

## Viral Hepatitis

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### ABSTRACT

**Background:** The primary goals of conducting surveillance for viral hepatitis are to direct prevention and control activities for these diseases and to evaluate the impact of these activities. Any person with a hepatitis virus infection is a potential source of infection to others. Surveillance would help accomplish the goals by providing information on:

1. Creating a network of laboratories for diagnosis of viral hepatitis. 2. Monitor trends in incidence of and risk factors for disease. 3. Assess burden of disease 4. Identify infected persons requiring counseling and /or post exposure prophylaxis. 5. Identify and control outbreaks.

**Methodology:** Laboratory based targeted surveillance in sentinel geographical regions/population. **Clinical Case Definition:** An acute illness with discrete onset of symptoms (e.g., fatigue, abdominal pain, loss of appetite, intermittent nausea, vomiting), and jaundice. (source www.cdc.gov.in) NCDC will be the nodal agency for implementation of the project.

**Results:** HBV, HCV and HDV are transmitted through contaminated blood or blood components or through the use of contaminated needles and syringes. In several populations, a common route of transmission of HBV infection is from infected pregnant women to their infants around the time of delivery. In many people with HBV or HCV infection, no route of transmission can be identified. In addition, specific vaccines and/or passive immune prophylaxis (use of specific immunoglobulin products) are also useful in preventing transmission of some infections. and also HAV vaccine is the most effective method for specific pre-exposure prophylaxis. and two different vaccines based on inactivated cell culture are available. Both vaccines are highly antigenic, especially in adults, and induce protective antibody levels in more than 95% of recipients after the first dose of vaccine. Individuals at high risk of repeated exposure to HBV, such as personnel Health Care Anti-HBs titer should be evaluated one month after the third dose. An Anti-HBs titer of 10 IU/L (or 10 mIU/mL) is protective. After reaching this titer, there is no need for further booster doses.

**Conclusion:** Viral hepatitis is a systemic infection affecting predominantly the liver and causing its inflammation. It may be acute (recent infection, relatively rapid onset) or chronic. Viral hepatitis is caused by infection with one of the five known hepatotropic viruses, which are named as hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and hepatitis E virus (HEV), respectively. These viruses are quite divergent in their structure, epidemiology, routes of transmission, incubation period, clinical presentations, natural history, diagnosis, and preventive and treatment options.

**Keywords-** Viral hepatitis, hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and hepatitis E virus (HEV).

## I. INTRODUCTION

Viral hepatitis refers to inflammation of the liver caused by a viral infection. There are several types of viral hepatitis, the most common being hepatitis A, hepatitis B, hepatitis C, hepatitis D, and hepatitis E. Each type of viral hepatitis is caused by a different virus and has distinct characteristics in terms of transmission, severity, and long-term consequences.

Hepatitis A is primarily transmitted through the consumption of contaminated food or water. It is typically a short-term infection and does not lead to chronic liver disease. Hepatitis B is transmitted through contact with infected blood, semen, or other body fluids. It can cause both acute and chronic infections, with the latter potentially leading to liver cirrhosis or liver cancer. Hepatitis C is mainly transmitted through exposure to infected blood, commonly through sharing needles or

other drug paraphernalia. It can also be transmitted through unsafe medical procedures or from mother to child during childbirth. Hepatitis C often becomes a chronic infection and can cause long-term liver complications if left untreated.

Hepatitis D is a unique type of hepatitis that only occurs in individuals who are already infected with hepatitis B. It is transmitted through contact with infected blood or sexual contact. Hepatitis D can lead to more severe liver disease than hepatitis B alone.(5)

Hepatitis E is primarily transmitted through the consumption of contaminated water or food, particularly in areas with poor sanitation. It is typically an acute infection, but it can be particularly dangerous for pregnant women, leading to severe complications.

Symptoms of viral hepatitis include fatigue, jaundice (yellowing of the skin and eyes), abdominal pain, loss of appetite, nausea, and dark urine.

However, some people may experience mild or no symptoms, especially in the early stages of infection. Prevention of viral hepatitis involves practicing good hygiene, maintaining safe sexual practices, avoiding sharing needles or other drug paraphernalia, and getting vaccinated for hepatitis A and B. Treatment options vary depending on the type of viral hepatitis and may include antiviral medications, supportive care, and lifestyle changes.

Viral hepatitis is a significant global health problem, affecting millions of people worldwide. (7)

It can lead to serious liver damage, liver failure, and even death if not properly managed. Public health efforts focus on raising awareness, improving sanitation, promoting vaccination, and ensuring access to testing, treatment, and care for those affected by viral hepatitis

## II. THE IMPORTANCE AND NECESSITY OF RESEARCH

Research on viral hepatitis is of utmost importance and necessity due to several reasons:

### *Understanding the Viruses:*

Research helps in deepening our understanding of the different viruses that cause hepatitis, including their structure, replication mechanisms, and interactions with the human immune system. This knowledge contributes to the development of effective prevention strategies, diagnostic tests, and therapeutic interventions.

### *Prevention and Vaccination:*

Research plays a crucial role in the development and evaluation of vaccines against hepatitis viruses. Vaccines have been highly successful in preventing hepatitis A and hepatitis B infections, and ongoing research aims to develop effective vaccines for other types of viral hepatitis, such as hepatitis C and hepatitis E. Research also helps identify high-risk populations and transmission routes, leading to targeted prevention efforts. (1)

### *Treatment and Therapies:*

Viral hepatitis can lead to chronic liver disease, cirrhosis, and liver cancer. Research is essential for developing antiviral drugs and therapies that can effectively treat and manage viral hepatitis infections. Advances in research have led to the development of direct-acting antiviral drugs for hepatitis C, which have revolutionized treatment outcomes and cure rates for this chronic infection. (14).

### *Screening and Diagnostic Tools:*

Research contributes to the development of sensitive and reliable screening tests for viral hepatitis. It helps in identifying biomarkers and molecular techniques that aid in early detection, accurate diagnosis, and monitoring of the disease progression. Timely diagnosis enables early intervention and appropriate management, reducing the risk of severe complications.

### *Public Health Strategies:*

Research provides evidence-based data that guide public health policies and strategies for the prevention, control, and management of viral hepatitis. It helps in assessing the burden of the disease, estimating the prevalence and incidence rates, and identifying risk factors. This information is crucial for allocating resources, implementing prevention programs, and evaluating the effectiveness of interventions. (1)

### *Global Health Impact:*

Viral hepatitis is a major global health concern, with millions of people affected worldwide. Research on viral hepatitis contributes to the global effort to eliminate hepatitis as a public health threat by 2030, as outlined by the World Health Organization. It aids in developing comprehensive strategies, fostering international collaborations, and promoting access to affordable diagnostics, treatments, and vaccines. In summary, research on viral hepatitis is critical for advancing our knowledge, developing effective prevention and treatment strategies, improving public health policies, and ultimately reducing the burden of this disease worldwide. Continued research efforts are necessary to achieve the goal of eliminating viral hepatitis as a major public health problem.

## III. BACKGROUND RESEARCH

Viral hepatitis is a well-studied area of research that has significantly advanced our understanding of the viruses, their modes of transmission, pathogenesis, and the development of prevention and treatment strategies. Here is a brief overview of some key areas of research on viral hepatitis:

### *Virology and Molecular Biology:*

Researchers have extensively studied the structure, genome, and replication mechanisms of hepatitis viruses. This has led to a better understanding of their life cycles, viral proteins, and interactions with host cells. Advances in molecular biology techniques have enabled the identification of viral genotypes, subtypes,

and variants, which have important implications for disease progression and treatment response. (7)

**Epidemiology and Global Burden:**

Numerous studies have investigated the global prevalence, incidence, and distribution of viral hepatitis infections. These studies have provided valuable data on the burden of disease, high-risk populations, and geographical variations. Research has also explored risk factors, such as injection drug use, unsafe sexual practices, blood transfusions, and vertical transmission, helping to inform targeted prevention strategies. (8)

**Prevention and Vaccination:**

Research has played a pivotal role in the development and evaluation of vaccines for hepatitis A and hepatitis B. Clinical trials and population-based studies have demonstrated the effectiveness of these vaccines in preventing infections and reducing the burden of disease. Ongoing research is focused on developing vaccines for other types of viral hepatitis, such as hepatitis C and hepatitis E.

**Diagnostic Tools and Biomarkers:**

Advances in research have led to the development of sensitive and specific diagnostic tests for viral hepatitis. (4)

Serological assays, nucleic acid amplification techniques, and point-of-care tests have improved the accuracy and accessibility of diagnosis. Researchers have also identified and validated biomarkers that aid in disease staging, prognosis, and treatment response monitoring. (3)

**Therapeutics and Treatment Strategies:**

The development of antiviral drugs and therapeutic approaches has been a major focus of research on viral hepatitis. For example, the discovery of direct-acting antivirals (DAAs) has revolutionized the treatment landscape for hepatitis C, resulting in high cure rates and shorter treatment durations. Research continues to explore novel targets, combination therapies, and strategies to overcome drug resistance. (8)

**Public Health Interventions and Elimination Efforts:**

Research has informed public health policies and interventions aimed at preventing and controlling viral hepatitis. It has guided the implementation of vaccination programs, harm reduction strategies for injection drug users, and screening recommendations for high-risk populations. Moreover, research has contributed to the global efforts to eliminate viral hepatitis as a public health threat by providing evidence-based strategies, monitoring progress, and evaluating the impact of interventions. (3)

Research on viral hepatitis is a dynamic field, driven by the need to address ongoing challenges such as the high burden of chronic infections, limited access to diagnostics and treatment, and emerging viral variants. Collaborative efforts among scientists, healthcare professionals, policymakers, and affected communities continue to drive advancements in our understanding and management of viral hepatitis. (5)

The Health Assembly has considered specific aspects of hepatitis prevention in past resolutions.

First, in 1992, in resolution WHA45.17 on immunization and vaccine quality it urged Member States to integrate cost-effective new vaccines, such as hepatitis B vaccine, into national immunization programmes in countries where it is feasible.

The Secretariat acted on this resolution by recommending that all countries integrate hepatitis B vaccine into national immunization programmes by 1997. (9)

Global support from the GAVI Alliance and the contribution of PAHO's Revolving Fund for Vaccine Procurement in the Region of the Americas for the introduction of hepatitis B vaccine have resulted in great increases in vaccination coverage in the past decade. As of 2007, more than 88% of Member States have introduced hepatitis B vaccine; overall coverage with three doses of vaccine was 65%, and globally 27% of newborn infants received the birth dose of hepatitis B vaccine. Secondly, in 2005, in resolution WHA58.22 on cancer prevention and control the Health Assembly called for including reduction in hepatitis B virus infection among the outcome objectives of national cancer control programmes; implementation of this resolution and its monitoring are still in progress.

Thirdly, as part of the Global plan of action on workers' health 2008–2017, endorsed by the Health Assembly in 2007 in resolution WHA60.26, the Secretariat's activities would include working with Member States for immunization of health-care workers against hepatitis B. Little progress has been made in the short time since the resolution endorsing the plan was adopted.

In addition, the Health Assembly has considered several hepatitis prevention issues relating to immunization, 1 safe blood supply, 2 food safety 3 and safe injections. 49

In 1998 the WHO-cosponsored Conference Regarding Disease Elimination and Eradication as Public Health Strategies (Atlanta, Georgia, United States of America, 23–25 February 1998) concluded that hepatitis B is "a primary candidate for elimination or eradication". In 1999, WHO joined UNICEF and UNFPA to recommend the exclusive use of autodisable syringes for all immunization injections by the year 2003. 5 Much progress has been made with the support of the GAVI Alliance for the procurement of non-reusable syringes for immunization. WHO has issued position papers on hepatitis B vaccines (2009) 6 and hepatitis A vaccine (2000). 7 In 2005, the Western Pacific Region set a goal of reducing chronic hepatitis B virus infection rates to less than 2% among five-year-old children by 2012. In 2008, WHO with FAO convened an expert meeting on viruses in foods in order to provide scientific advice in support of risk-management activities. Recently, the European Region has developed clinical protocols for the management of hepatitis B virus/HIV coinfection,

hepatitis C virus/HIV coinfection, and prevention of hepatitis A, B and C virus infections in people living with HIV. In November 2008, WHO's Strategic Advisory Group of Experts on immunization recommended that "all regions and associated countries develop goals for hepatitis B control appropriate to their epidemiologic situations". The Regional Committee for the Eastern Mediterranean adopted a resolution (EM/RC56/R.5) for hepatitis B and C control and set a target for reduction of the prevalence of chronic hepatitis B to less than 1% among children below five years of age by 2015 at its fifty-sixth session (Cairo, 3–6 October 2009). Several countries have established national goals for the elimination of transmission of hepatitis B virus.

**Objectives:**

- 1) To establish a laboratory network for testing of various types of hepatitis
- 2) To provide trends in the incidence and risks in acute cases (Hepatitis A, B, C and E) needed to
- 3) develop evaluation and prevention strategies
- 4) Identifying chronic hepatitis cases (hepatitis B and C) and measuring their prevalence Accurate estimate of burden of disease

**Questions:**

- 1) How is the laboratory network for testing different types of hepatitis created?
- 2) How was the presentation of the trend in incidence and risks in acute cases (hepatitis A, B, C and E)?
- 3) What has been the role of hepatitis evaluation and prevention strategies?
- 4) Identification of cases of chronic hepatitis (hepatitis B and C) and how prevalent was the measurement?

**Methodology:**

Laboratory based targeted surveillance in sentinel geographical regions/population. Clinical Case Definition: An acute illness with discrete onset of symptoms (e.g. fatigue, abdominal pain, loss of appetite, intermittent nausea, vomiting), and jaundice. (source [www.cdc.gov](http://www.cdc.gov)) NCDC will be the nodal agency for implementation of the project.

#### IV. THE SCOPE OF THE RESEARCH

The scope of research on viral hepatitis is multidisciplinary, involving virologists, epidemiologists, clinicians, immunologists, public health experts, and policymakers. It encompasses basic science, clinical research, translational studies, and health system research. Collaboration between researchers, healthcare providers, governments, and affected communities is essential to address the complex challenges posed by viral hepatitis and work towards its prevention, control, and elimination.

#### V. RESULTS

For any disease condition, prevention is often better than cure from both public health and clinical perspectives. Prevention is even more important when a

particular condition is very common, is difficult to treat, is associated with serious health-related or economic consequences, and if preventive measures are simple,(2) safe and cost-effective. For infectious diseases, preventive measures are aimed primarily at reduction or elimination of transmission of the agent. This results not only in reduction of new cases, thereby reducing the overall disease burden, morbidity, mortality and healthcare expenditure, but eventually also in a reduced pool of infectious persons, contributing by itself to a reduced risk of disease transmission. Preventive measures for an infectious disease depend on its modes of spread. Various hepatitis viruses differ in their modes of transmission (Table 1-1). HAV and HEV are transmitted primarily through contaminated food and water, whereas HBV, HCV, and HDV are transmitted through exposure to contaminated blood or blood components, or use of contaminated needle and syringes.

In several populations, a common mode of transmission of HBV infection is from infected pregnant women to their newborns around the time of delivery. In several persons with HBV or HCV infection, no route of transmission can be identified; these cases appear to be related to in apparent parenteral transmission through contact with skin cuts, etc. In addition, HBV and HDV can also be transmitted by unprotected sex. For HCV infection, mother-to-child and sexual transmission though known to occur are responsible for a much smaller proportion of cases with this disease. Because of the shared modes of transmission of various hepatitis viruses, some preventive measures are effective against more than one hepatotropic viruses. These include changes in practices related to water hygiene and sanitation, percutaneous injections, transfusion of blood or blood products, sexual habits, and antenatal care (Table 1-2). In addition, specific vaccines and/or passive immune prophylaxis (use of specific immunoglobulin products) are also useful in preventing transmission of some infections. (Table 1-1). (Table 1-2).

**Water & Food Hygiene and Sanitation:**

HAV and HEV are predominantly transmitted through fecal-oral route. This often involves consumption of contaminated food or water. The best possible way to prevent the transmission of these viruses thus is to improve food hygiene and sanitation facilities, such as access to safe drinking water, consumption of hygienically cooked fresh food, proper disposal of excreta particularly from persons with viral hepatitis. These measures have the potential to greatly reduce the disease burden due to HAV and HEV infection. Legislation and enforcement of guidelines related to preparation, packaging and sale of various food items may also be useful.(8)

**Safe injection practices:**

A large proportion of infections with HBV or HCV are acquired through unsafe percutaneous injection exposure. Such exposure can occur when injection equipment such as needles and syringes are reused

without proper sterilization. This may happen either in healthcare facilities or among injection drug users, who tend to share syringes and needles. A less common mode for such transmission is through needle stick injuries to health care personnel. Several measures can substantially reduce transmission of hepatitis viruses through injections, such as avoidance of unnecessary percutaneous injection (through use of alternative non-percutaneous routes of drug administration, such as oral or topical applications), promotion of the use of disposable single-use (auto disable) syringes which cannot be used after initial use, and safe disposal of used needles and other sharps.(9)

Used needles and other sharps also pose an occupational hazard to healthcare workers, with needle stick injuries resulting in transmission of HBV and HCV, besides other blood-borne infections. Such exposure can be prevented by reducing the use of sharps and laying down, training in and meticulous adherence to safe work practices. In case of an injury, the affected area should be rinsed and washed thoroughly with soap and water; the practice to "milk out" more blood is controversial and not recommended. Another related mode of transmission is the re-use of other hospital equipment (e.g., surgical instruments or endoscopes) without adequate decontamination. Hepatitis C infection is one of the important infections in patients undergoing Hemodialysis. Prevalence of HCV RNA in the Hemodialysis population is 27.7%. Duration of dialysis, getting dialysis at more than one center, elevated transaminase levels, and low serum albumin are important associations for HCV RNA positivity. Interruption of such transmission requires meticulous adherence to hospital infection control practices.

#### **Safe blood transfusion:**

Transfusion of contaminated blood or blood products is the most common route of HCV transmission. This route is also responsible for a proportion of cases with HBV and HDV infection. Such transmission can be markedly reduced through the use of following steps:

- a. Use of unpaid voluntary blood donors in preference to replacement or commercial donors, Screening of blood for infectious diseases
- b. Avoidance of undictated blood transfusions. (7)

Besides HCV and HBV infection, these measures also serve to prevent other transfusion transmitted diseases, such as syphilis.

#### **Safe sex practices:**

Unprotected sex is a common method for acquisition of HBV infection among young adults, and for some cases of HCV infection. Such transmission is particularly efficient among men who have sex with men. Sexual transmission of these hepatitis viruses can be prevented by promoting monogamous relationship; use of barrier methods (condoms) during the sexual act; avoiding sex with a person who has an ulcerative genital tract infection (e.g., a sexually-transmitted genital tract

infection), and screening of commercial sex workers for infection with HBV or HCV.

#### **Prevention of Mother-to-child transmission:**

HBV can be transmitted efficiently from pregnant mothers to their newborns, particularly if the mother has a high viral load. This transmission may occur either in utero (during third trimester of gestation), during birth (passage of the baby through birth canal where it comes in contact with the maternal body secretions), or in the period after delivery (through close contact between mother and baby). Since HBV infection in infancy is much more likely to become chronic and hence lead to liver cirrhosis or liver cancer, prevention of HBV infection is focused particularly on such transmission. Mother-to-child HBV transmission can be interrupted through administration of hepatitis B vaccine to newborn babies, beginning with the first dose within 24 hours of birth. If a pregnant woman is known to have HBV infection and also has a positive HBeAg test or a high viral load, administration of specific hepatitis B immunoglobulin (HBIG) to the baby at birth and/or of oral anti-viral drugs to the mother in the third trimester of pregnancy may provide some additional protection. This issue is discussed in greater detail in the section on hepatitis B. (1)

#### **Vaccines and immunoglobulins**

Active and passive monoprophylaxis (using specific vaccine and immunoglobulin, respectively) are available for preventing HAV and HBV infections. These are discussed below in sections relating to each virus. A vaccine has been developed against hepatitis E virus; however, it is not yet approved or available in India. No vaccine has yet been developed against HCV infection. (14)

#### **Prevention and control of HAV infection**

HAV is transmitted primarily through the fecal-oral route. The virus is shed in stools of infected persons, with peak viral excretion occurring in the two weeks preceding the onset of jaundice and during the initial phase of clinical illness. The virus can then contaminate food and water, or may be transmitted through contaminated fomites. (5)

Person-to-person spread through close personal contact is the most common mode of spread, with frequent occurrence of secondary cases among household or school contacts of those infected. Transmission of HAV infection to sexual partners has been reported, particular among men who have sex with men. Transmission among groups who share intravenous drug injection equipment has been reported – this is related to fecal contamination of injection equipment rather than through contamination with blood. In India, HAV infection is very common but usually occurs in early childhood. Infection at this age is most often asymptomatic and leads to life-long immunity against reinfection. Hence, disease due to this infection is distinctly infrequent. (7)

However, in some areas, some children escape exposure to HAV and develop hepatitis A from exposure during adolescence or young adulthood. Prevention and control of HAV infection relies on breaking the chain of transmission using one or more of the following measures: (a) improving hygiene and sanitary measures, (b) pre-exposure prophylaxis for those at a high risk of exposure (c) post-exposure prophylaxis for those who have recently been exposed to HAV. (13)

#### **Pre-exposure prophylaxis**

HAV vaccine is the most effective method for specific pre-exposure prophylaxis. Two different inactivated cell-culture based vaccines are available. These vaccines are administered intramuscularly in the deltoid muscle as two doses given 6-18 months apart; the dose of vaccine depends on the person's age (Table 1-3). Both the vaccines are highly antigenic, particularly in adults, inducing protective antibody levels in >95% of recipients after the first vaccine dose.(12)

Standard guidelines in several countries recommend administration of one of the hepatitis A vaccines in persons at high risk of this disease, namely adults with high-risk behaviors such as men who have sex with men and injection drug users, people at risk of occupational exposure to HAV, hemophiliacs, persons with chronic liver disease (since disease caused by hepatitis A may be more severe in them). This is not applicable to India where most adults have already been exposed to and are thus protected against hepatitis A.

In some developed countries, universal childhood vaccination against HAV is recommended. In India, for the reason indicated above, universal vaccination is not needed. (Table 1-3).

#### **Post-exposure prophylaxis**

Post-exposure monoprophylaxis against hepatitis A disease involves administration of either HAV immunoglobulin (HAVIg) or one of the hepatitis A vaccines within 2 weeks of exposure to a confirmed hepatitis A case. This is recommended for:

1. Close family contacts of hepatitis A cases, or
2. Susceptible staff and attendees of child care centers or school with hepatitis A cases.
3. Active immunization (hepatitis A vaccine), with its life-long protection, is preferred because passive monoprophylaxis (HAVIg) has only a short-term efficacy.

HAVIg is administered as a single dose of 0.02 ml/Kg body weight intramuscularly. It is preferred over HAV vaccine in those groups where response to the vaccine may be suboptimal (children under 12 months of age, adults > 40 years old, immunocompromised individuals, etc.) or those in whom the vaccine is contraindicated. (9)

Post-exposure prophylaxis against HAV for close healthy adult contacts is not useful in India because of the reasons mentioned above.(3)

#### **Prevention and control of HBV infection**

HBV is transmitted primarily through percutaneous routes, including

1. Transfusion of contaminated blood or blood products,
2. Use of unsterile needles for percutaneous injections,
3. Unprotected sexual contact, and
4. Perinatal transmission from HBV-infected mothers to their newborns.

Transmission of HBV through the first three routes can be prevented through the use of safe blood and blood products, use of disposable needles and syringes for percutaneous injections, and safe sex practices, as discussed above. In addition, for persons at high risk of HBV infection, such as persons frequently receiving blood and blood products (persons with thalassemia, hemophilia, etc.), injection drug users, healthcare workers, sexual contacts and family members of persons infected with HBV, pre-exposure prophylaxis through administration of hepatitis B vaccine is recommended. Pre-exposure prophylaxis using hepatitis B vaccine Hepatitis B vaccines are available from several manufacturers and can be either recombinant or plasma-derived.

All the vaccines have comparable and high protective efficacy of more than 95% when administered prior to exposure. These vaccines, which contain the hepatitis B surface protein, are given as three age-appropriate doses (Table 1-4) as deep intramuscular injections into the deltoid muscle. For pre-exposure prophylaxis, the doses are given at 0, 1 and 6 months.

No boosters are recommended. In normal-risk recipients, no follow-up testing is recommended. However, in persons at high risk of frequent exposure to HBV, such as health care personnel, anti-HBs titer should be assessed one month after the third dose. Anti-HBs titer of 10 IU/L (or 10 mIU/mL) is protective; once this titer is reached, no further booster doses are needed. In immunosuppressed persons, higher doses of vaccine are used; despite this, the protective antibody response may be suboptimal. Decision on testing of antibodies and administration of further doses of the vaccine in such patients may need to be individualized. (Table 1-4).

#### **Prevention of HBV infection in childhood**

As indicated above, prevention of childhood HBV infection is particularly important since infection occurring early in life has a very high risk of becoming chronic. (2)

For instance, nearly 90% of infections acquired at birth and 30-40% of those acquired under 6 years of age become chronic, compared to only about 5% of infections acquired in later childhood or as adults. Administration of hepatitis B vaccine to all newborns is the most effective strategy for preventing such infection. (5)

In addition, given the serious consequences of HBV infection, and availability of cheap, safe and effective hepatitis B vaccines, the latter are included in

universal childhood immunization programs of most countries in the world, including India. The risk of HBV infection is higher in infants born to HBV-infected mothers, particularly those who are also positive for another serological marker known as hepatitis B e antigen or HBeAg. In these infants, it is important that the first dose of vaccine is administered as soon as possible, i.e., within 24 hours, after birth.

Since antenatal screening of maternal HBV infection status is not possible in our country, it is recommended that the birth dose of hepatitis B vaccine is administered to all newborns, wherever possible. Some additional steps may further reduce the risk of acquisition of HBV infection for infants born to HBV-infected mothers.

Administration of HBIG (0.5 mL intramuscular) in addition to birth dose of hepatitis B vaccine soon after birth provides some additional benefit over the birth dose of vaccine alone, in infants born to HBV-infected mothers who are also positive for HBeAg. There is some evidence that administration of anti-viral drugs during pregnancy to HBV-infected pregnant women with high viral load in their blood may reduce the risk of HBV infection in their newborns. However, both these approaches require prior knowledge that a pregnant woman is infected with HBV and additional specialized blood testing, which are not easily available.

**Post-exposure prophylaxis for HBV**

If a person has been exposed to HBV, e.g., through a needle stick injury from a person infected with HBV, a combination of passive (single dose of HBIG) and active monoprophylaxis (complete three-dose vaccination) should be used (Table 1-5). HBIG and first dose of the vaccine should be administered at separate sites. This schedule has a protective efficacy rate of 90-95%, if instituted soon after exposure. If a person has previously been vaccinated against hepatitis B, as is likely for healthcare workers, the algorithm shown in Table 16 should be followed. (7)

HBIG is administered intramuscularly in a dose of 0.5 mL for newborns and 0.06 mL/Kg in children and adults. (Table 1-5).

**VI. DISCUSSION**

Preventive measures for an infectious disease depend on its mode of transmission. Different hepatitis viruses differ in their modes of transmission (Table 1-1). HAV and HEV are mainly transmitted through contaminated food and water, while HBV, HCV, and

HDV are transmitted through exposure to contaminated blood or blood components or the use of contaminated needles and syringes. Transmission of HBV infection is common from infected pregnant women to their babies around the time of delivery. In many people with HBV or HCV infection, no route of transmission can be identified. These cases appear to be related to apparent injection transmission through contact with skin incisions, etc. (Table 2-1). In addition, specific vaccines and/or passive immune prophylaxis (use of specific immunoglobulin products) are also useful in preventing the transmission of some infections. HAV vaccine is the most effective method for specific pre-exposure prophylaxis. Two different inactivated cell culture-based vaccines are available. These vaccines are injected intramuscularly in the deltoid muscle in two doses with an interval of 6-18 months. The dose of the vaccine depends on the age of the person (Table 1-3). Both vaccines are highly antigenic, particularly in adults, and induce protective antibody levels in more than 95% of recipients after the first vaccine dose. Standard guidelines in several countries recommend the administration of one of the hepatitis A vaccines in persons at high risk for the disease, i.e., adults with high-risk behaviors such as men who have sex with men and injecting drug users, persons at risk of occupational exposure to the disease. They recommend in (Table 1-4) they are prescribed as deep intramuscular injection in the deltoid muscle. For pre-exposure prophylaxis, doses are administered at months 0, 1, and 6. No boosters are recommended. In normal-risk recipients, no further testing is recommended. However, in individuals at high risk of repeated exposure to HBV, such as health care personnel, the anti-HBs titer should be evaluated one month after the third dose. An Anti-HBs titer of 10 IU/L (or 10 mIU/mL) is protective. After reaching this titer, there is no need for further booster doses. If a person has been exposed to HBV, for example, through a needlestick injury from an HBV-infected person, a combination of passive (single-dose HBIG) and active monoprophylaxis (complete vaccination with three doses) should be used (Table 1-5). HBIG and the first dose of vaccine should be injected at separate sites.(1)

This program has a protective effectiveness rate of 90-95% if applied immediately after exposure. If the individual has previously been vaccinated against hepatitis B, as is likely for healthcare workers, the algorithm shown in Table 16 should be followed. HBIG is administered intramuscularly at a dose of 0.5 ml for infants and 0.06 ml/kg for children and adults. (Table 1-5).

**Table 1-1: Virological, Epidemiological, and Clinical features of various hepatitis viruses**

Feature	Virus				
	HAV	HBV	HCV	HDV	HEV
Clinical syndromes	Acute viral hepatitis (AV H) Acute liver failure (ALF)	Acute viral hepatitis Chronic hepatitis Acute liver failure	Chronic hepatitis Acute viral hepatitis (infrequent)	Acute viral hepatitis Chronic hepatitis A acute on	Acute viral hepatitis Acute liver failure



				chronic liver disease	
Incubation period	2 weeks – 6weeks	6 weeks – 6months	2weeks –6 months	2 weeks – 8 weeks	2 weeks – 10 weeks
Route(s) of transmission	Contaminated food and water Close person to-person contact	Percutaneous Blood and blood products Unprotected sex Mother-to-child	Percutaneous Blood and blood products Rarely, Unprotected sex or mother-to child	Percutaneous Blood and blood products Unprotected sex	Contaminated drinking water supplies Contaminated food
Chronicity	No	Yes; may lead to cirrhosis and liver cancer	Yes; may lead to cirrhosis and liver cancer	Yes, with chronic HBV infection	Rare, in transplant recipients and immunosuppressed persons (reported in developed countries)
Vaccine availability	Yes	Yes	None	Yes (HBV vaccine)	Developed but not yet approved in India

**Table1-2: Summary of preventive measures that are effective for Hepatitis viruses A to E**

Preventive measures	Hepatitis A virus	Hepatitis B virus	Hepatitis C virus	Hepatitis D virus	Hepatitis E virus
Water and food hygiene, and sanitation measures	Yes				Yes
Safe injection practices		Yes	Yes	Yes	
Safe blood and blood product transfusion		Yes	Yes	Yes	
Safe sex practices		Yes		Yes	
Ante-natal screening	Yes				
Vaccination	Yes	Yes		Yes (using hepatitis B vaccine)	
Immunoglobulin	Yes	Yes			

**Table 1-3: Recommended doses and schedules for the two available Hepatitis A vaccines**

Vaccine	Age (years)	Dose (ml)	Number of doses	Schedule (month)
Havrix®(GSK)	1-18	0.5 (720 EL units)	2	0, 6-12
	>18	1.0 (1440 EL units)	2	0, 6-12
Vaqta®(Merck)	1-18	0.5 (25 units)	2	0, 6-18
	>18	1.0 (50 units)	2	0, 6-18

**Table 1-4: Dose and schedule of Hepatitis B vaccine**

Group	Vaccine dose (20 µg/mL)	Schedule
Newborn	0.5 mL (10µg)	<24 hours, 6 weeks, 14 weeks (if administration of first dose within 24 hours of birth is not possible, then 6, 10 and 14 weeks)
Healthy persons aged ≤19 years	0.5 mL (20 µg)	0, 1, 6 months



Healthy persons aged $\geq 20$ years	1.0 mL (20 $\mu$ g)	0, 1, 6 months
Persons on hemodialysis or immunocompromised persons	2.0 mL (40 $\mu$ g)	0, 1, 2, 6 months

**Table 1-5: Post-exposure prophylaxis after exposure to HBV infection**

Immune status of exposed person	Post-exposure prophylaxis
Unvaccinated	Administer one dose of HBIG and begin 3-dose vaccine schedule.
Known vaccine responder	Neither vaccine nor HBIG is needed
Known vaccine non-responder	Administer one dose of HBIG and start 3-dose vaccine schedule (preferable) or Administer two doses of HBIG, 4 weeks apart
Vaccinated but unknown response	Test the exposed person for anti-HBs titer. If the titer is $< 10$ IU/L, administer one dose of HBIG and a booster dose of hepatitis B vaccine If the titer is $\geq 10$ IU/L, neither HBIG nor vaccine is needed.

## VII. CONCLUSION

Viral hepatitis is a systemic infection affecting predominantly the liver and causing its inflammation. It may be acute (recent infection, relatively rapid onset) or chronic. Viral hepatitis is caused by infection with one of the five known hepatotropic viruses, which are named as hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and hepatitis E virus (HEV), respectively. These viruses are quite divergent in their structure, epidemiology, routes of transmission, incubation period, clinical presentations, natural history, diagnosis, and preventive and treatment options. The most common clinical consequence of infection with HAV or HEV is an illness characterized by sudden onset of fever and systemic symptoms, which is followed a few days later by jaundice. Majority of people with acute viral hepatitis recover spontaneously within a few weeks, without any residual consequences. However, in some persons, the illness is complicated by occurrence of a severe form of the disease, known as acute liver failure (ALF), which is characterized by altered sensorium and bleeding tendency (coagulopathy). Patients with ALF have a high case-fatality rate, in the absence of liver transplantation, which is either inaccessible or non-affordable for a large majority of Indian population.

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