Hepatitis B viral infection: Transmission and Prevention

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INTRODUCTION

Approximately 30% of the world population has been infected with hepatitis B virus at some time in their lives. These two billion people include 350 million life-long carriers which are capable of transmitting the virus to others. Universal precautions and vaccination are the best methods of protection. Hepatitis B can cause hepatocellular carcinoma, representing the first cancer for which vaccine became available. Persons with chronic HBV infections are often asymptomatic until they experience liver problems, therefore, known as "silent carriers". The only means of detecting them is by identifying the presence of Hepatitis B surface antigen (HBsAg) in blood. HBsAg positive does not necessarily mean infectivity; it is determined by the presence of HBeAg and viral DNA in the blood. Therefore, simple detection of HBeAg in serum along with routine detection of HBsAg helps in determining the status of infection and infectivity of a patient. The purpose of this article is to emphasize need for immunization and checking infectivity in subjects/ patients for the healthcare workers, especially those involved in interventional and surgical branches, including dentistry.

REVIEW OF LITERATURE:

India has intermediate endemicity of Hepatitis B, with Hepatitis B surface antigen (HBsAg) prevalence between 2% and 7% among populations studied . Mortality due to hepatitis B reaches around one million each year due to chronic hepatitis, cirrhosis or hepatocellular carcinoma. In India, over one lakh are affected with a chronic carriage rate of 1.62 to 4% among general population (intermediate seroprevalence).

The early cases of HBV infection were linked to the use of conventional viral vaccines, which were prepared from or contained human serum; hence the term serum hepatitis for this disease. Hepatitis B is a blood borne infection and is transmitted from person to person through blood, saliva, vaginal fluids or other body fluids. Infection is not transmitted through breast feeding, tears, sweat, urine, stools, or droplet nuclei. It may be transmitted during birth from mother to baby, through needles contaminated with Hepatitis B virus from an infected person, sexually after contact with blood or other body fluids, social transmission between children during play through cuts, scrapes, and scratches, etc. Small children and adolescents are particularly vulnerable. Though they rarely develop acute hepatitis, they are at the highest risk of developing chronic Hepatitis B, which may cause liver complications later. Unsafe injections transmit 80 million to 160 million Hepatitis B virus infections according to WHO estimates.

The virus replicates to high titers in the blood (108 to 1010 virions per milliliter), especially during acute phase of illness. The source of infection of hepatitis B infection is usually from chronic asymptomatic carriers having high viremia, usually transmitting the disease between one and two months before and after the onset of symptoms. Those who are HBeAg positive have more than 106 virions per ml compared to antiHBe positive patients. This explains higher incidence of transmission from HBeAg positive than antiHBe positive carriers. This holds true for perinatally transmitted HBV infection also. The risk of infection among infants born to HBV-infected mothers ranges from <10% to >85%, with higher rates of transmission from HBeAg-positive mothers compared to HBeAg-negative. In such cases, rate of spontaneous HBeAg clearance has been estimated to be approximately 15% even after 20 years of infection.In addition, T-cell tolerance for the viral proteins HBeAg and HBcAg contributes to viral persistence. Transmission of HBV can also occur from health care workers to patients if the health care worker is highly infectious (HBeAg positive), during surgery or procedure on patients, or if the health care worker has dermatitis or traumatic or open lesions of the skin during work.

The serological markers in various conditions with Hepatitis B exposure are listed in table 1. As seen in this table, HBe antigen, considered a marker of infectivity is present during both acute and chronic phases of hepatitis B infection, while anti HBe signals control of viral replication. HBeAg is a secretory protein that is processed from the precore protein. However, some patients continue to have active liver disease and detectable HBV DNA in serum after HBeAg seroconversion. Highly sensitive nucleic acid tests can detect HBV DNA in the serum of an infected person 10-20 days before detection of HBsAg.

Loss of serological markers HBV DNA, HBeAg, HBsAg, and IgM anti-HBc and development of anti-HBe and anti-HBs characterize immunity. In persons who recover from HBV infection, HBsAg is eliminated from the blood, usually within 3--4 months, and anti-HBs develops during convalescence. The presence of anti-HBs typically indicates immunity from HBV infection. Anti-HBs can be detected for several months after hepatitis B

immune globulin (HBIG) administration. Presence of HBeAg in blood does not warrant treatment unless associated with serum alanine transferase (ALT) levels more than twice normal or in patients with concomitant cirrhosis. Various reports highlighting the incidence of HBeAg positivity in HBsAg positive subjects are tabulated in table 2.

There is no specific therapy for acute HBV infection. The easiest way to prevent Hepatitis B infection is through vaccination which not only protects against hepatitis B but also against sequelae of chronic hepatitis B infection. Hepatitis B vaccine also protects against HDV infection since HDV is an incomplete virus that requires the presence of HBV for replication.

A safe and effective vaccine against Hepatitis B has been available since 1982 and is routinely administered in 120 countries. The World Health Organization recommends that all countries include Hepatitis B vaccine in their routine infant immunization programmes.

Two types of hepatitis B vaccine are available, plasma-derived and recombinant. Plasma-derived vaccine is prepared from purified HBsAg from the plasma of persons with chronic HBV infection, hence cheaper. Recombinant hepatitis B vaccine is made using HBsAg synthesized by genetic engineering techniques. There are no significant differences in safety, immunogenicity, or efficacy between the two types of hepatitis B vaccines but the choice between the two types of vaccines is based on cost, availability and other considerations especially in areas of high endemicity. Since anti-HBs alone is sufficient for protection against hepatitis B, most recombinant vaccines express HBsAg only. Two thimerosal-free vaccines that express HBsAg (Engerix-B: GlaxoSmithKline Biologicals and Recombivax HB: Merck & Co., Inc.) are widely available. These vaccines contain 20 g/ml HBsAg and are approved for use in all age groups. A combination vaccine (Twinrix), which expresses both HBsAg and hepatitis A virus, is also available and is approved for use in adults in the United States and Europe, typically when protection against both viruses is needed.

Table 1: Laboratory markers of Hepatitis B

Condition	Laboratory Markers for Hepatitis B					
	HBsAg	HBeAg	HBV DNA	Anti HBs	Anti HBe	IgM Anti HBc
Acute Infection	+	+	+	-	-	+
Chronic Infection	+	+	+/-	-	-	+
Fulminant hepatitis	+/-	+	+	-	-	+
Vaccinated person	+#	-	-	-	-	-
Infection immunity	-	-	-	+	+/-	-
Healthy carrier	+	-	-	-	+	+

#Transient HBsAg positivity has been reported for up to 18 days after vaccination and is clinically insignificant

Table 2: Reports of HBeAg positivity in HbsAg positive subjects

Reports	HBeAg in HBsAg positive patients	Subject population	Place of study
Amarapurkar DN *et al*	39%	Chronic HBV infection	Mumbai
Choudhary *et al*	10%	Community based epidemiological study	West Bengal
Nayak et al	7.8%	Pregnant females	North India
Thyagarajan SP*	34.2%	HBV Carriers	Madras
Chawla YK*	47%	HBV Carriers	Chandigarh
Dixit VK et al	21%	Chronic HBV infection	Varanasi
De Franchis R et al	40%	Adult asymptomatic carriers	Japan
Richer G, et al	5%	Blood donors	Montreal, Canada
Bastiaans MJ, et al	15%	Blood donors	USA
McMahon BJ, et al	42%	Chronic HBV infection	Alaska natives

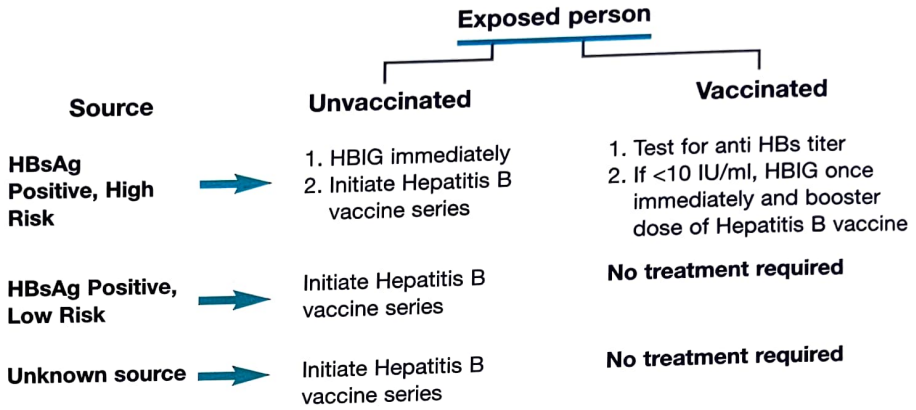
Comvax (Merck & Co., Inc., New Jersey) and Pediarix (GlaxoSmithKline Biologicals, Belgium) are used for vaccination of infants and young children. Comvax contains recombinant HBsAg and Haemophilus influenzae type b (Hib) polyribosylribitol phosphate conjugated to Neisseria meningitidis outer membrane protein complex. Pediarix contains recombinant HBsAg, diphtheria and tetanus toxoids and acellular pertussis adsorbed (DTaP), and inactivated poliovirus (IPV).

The Hepatitis B Project was initiated in India in the year 2002 with support of Global Fund for vaccines & Immunization (GAVI) and from year 2005, this project included injection safety also. . Current immunization program includes Hepatitis B recombinant DNA vaccine, given along

with DPT vaccine at 6, 10, and 14 weeks, these three doses 0.5 ml each given intramuscular at an interval of 4 weeks in the antero-lateral aspect of the thigh (infants) or the deltoid muscle (adults). It can safely be administered at the same time as other vaccines such as DPT, polio, measles, and BCG but the vaccines should be administered in opposite limbs. It is a cloudy liquid that comes in ten-dose vials and does not require reconstitution. It requires storage between 2°C to 8°C and shaking before administration to mix the vaccine. Booster doses of vaccine are not necessary since immunity remains for more than 13 years after immunization. If a dose is missed, the next dose should be given as soon as possible. There is no need to start the schedule anew.

Hepatitis B vaccine is a safe vaccine. The most common potential side effects are redness, swelling, and pain at the injection site (about 1 of 11 children vaccinated). These side effects usually start within one day following vaccination and last between one to three days. Less commonly, fever may occur for a short time following administration. A protective level of immune response after vaccination is defined as a titer of anti-HBs of ? 10 IU/L. Overall about 95% healthy adults seroconvert and show higher titers of anti HBs.

Figure 1: Recommendations for Hepatitis B prophylaxis following percutaneous exposure



INDICATIONS FOR VACCINATION

1. Universal immunization of infants: In areas with Intermediate or high endemicity of HBV infection, infection tends to predominate among infants and children. It is at this age that acute infection is more likely to develop into chronic infection, therefore the importance of vaccination soon after birth.
2. All children and adolescents aged < 19 years.
3. All medical / paramedical personnel especially the Health care workers involved in activities with potential exposure to human blood.
4. Medical/ dental/ nursing college students or laboratory technology students undergoing training at medical institutions.
5. Patients frequently receiving blood/ blood products: thalassemia, haemophilia patients.
6. Patients undergoing hemodialysis.
7. Chronic renal failure or renal transplant recipients.
8. Chronic liver disease patients.
9. Individuals at high risk of infection; HIV infected patients, multiple sexual partners, men having sex with males, intravenous drug users.
10. Household contacts or sexual partners of persons infected with acute or chronic hepatitis B.
11. For post-exposure prophylaxis in non immune individuals who have percutaneous, sexual contact, ocular, or mucous membrane exposure to blood, needle stick injuries or human bites.

CONTRAINDICATIONS TO HEPATITIS B VACCINATION

Known hypersensitivity to any component of the vaccine or in subjects showing signs of hypersensitivity after previous hepatitis B vaccine administration.

Passive immunization (HBIG): HBIG provides passively acquired anti-HBs and temporary protection (i.e., 3--6 months) when administered in standard doses. HBIG is prepared from the plasma of donors with high concentrations of anti-HBs. The plasma is screened to eliminate donors, who are positive for HBsAg, antibodies to HIV and hepatitis C virus (HCV), and HCV RNA. Postexposure prophylaxis with HBIG and vaccine is recommended for all nonimmune individuals who have percutaneous, sexual contact, ocular, or mucous membrane exposure to blood, including human bites that penetrate the skin. The first dose of 0.06 mL/kg (or 5 mL for adults) should be administered as soon as possible, preferably within 12 hours, , maximum seven days followed by the remainder of the series. (Figure 1)

INDICATIONS OF POST EXPOSURE PROPHYLAXIS:

1. Neonates of HBsAg positive mothers.
2. Percutaneous exposure in non immune individuals.
3. Accidental exposure of an unvaccinated individual to high risk hepatitis B infected individual.

Detection of HBsAg in the serum of an individual indicates that the person is currently infected with the virus. Detection of hepatitis B e antigen (HBeAg) in serum correlates with greater viremia and greater infectivity. Seroprevalence determination based on HBV DNA is not cost effective and is therefore not encouraged. Therefore determination of HBeAg status can be done along with HBsAg testing in an intermediate to high endemicity setting and can serve as an important source of information for determining infection transmission in a population. Since there is no treatment available for hepatitis B infection but prevention through vaccination has an efficacy close to 100% after 3 doses, vaccination of all high risk groups is strongly recommended.