharkawy et al., 2014). This high prevalence is partly due to the historical use of unsafe injection practices during mass schistosomiasis vaccination campaigns in the 1970s, which inadvertently facilitated the spread of hepatitis B. Conversely, Gulf countries, including Qatar and the UAE, report lower rates of hepatitis B due to stricter public health policies, including the implementation of universal vaccination programs (Al-Bader et al., 2010).

❖ **Hepatitis B in Iraq**

In Iraq, hepatitis B is a significant public health issue, with the country experiencing relatively high rates of infection. Studies estimate that approximately 4-6% of the Iraqi population is chronically infected with hepatitis B (Kakamad et al., 2017). Several factors contribute to the spread of hepatitis B in Iraq, including poor sanitation, limited access to healthcare, and the use of unsterilized medical instruments.
The country's history of conflict has also played a significant role in the spread of hepatitis B, as wars have disrupted healthcare infrastructure and led to the increased use of unsafe medical practices such as needle reuse and lack of proper sterilization (Hossain & Karim, 2019). Furthermore, political instability and limited resources have hindered the full implementation of nationwide vaccination programs, though some progress has been made in reducing new infections among children (Mahmud et al., 2012).
Hepatitis B is particularly prevalent among certain groups in Iraq, such as healthcare workers, military personnel, and individuals with a history of intravenous drug use. The prevalence of hepatitis B is also higher in rural areas where healthcare access is more limited (Al-Sarraj et al., 2010).

Pathophysiology

Hepatitis B virus is transmitted via percutaneous inoculation or through mucosal exposure with infectious bodily fluids. Oral-fecal transmission is possible but considerably rare. The incubation period of HBV infection is typically between 30 and 180 days, and while recovery is common in immunocompetent patients, a small percentage can progress to a chronic state, serologically defined as the presence of HBsAg for greater than six months. HBsAg is transmitted via blood contact or body secretions, and the risk of acquiring hepatitis B is considerably higher in individuals with close contact with HBsAg-positive patients.
The pathogenesis of liver disease in HBV infection is mainly immune-mediated, and in some circumstances, HBV can cause direct cytotoxic injury to the liver. HBsAg and other nucleocapsid proteins that are present on cell membranes promote T cells-induced cellular lysis of HBV-infected cells. Cytotoxic T cell response to HBV-infected hepatocytes is relatively ineffective; a significant majority of HBV DNA is cleared from the hepatic system prior to maximal T cell infiltration, suggesting that the immune response is likely more robust in the early stages of infection. The immune

response may not be the sole etiology behind hepatic injury in hepatitis B patients. Hepatitis B-associated injury is also seen in post-liver transplant patients with hepatitis B that are on immunosuppressant therapy. The histological pattern that follows from this infection is termed fibrosing cholestatic hepatitis and is thought to be associated with an overwhelming exposure to HBsAg. This lends credence to the idea that hepatitis B may possess pathogenicity regardless of the immune system's response.[10]

Evaluation

Diagnosis of Hepatitis B is based on proper history taking, physical examination, laboratory works, and imaging. Initial symptoms are nonspecific and can include anorexia, nausea, vomiting, abdominal pain, dark urine, clay-colored stool, and jaundice. In cases of severe liver damage, advanced findings specific to liver damage are common and can include hepatic encephalopathy, confusion, coma, ascites, gastrointestinal bleeding, coagulopathy, or infections. In cases of chronic hepatitis B, patients can have a chronic inactive infection, or they can develop findings of acute hepatitis known as chronic active hepatitis. The diagnosis of hepatitis B relies on the appropriate history/physical and evaluation of serum or viral biomarkers. Viral serology of hepatitis B is usually detectable 1-12 weeks after initial infection with the primary viral marker being hepatitis B surface antigen (HBsAg) (2).

The presence of HBsAg rarely persists beyond 6 months after infection and typically precedes detectable quantities of the corresponding antibody to surface antigen (Anti-HBsAg). The period of time between the disappearance of HBsAg and the appearance of Anti-HBsAg is termed "the window period" or "serological gap." During the window period, other viral serology could also be undetectable. HBsAg is the first virological marker to be detected thanks to its exposure on the viral surface and is indicative of an acute infection. Immune-mediated destruction of the nucleocapsid allows exposure of core antigen (HBcAg) or e antigen (HBeAg) with subsequent antibody development. Liver enzymes are typically elevated within the latter part of the replicative phase on infection thanks to active inflammatory processes, otherwise, liver transaminases could also be within their reference ranges. Hence, liver transaminases should not be a sole guide to diagnosing suspected hepatitis B infection.The presence of antibodies to HBsAg indicates immunized status while the presence of antibodies to HBeAg refers to a possible chronic infection state. Seroconversion refers to the transition between an acute, immune-active phase to an inactive carrier state and is marked by the spontaneous development of antibodies to HBeAg. Earlier seroconversion has been related to more favorable outcomes while later seroconversion, in conjunction with recurrent bouts of reactivation and remission, is more liable to complications like liver cirrhosis, thus resulting in poorer outcomes.[11]The persistence of serum HBsAg for a duration of 6 months or greater delineates acute hepatitis B infection from chronic hepatitis B infection. Following groups of people should be screened for hepatitis B:[4]

Persons born in high or intermediate endemic areas (HBsAg prevalence of greater than or equal to 2%). African countries, countries from North, Southeast, and East Asia. All countries from Australia and South Pacific (except for Australia and New Zealand). All countries from the Middle East (except for Israel and Cyprus). All countries from Eastern Europe (except for Hungary), Western Europe (Spain, Malta, and the indigenous population of Greenland), North America (Alaskan natives and indigenous populations of Northern Canada), Mexico, Guatemala, and Honduras. South America (Ecuador, Guyana, Suriname, Venezuela, and Amazonian areas). Caribbean (Antigua, Barbuda, Dominica, Grenada, Haiti, Jamaica, Saint Kitts and Nevis, Saint Lucia, and Turks and Caicos Islands).

The unvaccinated U.S. citizens whose parents were born in high prevalence areas.

- ✓ History of illicit intravenous drug use.
- ✓ Men who have sex with men.
- ✓ Persons on immunosuppressive therapy.
- ✓ Persons with elevated ALT or AST of unknown origin.
- ✓ Blood, plasma, organ, tissues, or semen donors.
- ✓ Persons with end-stage renal disease.
- ✓ All pregnant women and infants born to HBsAg-positive mothers.
- ✓ Persons with chronic liver disease and HIV.
- ✓ Close contacts of HBsAg-positive persons, such as household, sexual, or needle-sharing.
- ✓ Persons with more than one sexual partner in the last six months.
- ✓ Persons requesting evaluation or treatment for sexually transmitted infections.
- ✓ Health care workers or public safety workers who are at risk for occupational exposure to blood or blood-contaminated body fluids.
- ✓ Residents and staff at facilities for developmentally disabled persons.

- ✓ Travelers to countries with an intermediate or high prevalence of Hepatitis B virus infection.
- ✓ Correctional facilities inmates.
- ✓ 19-59-year-old persons with diabetes who have not been vaccinated for Hepatitis B.
- ✓ Persons who are the source of blood or body fluid exposures that might require post-exposure prophylaxis.

Interpretation of Serologic Markers

Following serologic markers are often tested: Hepatitis B surface antigen (HBsAg), antibody to Hepatitis B surface antigen (anti-HBs), Hepatitis B core Ab (Anti-HBc) IgM, Hepatitis B core Ab (Anti-HBc) IgG, Hepatitis B e antigen (HBeAg), and Hepatitis B e antibody (anti-HBe).[11]

- HBsAg: Acute infection (less than 6 months) or chronic infection (more than 6 months).
- Anti-HBs: Recovery from acute infection or immunity from vaccination.
- HBeAg: Mostly associated with high viral load.
- Anti-HBe: Low replicative phase.
- Anti-HBc IgM: Acute infection, an only marker present in the window period, can be present during exacerbation of chronic infection.
- Anti-HBc IgG: Exposure to infection, chronic infection (if present along with HBsAg), recovery from acute infection (if present with anti-HBs), if isolated presence, may represent occult infection.
- Other markers are: Hepatitis B viral DNA is for detection of viral load. Hepatitis B genotype provides input about disease progression and response to interferons.[12]

Reference

1. Tripathi N, Mousa OY. Hepatitis B. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-
2. Beasley RP, Hwang LY, Lin CC, Leu ML, Stevens CE, Szmuness W, Chen KP. Incidence of hepatitis B virus infections in preschool children in Taiwan. J Infect Dis. 1982 Aug;146(2):198-204. [PubMed]
3. Alter MJ, Hadler SC, Margolis HS, Alexander WJ, Hu PY, Judson FN, Mares A, Miller JK, Moyer LA. The changing epidemiology of hepatitis B in the United States. Need for alternative vaccination strategies. JAMA. 1990 Mar 02;263(9):1218-22. [PubMed]
4. Terrault NA, Lok ASF, McMahon BJ, Chang KM, Hwang JP, Jonas MM, Brown RS, Bzowej NH, Wong JB. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology. 2018 Apr;67(4):1560-1599. [PMC free article] [PubMed]
5. Kowdley KV, Wang CC, Welch S, Roberts H, Brosgart CL. Prevalence of chronic hepatitis B among foreign-born persons living in the United States by country of origin. Hepatology. 2012 Aug;56(2):422-33. [PubMed]
6. Higgins DC, Kuncio DE, Johnson CC, Viner KM. Influence of birth origin and risk factor profile on hepatitis B mortality: Philadelphia, PA 2003-2013. Ann Epidemiol. 2018 Mar;28(3):169-174. [PubMed]
7. Nebbia G, Peppa D, Maini MK. Hepatitis B infection: current concepts and future challenges. QJM. 2012 Feb;105(2):109-13. [PMC free article] [PubMed]
8. Kuo A, Gish R. Chronic hepatitis B infection. Clin Liver Dis. 2012 May;16(2):347-69. [PubMed]
9. Chisari FV, Isogawa M, Wieland SF. Pathogenesis of hepatitis B virus infection. Pathol Biol (Paris). 2010 Aug;58(4):258-66. [PMC free article] [PubMed]
10. Mani H, Kleiner DE. Liver biopsy findings in chronic hepatitis B. Hepatology. 2009 May;49(5 Suppl):S61-71. [PubMed]
11. Trépo C, Chan HL, Lok A. Hepatitis B virus infection. Lancet. 2014 Dec 06;384(9959):2053-63. [PubMed]
12. Kim BK, Revill PA, Ahn SH. HBV genotypes: relevance to natural history, pathogenesis and treatment of chronic hepatitis B. Antivir Ther. 2011;16(8):1169-86. [PubMed]