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HEPATITIS-B; A PUBLIC HEALTH CONCERN - NEED FOR AN ACTION.

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ABSTRACT

Hepatitis B (HBV) infection is a serious global health issue with 2 billion people infected worldwide and 350 million suffering from chronic HBV infection. As hepatitis B is the only vaccine preventable disease among all forms of viral hepatitis- mass immunization program, standard precautions and effective treatment are essential for eliminating HBV infection and reducing global HBV-related morbidity and mortality. However, not all countries have adopted these recommendations and there remain a large number of issues that need to be addressed for achieving the desired results.

KEYWORDS: Hepatitis B vaccine, Endemicity, Post exposure prophylaxis.

INTRODUCTION

Epidemics of blood borne pathogens have affected the entire developing world. Hepatitis B is one such disease which imposes a heavy burden on national economy and individual family due to rising cost from acute and chronic morbidity. The severe pathological consequences of persistent HBV infections include the development of chronic hepatic insufficiency, cirrhosis, and Hepatocellular carcinoma (HCC). World Health Organization (WHO) estimates that about 90% of HBV-related deaths are associated with chronic HBV infection (70% from Hepatocellular carcinoma with or without cirrhosis and 20% from cirrhosis) while less than 10% are associated with acute infection).[1]

Current scenario

Global:- HBV infection is a global problem and is endemic all over the world. WHO has estimated that there are more than 2 billion HBV infected people (one third of the population).In addition approximately 4.5 million new HBV infections occur worldwide each year, of which a quarter progresses to liver disease. About 378 million (5–7% of the world's population) are chronic carriers worldwide. Nearly 25% of all carriers develop serious liver diseases such as chronic hepatitis, cirrhosis and primary hepatocellular carcinoma. There are approximately 6,20000 HBV related deaths each year.[1] Despite being ten times more common than HIV infection, hepatitis B has not commanded the same public health response worldwide, as other infectious diseases particularly HIV/AIDS and Hepatitis C.[2] Based on HBsAg prevalence countries are classified as **High endemic zone (≥8%):** Areas of high endemicity include South-East Asia, China, most of Africa, most of Pacific Islands, the Amazon basin and parts of the Middle-East. **Intermediate endemic zone (2–7%):** include South Asia, Eastern and Southern Europe, Russia and Central and South America. **Low endemic zone (< 2%)**: includes United States, Western Europe and Australia.

Indian scenario: India has intermediate to high endemicity for hepatitis B surface antigen (HBsAg) and an estimated 40 million chronic HBV infected people constituting approximately 11% of the estimated global burden.[3] An extensive review by the Indian National Association for the study of liver diseases estimates the average national prevalence rate to be 4.7 (2-10%).[4] India has over 40 million HBV carriers and accounts for 10–15% of the entire pool of HBV carriers of the world. Every year over 100,000 Indians die due to illnesses related to HBV infection. Predominant mode of transmission in India is horizontal due to contact of non-intact skin or mucous membranes with tears, saliva or blood containing secretions or through sharing of tooth brushes.[5] Chronic HBV infection accounts for 40-50% of hepato-cellular carcinoma (HCC) and 10-20% cases of cirrhosis in India. Outbreaks of acute and fulminant hepatitis B still occur mainly due to improperly sterilized needles and syringes, as demonstrated by outbreaks of acute hepatitis B in Modasa town of Gujarat.[6]

EPIDEMIOLOGY

Agent factors:- HBV is a small, double-shelled virus in the family Hepadnaviridae discovered in 1963 by Blumberg. The virus has a small circular DNA genome that is partially double-stranded. HBV contains numerous antigenic components, including HBsAg, HBcAg, and HBe antigen. HBV is relatively resilient and in some instances, has been shown to

remain infectious on environmental surfaces for more than 7 days at room temperature. There are eight genotypes of HBV (A–H) which are geographically distributed. Genotypes B and D predominate in Asia-Genotype B is more likely to resolve, with a lesser risk of cirrhosis and liver cancer than genotype C. In U.S.A Genotypes A–G are prevalent with Genotype B causing less severe liver disease than A. In Africa, Genotype E (Central Africa) has lower viral load and less peri-natal transmission than A or D.[7]

***Reservoir of infection*:-** Human beings are the only known reservoir of infection. Such a reservoir may be a case or carrier. The risk of becoming a carrier is 5 to 10% among adults and about 50% among infants.

Host factors:- Humans are the only known host for HBV although some non human primates have been infected in laboratory conditions.

***Age incidence*:-** Outcome in hepatitis is age dependent. Acute hepatitis B occurs in 1% perinatal, 10% early childhood (1-5 yrs.) and 30% in older children (>5 yrs). 90% of exposed infants, 30-50% children and 10% of exposed adults will develop chronic infections.[8]

Modes of transmission

HBV is transmitted through percutaneous or parenteral contact with infected blood, body fluids and by sexual intercourse.[9] Virus can survive outside the body for 7 days, whereas HIV can survive for only few hours outside the body. HBV is 50-100 times more infectious than HIV.'[10]

Percutaneous transmission

Occurs due to contact of open skin or mucous membrane with infected materials, usually occurring due to occupational exposure in health settings by way of needle-stick injury, surgical procedures, handling infected materials. HBV risk varies depending on e-antigen status, if positive risk is 30% and if e antigen is negative risk is 1-7%. Contaminated needles cause 8–16 million HBV infections each year, compared with 2.3–4.7 million hepatitis C virus infections, and 80000–160000 HIV infections.[11]

Sexual transmission

It is the major route of infection in all areas of the world especially in the low endemic areas. Homosexual men are at highest risk of infection due to sexual contact.[12] Heterosexual

factors associated with increased risk of HBV infection include number of sexual partners, duration of sexual activity, history of STD. Sexual partners of injection drug users, prostitutes, and clients of prostitutes are at particularly high risk for infection.

Perinatal transmission

HBsAg and HBeAg positive mothers with HBV DNA level $\geq 10^6$copies/ml are at greatest risk of transmitting HBV to their infants. The overall rate of transmission ranges from 5-90 % in the absence of immunoprophylaxis**.** Those with a positive HBeAg test have a transmission rate of 70-90% where as those with a negative HBeAg test have a rate of transmission less than 10%.[13] Currently there is no special recommendation regarding the mode of delivery in HBsAg-positive patients. There is no evidence that breast feeding increases the risk of mother to child transmission.[14]

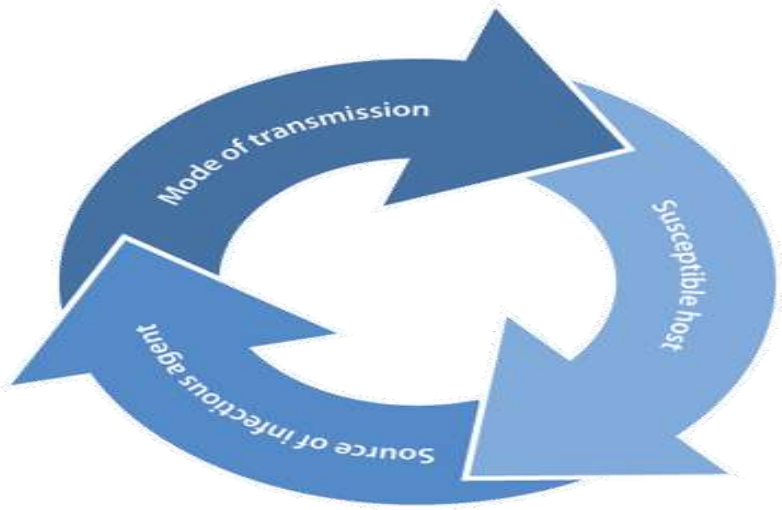
High risk groups

People who have been vaccinated successfully or those who have developed anti-HBs antibodies after HBV infection are immune to HBV infection. Persons with congenital or acquired immunodeficiency including HIV infection, and those with immunosuppression including those with lymphoproliferative disease, and patients treated with immunosuppressive drugs including steroids and by maintenance haemodialysis are more likely to develop persistent infection with HBV.CDC provides a list of individuals that fall in high risk category.[15]

- Infants born to HbsAg positive mothers.
- Sexual/ household contacts of infected persons.
- Intravenous drug abusers.
- People with multiple sex partners.
- Hemophiliacs and other patients requiring blood and blood products.
- Health care personnel.
- Residents and staff members of institutions for the mentally retarded.
- Travelers to countries with intermediate or high prevalence of HbsAg infection.

PREVENTION AND CONTROL

Aim of prevention is to break the chain of transmission by targeting the source of infection, susceptible host and an established route of transmission.



1. Control of source of infection by early identifications and treatment of cases: Control of infectious source can be achieved through early identification and timely treatment of cases, so that viral load can decrease to undetectable levels and infection does not spread rampantly.

CDC provides the following list of individuals that need to be screened.[16]

- Household, needle sharing or sexual contacts of Persons known to be HBsAg positive.
- Donors of blood, plasma, tissue and semen.
- Person with elevated AST/ALT of unknown etiology.
- All pregnant women.
- Injection drug use.
- Men who have sex with men
- Persons needing immunesuppressive therapy**.**

Diagnosis of hepatitis is made by biochemical assessment of liver function.[17] Initial laboratory evaluation should include: total and direct bilirubin, ALT, AST, alkaline phosphate, prothrombin time, total protein, albumin, and globulin, complete blood count, and coagulation studies. Diagnosis is confirmed by demonstration in sera of specific antigens and/or antibodies. Three clinical useful antigen-antibody systems have been identified for hepatitis B.

- Hepatitis B surface antigen (HBsAg) and antibody to HBsAg (anti-HBs).
- Antibody (anti-HBc IgM and anti-HBc IgG) to hepatitis B core antigen (HBcAg).
- Hepatitis B e antigen (HBeAg) and antibody to HBeAg (anti-HBe).

Tests	Results	Interpretation
HbsAg	**negative**	**Susceptible**
Anti-HBc	**negative**	
Anti-HBs	**negative**	
HbsAg	**negative**	**Immune due to infection**
Anti-HBc	**positive**	
Anti-HBs	**positive**	
HbsAg	**negative**	**Immune due to hepatitis B vaccination**
Anti-HBc	**negative**	
Anti-HBs	**positive**	
HbsAg	**positive**	**Acutely infected**
Anti-HBc	**positive**	
IgM anti-HBc	**positive**	
Anti-HBs	**negative**	

HbsAg	Positive	Chronic carrier
Anti-HBc	Positive	
IgM anti-HBc	Negative	
anti-HBs	Negative	
HbsAg	Negative	May be recovering from acute HBV infection. May be distantly immune and test not sensitive enough to detect very low level of anti-HBs in serum. May be susceptible with a false positive anti-HBc May be undetectable level of HbsAg present in the serum and the person is actually a carrier
Anti-HBc	Positive	
Anti-HBs	Negative	

Treatment of cases: The aim of treatment is sustained suppression of HBV replication and elimination of infectivity in order to prevent transmission and spread and achieve remission of liver disease by decreasing rate of development of cirrhosis and hepatocellular carcinomas. Anti-virals like Lamivudine, Adefovir, Tenofovir, Telbivudine and Entecavir are aimed at suppressing or destroying HBV by interfering with viral replication. Immune-modulators like Interferon alpha-2a and PEG-ylated interferon alpha aimed at helping the human immune system to mount a defence against the virus are also used.

2. Protection of Susceptible (Immunization of the host): Hepatitis B virus infection is a preventable disease. Vaccine against this disease has been available since 20 years and is

95% effective in preventing the development of chronic infection. Following are types of vaccine that are available against hepatitis B.

Monovalent vaccines: Engerix-B.

Combination vaccines

Pentavalent: HBV + Haemophilus- influenza type B+DPT

Pediarix: HBV+Diphtheria+Tetanus+Pertussis+polio.

Comvax : HBV + Haemophilus influenza type B.

Twinrix: HBV + hepatitis A.

Hepatitis B vaccine has been included in the national immunization programs of nearly 175 WHO member countries by the end of 2009 compared with 31 countries in 1992, when WHO passed a resolution recommending global vaccination against hepatitis B.[18] Government of India has included hepatitis B vaccine in the National universal immunization program in the entire country in 2011-2012. Vaccination is the most effective tool in preventing the transmission of HBV infection. Strategies targeting high risk groups cannot control HBV infection throughout the population. Broader vaccination programmes are required. CDC provides guidelines regarding individuals who should receive Hepatitis-B vaccine.[19] Infants as a part of (universal immunization).

AGE	SCHEDULE
Infant (up to 1 year) Term	Birth dose (Monovalent) 2 month, 4 month and 6 month. (Pentavalent).
Preterm (weight <2000g)	Delay 1st dose until age of 1 month or hospital discharge. Complete the vaccine series.
Children(1 – 10 years)	0, 1 and 6 months 0, 1, 2 and 12 months
Adolescents (11 – 19 years)	0, 1 and 6 months
Adults(≥ 20)	0, 1 and 6 months

Adult immunization is recommended for

1. Children and adolescents not vaccinated previously (catch-up vaccination).
2. Persons with occupational risk (exposure to blood or blood-contaminated. environments) and students of health-care professions before they have blood contact.
3. Household contacts and sex partners of HbsAg positive.
4. Persons with end-stage renal disease, diabetes mellitus, HIV infection, treatment for STDs.

5. Transplant candidates, haemodialysis patient's recipients of frequent or large volumes blood or blood components.
6. Injecting drug abusers.

Post vaccination testing

Testing for anti-HBsAg (1–2 months) after completing the vaccination series is recommended in the following groups.[20]

1. Sexual partners of HBsAg positive person.
2. Infants born to HBsAg-positive mothers: Test for both HBsAg and anti-HsAg 9–18 months of age.
3. Health care and public safety workers.
4. Hemo-dialysis patients and other immune-compromised persons (e.g. HIV/AIDS).

Health care personnel should be tested for (anti-HBsAg) 1-2 months after completing three dose series, if tested >10mIU/ml label them as (protected) if <10mIU/mL (complete a second series of vaccine (0, 1, 6) months. Re-test for (anti-HBs) after 1-2 months. If titres are >10mIU/ml then label them as protected. If <10mIU/ml label them as non-responder. Non responders constitute less than 5% of the vaccine recipients. Check for HBs Ag status among the non responders.

Interruption of route of transmission:- Can be achieved by educating and increasing awareness of public and medical personnel on different aspects of hepatitis B. World hepatitis day (28th July) is marked by WHO and plays an important role in spreading awareness about hepatitis B.

Interruption among high risk groups:- laying stress on standard precautions among health care personnel to interrupt transmission. Essential components of standard precautions include.

- Hand hygiene
- Personal protective equipment --PPE.
- Environmental controls.
- Safe handling and disposal of potentially infectious material (Waste, *Sharps, Laboratory Specimens,* Proper handling of linen).
- Appropriate reprocessing of instruments and equipment following use—.
- Aseptic practices.

- Respiratory Hygiene/Cough Etiquette.
- Safe injection practices.
- Use of masks for insertion of catheters or injection of material into spinal or epidural spaces via lumbar puncture procedure (e.g. myelogram, spinal or epidural anesthesia).

Post exposure prophylaxis: In case of accidental exposure among health care personnel in health care settings.

- Clean wounds with soap and water.
- Flush mucous membrane with water.
- Avoid application of disinfectant, bleach or any other agent.

SOURCE	RECIPIENT VACCINATION STATUS			
	Unvaccinated Not fully vaccinated <3 doses	Fully vaccinated (Titres) unknown)	Non responder	Responder >10IU/ml
Source HBsAg positive / Source unknown Source HBs Ag negative	Complete Hepatitis B vaccination. +(HBIG) Complete vaccination	Test for anti-HBs. If <10mIU/ ml. Give HBIG. Initiate Re-vaccination . If>10mIU/ml No action needed Same action as above	Give two doses (HBIG) one month apart No action	No action No action

Issues in Hepatitis B control and recommendations to address them

1) **Issue 1:** Low rate of hepatitis B screening among asymptomatic population in the communities.

Recommendations

- Screening of sexual and household contacts of hepatitis B positive patients.
- Advocacy for increasing funds for screening among high-risk population.
- Develop infrastructure and resources for vaccinating and treating such high-risk groups.

2) **Issue 2: Data base for hepatitis B needs to be strengthened.**

Recommendations

Registries can be used to distinguish newly reported cases of infection from previously identified cases, facilitate and track case follow-up, enable communication with case contacts**.**

Issue 3: Focus on health care associated hepatitis B infection is limited.

Recommendations

- Develop written hospital infection control policies and procedures based upon evidence-based guidelines, regulations or standards.
- Adequate resources should be dedicated for infection prevention and control.
- Assure sufficient and appropriate supplies necessary for adherence to standard precautions.e.g. Hand hygiene products, personal protective equipment, and injection equipment.
- Health care providers should receive training to recognize and report exposures have system in place to facilitate reporting and post exposure assessment.
- Post exposure prophylaxis should be readily available for timely administration.

3) Issue 4: There is an urgent need to increase vaccination education, awareness and funding at the community level.

Recommendation

- Share educational resources and collaborate to increase vaccination rates.

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