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# Prevention of Hepatitis B Virus (HBV) Is Essential to Avoid Chronic Liver Disease

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**Abstract**

Hepatitis B is a viral infection that is caused by hepatitis B virus (HBV), which becomes a severe public health problem worldwide. It is a short-term acute illness or a lifelong chronic infection that may be a cause of life-threatening liver cirrhosis, liver failure, liver cancer, and hepatocellular carcinoma (HCC). Persistence of HBV infection may remain for six months or more indicates chronic liver infection. Hepatitis B is transmitted by body fluids, such as blood, semen, vaginal secretions of hepatitis B patient; by sharing shaving razors, needles, syringes, etc. contaminated with HBV; having any kind of unprotected sex, such as vaginal, anal and oral sex with HBV infected patients; HBV infected mother to new born babies; use of surgical and dental tools of contaminated with HBV; use of tattooing or body piercing equipment of HBV patient, and so on. The HBV is endemic in Asia, Pacific Islands, Africa, Southern Europe, and Latin America. An attempt has been taken to discuss the HBV infection, its treatment, and prevention through the vaccination.

**Keywords:** HBV, immunity, genotypes, chronic hepatitis, viral mutation, vaccination

## 1. Introduction

Hepatitis B is a viral infection that attacks the liver and can cause acute or chronic illness. The hepatitis B virus (HBV) is an enveloped, hepatotropic, non-cytopathic virus (Huang et al., 2013). Chronic HBV infection is treatable, but not curable. This fatal infection is one of the important global health problems (Zhang et al., 2013). It is considered as the 10$^{th}$ leading cause of death worldwide that causes 0.5 to 1.2 million deaths per year. About 5% of immunocompetent adults are unable to clear the virus (Schmidt et al., 2013).

Many viral factors, such as viral load, genotype, and specific viral mutations, are known to affect disease progression (Sunbul, 2014). The HBV is the only known DNA virus that has hepatocytes specificity and spherical with a diameter of 42nm (nanometers) (Lu et al., 2004). It belongs to a family of DNA viruses called Hepadnaviridae and consists simply of a core particle and a surrounding envelope. The inner protein shell is capsid, having a diameter of 34nm in cryoelectronic microscopy (Hanazaki, 2004). The HBV is a highly resilient, blood-borne and sexually transmitted virus (Kuruuzum et al., 2008). It is transmitted through the contact with blood or other body fluids of the infected person (Gerlich, 2013). Humans are actually the only reservoir of HBV (WHO, 2016).

About one-third of the world population has been infected with HBV, and about 5% of them are chronically infected. In 1997, about 530,000 cases (82%) of liver cancer per year worldwide were caused by viral hepatitis infection, with 316,000 cases were associated with hepatitis B (Lee, 1997). In 2018 in the USA, a total of 1,649 deaths were reported due to hepatitis B. In 2020, an estimated 14,000 people in the USA were newly infected with the HBV and 39 States reported 11,635 newly diagnosed chronic hepatitis B infections (Honer et al., 2017). From 1990 to 2019, the incidence rates of HAV, HCV and HEV infection have remained stable, but the incidence

of HBV infection has declined due to increases in HBV vaccination rates. In 2020, HBV and HCV related disease led to 1.1 million deaths worldwide (Zeng et al., 2016).

It is estimated that in 2019 the prevalence of HBsAg in the population was 3.8% worldwide, with about 1.5 million new infections. Also, there were 296 million chronic HBV carriers worldwide and more than 820,000 deaths occur each year due to its complications, such as cirrhosis and hepatocellular carcinoma (HCC) (WHO, 2021). Majority of the HBV infected patients do not have access to life saving medications. In the absence of vaccination most exposed neonates and young children will be infected and become lifelong carriers (Gow & Mutimer, 2001).

The HBV was discovered in 1965 by American physician and geneticist Baruch Samuel Blumberg (1925-2011) (Blumberg, 2002). At present HBV infection becomes a global health problem that can cause acute or chronic infection that leads to fibrosis or liver cancer may reach death. Diagnostics testing, vaccination, and treatment are the keys to eliminate HBV (Zeng et al., 2021). World Health Organization (WHO) invited all the countries of the world to work together in the effort to eliminate viral hepatitis B and C as a public health threat by the year 2030 (WHO, 2016).

## 2. Literature Review

In any research, the literature review section is an introductory unit of research, where activities of previous researchers focus briefly (Polit & Hungler, 2013). It helps the new researchers to appreciate the subject matter, and also it serves as an indicator of the subject that has been carried out before (Creswell, 2007). Hossein Hadinedoushan and his coauthors have shown that HBV has been divided into eight genotypes (A to H) and sub-genotypes of A, B, C and F by using INNO-LiPA HBV genotyping assay (Hadinedoushan et al., 2015). Chih-Lin Lin and Jia-Horng Kao have highlighted on ten HBV genotypes (A to J) with distinct geographic distributions and several HBV mutants, including pre-core/core promoter mutations and pre-S/S deletion mutations (Lin & Kao, 2015). Anna Kramvis has discussed HBV genotypes and sub-genotypes and genetic variability of HBV that are useful in epidemiological and transmission studies, tracing human migrations, and in predicting the risk for the development of severe liver disease and response to antiviral therapy (Kramvis, 2014).

Hong You and her coauthors have provided the guidelines of HBV that focuses on active prevention, large scale testing, and expansion of therapeutic indication of chronic hepatitis B with the aim of reducing the hepatitis B related disease burden (You et al., 2023). Senko Tsukuda and Koichi Watashi have provided an update on the current knowledge of HBV biology and its life cycle that may help to identify new antiviral targets (Tsukuda & Watashi, 2020). Kathy Jackson and her coworkers have realized that several biomarkers are available to accurately diagnose the complex and evolving viral infection in clinical practice. Developmental and future biomarkers will be crucial to monitor clinical and virological outcomes through the emergence of new therapies (Jackson et al., 2018).

Luisa Romano and Alessandro R. Zanetti have advised that vaccination is the most effective way to control and prevent acute and chronic hepatitis B, including cirrhosis and hepatocellular carcinoma (HCC) on a global scale (Romano & Zanetti, 2022). Bader S. Alotaibi has tried to discuss the most recent developments in the structure, and epidemiology and biology of the HBV with the current treatment facilities. He has observed the advancements in genetics, the prospect for vaccinations, and tailored management to target the integration of virus with host (Alotaibi, 2023).

Jodie Dionne-Odom and her coauthors have tried to aid clinicians in counseling their patients regarding perinatal risks and management options available to pregnant women with hepatitis B infection through the routine screening during pregnancy for HBV infection with maternal HBsAg testing, and taking hepatitis B vaccine and HBV immunoglobulin within 12 hours of birth to all newborns of HBsAg-positive mothers (Dionne-Odom, et al., 2016). In some unpublished papers, Haradhan Kumar Mohajan has discussed the aspects of liver disease. In these papers, he wants to conscious the people about the healthy food and healthy lifestyle (Mohajan, 2024b-g).

## 3. Research Methodology of the Study

Research is a hard-working search, scholarly inquiry, and investigation that aim for the discovery of new facts and findings (Adams et al., 2007). It is a vital and significant device to the academicians to lead in academic world (Pandey & Pandey, 2015). Methodology in any creative research is the organized and meaningful procedural works that follow scientific methods efficiently (Kothari, 2008). It relates the nature and power to science, truth, and epistemology (Ramazanoglu & Holland, 2002). Therefore, research methodology is a strategy for planning, arranging, designing and conducting fruitful research confidently to obtain a successful result (Legesse, 2014). To rationalize the selection of a research methodology, a researcher must understand its philosophical origins and unique characteristics (Rieger, 2019). To prepare this article we have dependent on the secondary data sources. I have used books of famous authors, handbooks, and theses. I have also collected valuable information from websites and internets to enrich the paper (Mohajan, 2017, 2018, 2020).

## 4. Objective of the Study

Main objective of this article is to discuss the hepatitis liver disease that is infected by the hepatitis B virus (HBV). The disease is one of the fatal global health problems. Vaccination policy has effectively reduced the prevalence of the disease worldwide. Other minor objectives of the study are as follows:

1) to focus on genotypes and virology of HBV,

2) to indicate the risk factors, symptoms, and transmission of HBV, and

3) to show the effective vaccination of HBV to prevent the disease.

## 5. HBV Genotypes

HBV is the smallest enveloped human DNA virus with a genome of 3,200 nucleotides in length and has a single-stranded gap of 600-2,100 nucleotides (Lau & Wright, 1993). HBV has genotypes and subtypes that can influence disease progression and response to antiviral therapy and also the presence of mutations (Sunbul, 2014). Covalently closed circular DNA (cccDNA) is synthesized using nucleus minus-strand DNA as a template. The cccDNA is difficult to eliminate and plays an important role in chronic infection (Peneau et al., 2022).

Pregenomic RNA (pgRNA) can be transcribed from cccDNA to serve as the template of negative-strand DNA and then fully double-stranded DNA through DNA polymerase within the nucleocapsid, finally with the assembly of envelope protein to form mature HBV virions (Beck & Nassal, 2003). The HBV can be integrated into the hepatocyte genome, which is closely related to persistent HBsAg positivity and HCC occurrence (Erken et al., 2022).

Ten HBV genotypes from A to J are identified that differ by 8-10% at the nucleotide level across the whole genome, and more than 40 subgenotypes (4-8% nucleotide divergence) within most genotypes (Kramvis, 2014). There are no sub-genotypes of E, G and H genotypes. Genotype A is distinguished by a nucleotide insert at the carboxyl terminus of the core gene. It has been classified into A1, A2, and A4 subgenotypes, and quasisubgenotype A3 (Pourkarim et al., 2011). It is highly prevalent in Africa, Northern Europe, India, and America (Bowyer et al., 1997).

The genotype B is linked to an earlier time of HBeAg seroconversion. The sub genotypes of B are B1, B2, B3, B4, B5, B6 B7, B8, B9, and QS-B3 (quasisubgenotype) (Shi et al., 2012a). The earliest HBV genotype is C. It has the most subgenotypes, C1-C16 that reflects the length of time that it has been endemic in humans (Shi et al., 2012b). Genotypes B and C are common in the Asia-Pacific region (Schaefer, 2007). The genotype D is found worldwide and it has nine (D1-D9) sub-genotypes (Mayerat et al., 1999). Its sub genotypes are found in different regions: subgenotype D1 is found in Iran, D2 in Russia and Europe, D3 in Alaska and Serbia, D4 in Somalia, and D4,5,6,7,8, and D9 in India, Nigeria and Indonesia (Yousif & Kramvis, 2013).

Genotype E possesses the distinctive serological subtype ayw4. The preS1 region losses its 3 nucleotides that distinguishes E genotype from other genotypes (Andernach et al., 2013). Genotype E is restricted to West Africa (Olubayo et al., 2021). The subgenotypes of F are F1 to F4 that are all members of the serological subtype adw4. Genotype F is found in Central and South America, Alaska, and other parts of the world (Livingston et al., 2007). Genotype G was first detected in a homosexual man of California infected with HIV. It has been reported in France, Germany, and the America (Suwannakarn et al., 2005).

Genotype H was reported in 2002. It is found in Central America and Mexico (Roman et al., 2010). Two subgenotypes of genotype I are I1 and I2, and their corresponding serological subtypes are adw2 and ayw2, respectively. Genotype I is isolated in Vietnam and Laos (Tran et al., 2008). Genotype J is new and is identified in Japan (Tatematsu et al., 2009). It is estimated that B and C variants may increase the risk for hepatocellular carcinoma (HCC) and liver cirrhosis (Sunbul, 2014).

### *5.1 Virology of HBV*

Hepatitis B virus (HBV) is partially double-stranded circular DNA virus that is a member of the Hepadnaviridae virus family (Hubschen et al., 2009). It has a nuclear capsule enveloped by an outer lipid layer containing hepatitis B surface antigen (HBsAg) that is reproduced in the cytoplasm of the hepatocyte and serves as an indicator of the carrier of the virus (Lee, 1997). Other antigenic determinants are hepatitis B core antigen (HBcAg) that is reproduced in the nucleus that contains DNA; hepatitis B e antigen (HBeAg) that appears in the cytoplasm that reflects the replication activity of the virus (Honer et al., 2017). The HBeAg is a non-structural secreted protein that has tolerogenic properties and immune-modulating activity (Thompson et al., 2010). It is the hallmark in diagnosing HBV infection (Gupta et al., 2015). It plays an essential role in persistence that can be used to distinguish the phase of chronic hepatitis B (Jackson et al., 2018).

HBV is highly resistant, but it can be inactivated at 65°C for 10 hours, at 100°C for 10 minutes. It can be effectively inactivated by ethylene oxide, glutaraldehyde, peroxyacetic acid, and iodophor. It can survive 7 days

outside the body (You et al., 2023). Expression of the viral gene products is regulated by four promoters directing the synthesis of a set of viral transcripts, which are heterogeneous at their 5′ ends but coterminal at their 3′ ends (Pasternak et al., 2004). Incubation period of HBV is usually 45-180 days with an average 60-90 days. The disease is successfully treated with oral medications. The disease usually terminates by a complete recovery. This virus has morphological and serological markers, and its particles are visible in an electron microscope in the nucleus and cytoplasm. It replicates in hepatocytes and to a lesser extent in stem cells in the pancreas, bone marrow and spleen. It is an irritation and swelling of the liver (Thakur et al., 2002).

Replication takes place exclusively in the liver and it is possible to assume that the virus becomes a component of the nuclear protein of the host cell and can take part in the development of hepatic tumors; hepatomas (Cooke et al., 2019). The course of the disease depends on a number of factors, such as the virulence of the virus and both immunocompetence and the age of the patients. The destruction of the hepatocyte and the elimination of the virus are carried out by the cells of the immune system (Gerlich, 2013).

*5.2 Risk Factors*

Heterosexual people who have several sex partners that are unvaccinated are in high risk of contaminated with HBV. Moreover, if they are homosexuals and have contact with sex workers, they are more vulnerable (Iqbal et al., 2015). People are at high risk of hepatitis B infection are males who have sexual contact with other males, households with hepatitis B, illicit drug users and their sexual partners, persons who have chronic liver disease, those who are HIV positive, teachers, staff and students in a childcare setting of infected with HBV (Ziraba et al., 2010). Drug misuse has been identified as the main risk factor for the spread of HBV (Nelson et al., 2011).

*5.3 Clinical Picture of HBV*

The clinical picture of HBV is the same as that of HAV, but the disease can proceed more severely than that of HAV (Mohajan, 2024a). It can cause acute hepatitis as well as chronic hepatitis. Sometimes it may develop to more serious liver diseases, and ultimately may cause liver damage (Zhang et al., 2013). Initial infection with HBV may be asymptomatic in up to 50% of adults and 90% of children. About 90% of adult HBV patients have a full recovery, but 5-10% of the patients will develop chronic hepatitis with complications, such as cirrhosis and hepatocellular carcinoma (HCC). Approximately 1% of cases manifest the symptoms of fulminant hepatitis (DePaola, 2003).

*5.4 Symptoms of HBV*

Many people infected with HBV do not show any signs or symptoms. Many cases are asymptomatic. However, symptoms may occur between 2 and 5 months after exposure. Symptoms usually last for several weeks to six months (Testoni et al., 2017). The liver becomes tender and swollen, may become permanent damage, such as scarring or liver cancer. Early symptoms of it are loss of appetite, fatigue, tiredness, low fever, muscle and joint aches, headache, nausea and vomiting, anorexia, abdominal pain, malaise, myalgia, rash and arthralgia, anorexia, dark urine, diarrhea, right upper quadrant pain, hepatomegaly, splenomegaly, clay-colored stool, and jaundice (Farooq et al., 2017).

*5.5 Transmission of HBV*

Different geographical regions have different predominance modes of HBV transmission (Alotaibi, 2023). HBV can be transmitted in human body through the bodily fluids (parenterally) that trigger an immune reaction through the sexual contact (unprotected sex, such as anal and oral sex), intravenous drug use, transfusion of blood and blood products, and pregnant mother to infant (Aghemo et al., 2012). Percutaneous exposure to blood, sexual transmission and perinatal transmission are the majority of the cases of HBV infections (horizontal transmission) in humans (Wang et al., 2002). Transmission from mother to neonate (vertical transmission) may occur through the maternal blood and other infectious fluids during labor, colostrum and rarely through breast milk or placental transmission (Thakur et al., 2002).

HBV can be transmitted through the infectious seminal fluid, menstrual blood, vaginal secretions and saliva during homosexual and heterosexual activity (Baars et al., 2009). It can be spread by unsterilized and contaminated surgical, dental, tattooing or body piercing equipment (Suslov et al., 2021). Sharing items, such as razors, toothbrushes, needles, syringes, or other drug-injection equipment, etc. with an infected person can spread the disease. Men who have sex with men are 10 to 15 times more likely to acquire the HBV than the general population (Trifan & Stanciu, 2003).

*5.6 Complications of HBV*

The virus will stay for six months or longer for chronic hepatitis B. About 15-40% of HBV carriers have a lifetime risk to develop cirrhosis, liver failure, or HCC (Fattovich et al., 2008). About 20% of patients with chronic hepatitis B develop liver cirrhosis that can take 10 to 20 years to develop, and around 10% with cirrhosis will develop liver cancer (Bakry et al., 2012). About 90% of children and 10% of adults HBV infected will

develop chronic hepatitis B that may lead to cirrhosis and cancer of the liver (You et al., 2023). On the other hand, about 15-40% of adults are at risk for cirrhosis or chronic liver failure, and about 5% for HCC and end-stage liver disease. Fulminate HBV infection is an important cause of acute liver failure. Patients that develop severe liver damage may need to undergo liver transplant (Pramoolsinsup, 2002).

*5.7 Diagnosis of HBV*

Diagnosis of HBV infection is usually through serological and virological markers. HBV is diagnosed by a blood test that measures certain enzymes and proteins in the bloodstream. Blood tests: such as anti-HBc, IgM, and HBsAg testing, etc. are required for diagnosing acute and chronic HBV infection (Pfefferkorn, 2021). HBsAg, HBeAg, serum glutamic-pyruvic transaminase (SGPT), and DNA of HBV are currently employed to determine the fatality and phase of the disease (Testoni et al., 2017).

*5.8 Treatment of HBV*

There is no specific treatment for the acute and chronic hepatitis B infection. Treatment of it is palliative and supportive. Supportive treatment for chronic hepatitis B depends on how badly the liver is affected. However, several medications are needed to slow the production of the virus, and slow progression of the disease. Consequently, prevents the liver damage, and can minimize liver cirrhosis and provide a way of long-term survival (WHO, 2015).

It is sufficient to get complete bed rest and healthy balanced foods are prescribed during the acute phase. Compensate loss of fluids resulting from diarrhea and vomiting (Lavanchy, 2004). Lamivudine is a safe effective antiviral drug for treating chronic HBV infection and Interferon Alfa is the only drug licensed for the treatment of it (Kim et al., 2009). Oral administration of entecavir, tenofovir, and tenofovir alafenamide can be used for the treatment of hepatitis B infection (Jonas et al., 2016).

*5.9 HBV Prevention Policy*

Prevention strategy is the best policy for the reduction of HBV infection globally. At present there are many preventive policies that may remarkably reduce the transmission of HBV (Saieed, 2007). Immunization of all the people with hepatitis B vaccine is the effective prevention strategy. HBV infection is largely preventable by vaccination among 90-100% produce sufficient antibody responses (Schmidt et al., 2013). Other preventive measures are adoption of personal hygiene, routinely screening of blood donors for HBsAg, human blood and body fluids should be tested HBV infection before use, etc. (Bett, L. J., 2014).

*5.10 Vaccination of HBV*

The hepatitis B vaccine is a non-infectious, vaccine prepared from recombinant yeast cultures, rather than human blood or plasma. It is highly effective and protects against hepatitis B infection and its complications, such as permanent liver damage, liver cancer, liver failure, and death. It prevents HBV infection in 90-100% of people who produce sufficient antibody responses (Schmidt et al., 2013).

The success of a program of vaccination depends on the availability of safe and highly effective vaccines and on the implementation of proper strategies of vaccination. Babies must be vaccinated as soon as possible after birth; ideally within 24 hours to prevent infections transmitted by mothers who carry HBV (Memon et al., 2007). Vaccination has clearly proven to be effective in reducing the incidence of the disease, carrier rates, and HBV-related mortality. Hepatitis B vaccine is recommended to induce active immunity against HBV among patients of all ages who are currently at increased risk of infection (Maher, 2008). It is very safe and highly effective in reducing the incidence of the disease, carrier rates, and mortality, and there is no convincing evidence of long-term undesirable squeals that can eradicate HBV infection worldwide efficiently. Hepatitis B vaccine is usually given as 2, 3, or 4 shots over 1 to 6 months. An infant can take vaccine at birth and will usually complete the series at 6 months of age (Lai et al., 2003).

Effective vaccines for hepatitis B virus have been available since 1982 (Lin & Kirchner, 2004). There are two vaccines available for HBV immunization that utilizes recombinant DNA technology: Engerix-B (GlaxoSmithKline) and Recombivax HB (Merck) that are about 95% effective in preventing hepatitis B. PreHevbrio is the only approved for adults age 18 and older (WHO, 2017). Both versions are developed by American microbiologist Maurice Ralph Hilleman (1919-2005) and his team that saves millions of lives every year (Tulchinsky, 2018). Pediarix is a new combination vaccine that protects infants against diphtheria, tetanus, pertussis (whooping cough), polio, and disease due to the HBV. Twinrix® (GlaxoSmithKline) and Ambirix® (GlaxoSmithKline) are combined vaccine can be used for the protection against both HAV and HBV (Jarvis & Figgitt, 2003; Beran, 2007).

The first vaccines against hepatitis B, known as plasma-derived vaccine that is inactivated and purified through treatments with a combination of urea, pepsin, formaldehyde, and heat (Francis et al., 1986). More than 190 countries in the world have introduced hepatitis B vaccination into their national childhood immunization

programs with an excellent profile of safety, immunogenicity, and effectiveness (WHO, 2016).

Risks hepatitis B vaccination is soreness, redness and swelling where the shot is given, fever, headache, and fatigue. Sometimes vaccinated people feel dizzy, vision changes or ringing in the ears. Acetaminophen or ibuprofen can be given for fever or soreness. Aspirin should not be given to anyone due to the risk of Reye syndrome. If the vaccinated individuals experience a life-threatening reaction, immediate treatment is necessary and next doses of the vaccination must be stopped (Resende et al., 2010).

## 6. Global HBV Burden

HBV infection poses a severe public health problem worldwide. More than 2 billion people are infected, among them an estimated 387 million are suffering from chronic HBV infection. About 90% of these cases live in developing countries and 50 million of which are in Africa (Bett, L. J., 2014). African and the South-East Asian regions carry a high share of the global HBV burden (Meheus & Dochez, 2008), and the top three countries carrying the highest burden are China (74 million), India (17 million) and Nigeria (15 million) that make up 29%, 6.6% and 5.8% of the global burden of HBV, respectively (Rochwerg et al., 2019). Healthcare providers have three to five times the rate of HBV infection compared to the general population (Levy et al., 1998). The virus accounts for three-quarters of the 1.1 million annual deaths from complications of liver cirrhosis but the incidence of it is declining worldwide due to vaccination (Cooke et al., 2019).

## 7. Conclusions

From this study, I have realized that HBV infects liver and in advanced stage it may cause chronic hepatitis, cirrhosis and hepatocellular carcinoma (HCC). HBV infection is increasing global morbidity and mortality due to million chronically infected people. The ultimate goal in treating hepatitis B is the reduction of HBsAg levels up to normal range. HBV genotype varies according to countries and ethnic backgrounds. Therefore, the physicians should identify disease-related risks and then start treatment according to fatality of the disease. At present the HBV vaccines are available, and also supportive treatments are also progressed, but yet about 296 million people are infected worldwide.

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